National Report on Medicines use in Italy Year 2017

AGENZIA ITALIANA DEL FARMACO

National Report on Medicines use in Italy Year 2017

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Dear Readers,
this is an extract/adaptation of 2017 OsMed Report. The original numeration of tables and figures was left unchanged in order to allow easy data consultation.

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Section 1

General characteristics of pharmaceutical use in Italy

National Report
on Medicines
use in Italy
Year 2017

Table 1.1.a Composition of pharmaceutical expenditure: 2017-2016 comparison (Table and Figure)

	Expenditure	%	Δ % 17-16
Gross outpatient NHS expenditure^	10,495	35	-1.3
Class A medicines by direct and *per conto* distribution	4,793	16	-13.7
Private Class A‡	1,317	4	0.6
Class C with prescription	2,874	10	8.8
OTC medicines	2,732	9	12.4
Malls	333	1	10.8
Local health authorities, Hospitals, Healthcare Residence and prisons*	7,267	24	10.3
Total	**29,811**	**100**	**1.2**

^ Including expenditure for vaccines (€ 248,734) and oxygen (€ 51.4 million) and class C drugs reimbursed in accordance with Law No.203 of 19 July 2000 (€ 24 million)

‡ Estimated on the basis of the historical series 2013-2016

* Including expenditure for vaccines (€ 487.4 million) and oxygen (€ 270.8 million). It does not include the expense for Class A drugs delivered in direct distribution and per conto

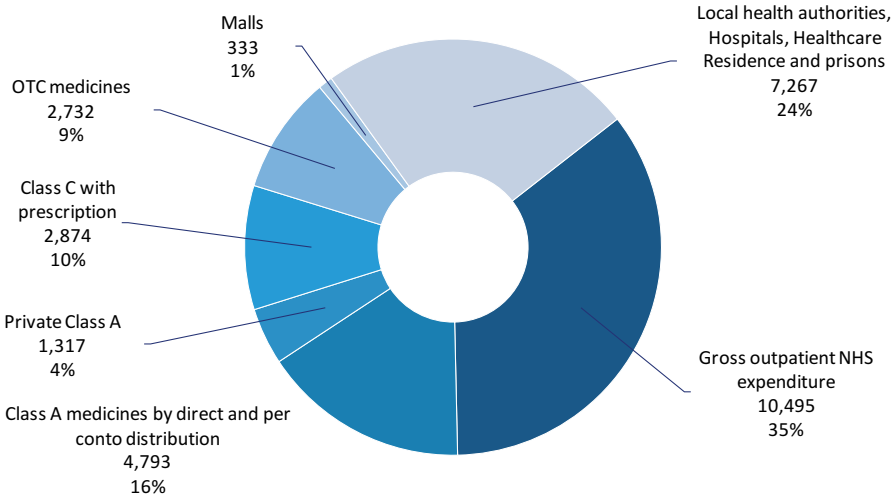
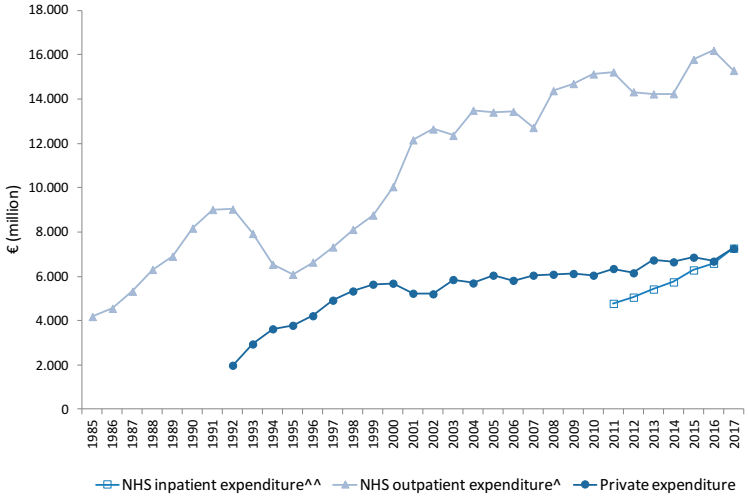


Figure 1.1.b Pharmaceutical expenditure in the period 1985 - 2017 (Figure and Table)



Years	Gross NHS outpatient expenditure *(million)*	Direct distribution Class A *(million)*	NHS outpatient expenditure^ *(million)*	Out of pocket expenditure *(million)*	Inpatient expenditure^^ *(million)*
1992	9,030		9,030	1,982	
1993	7,929		7,929	2,942	
1994	6,539		6,539	3,625	
1995	6,087		6,087	3,785	
1996	6,638		6,638	4,216	
1997	7,321		7,321	4,919	
1998	8,113		8,113	5,332	
1999	8,760		8,760	5,640	
2000	10,041		10,041	5,684	
2001	12,154		12,154	5,232	
2002	12,644		12,644	5,204	
2003	12,354		12,354	5,849	
2004	13,491		13,491	5,694	
2005	13,408		13,408	6,046	
2006	13,440		13,440	5,814	
2007	12,712		12,712	6,046	
2008	12,724	1,651	14,375	6,088	
2009	12,928	1,767	14,695	6,122	
2010	12,985	2,144	15,129	6,046	
2011	12,387	2,832	15,219	6,346	4,774
2012	11,488	2,837	14,325	6,152	5,055
2013	11,226	3,003	14,229	6,732	5,421
2014	10,988	3,250	14,238	6,648	5,744
2015	10,863	4,921	15,784	6,859	6,282
2016	10,638	5,556	16,194	6,645	6,587
2017	**10,495**	**4,793**	**15,288**	**7,257**	**7,267**

^ inclusive of the reimbursed pharmaceutical expense (gross of the pay-back and discount) and of the direct distribution and *per conto* of the class A, including the quote paid by the citizen

^^ Expenditure on public health facilities (gross of pay-back) net of direct distribution and *per conto* of class A

Source: OsMed processing of data from the Ministry of Economy and Finance and from "Tracebility of medicines" flow. Processing of IMS Health data for the estimate of private expenditure for years prior to 2017

1.1. Outpatient pharmaceutical expenditure

In 2017 the overall outpatient pharmaceutical expenditure, that is composed by public and private expenses, amounts to 21,715 millions of Euros, decreasing by -1.6% compared to 2016. The NHS outpatient pharmaceutical expenditure covers medicines supplied according to standard distribution (Tables 1.1.1 and 1.1.2) and Class A medicines supplied through direct and *per conto* distribution channels. This expenditure amounts to 12,909 millions of Euros (€ 213.05 per capita), and represent 59.4% of the total outpatient pharmaceutical expenditure. The pharmaceutical expenditure decreased by -6.5% compared to 2016. This decrease is mainly due to a reduction of the expenditure for class A medicines supplied according to direct and *per conto* distribution (-13.7%). Furthermore, a slight reduction of the net standard distribution expenditure (-1.7%) has also been reported.

The citizen pharmaceutical expenditure (Out of pocket expenditure) (Table 1.1.2) amounted to € 8,806 million (+7.1% compared to 2016). It is composed by: per citizen co-payments (regional prescription/package ticket and the difference in price between an off-patent medicine and its lowest reference price), expenditure for class C medicines and for Class A medicines privately purchased by citizens.

This change was due to an increase in the consumption of self-medication medicines (SOP and OTC medicines) (+12.4%), in the expenditure for medicinal products purchased in stores (+10.8%), and in the expenditure for Class C medicines with medical prescription (+8.8%) and to a slight increase of citizen co-payment (+0.6%).

The citizen cost-sharing (Table 1.1.1 and 1.1.2) amounted to € 1,549 millions (approximately € 25.6 per capita); this amount represented 14.8% of the standard distribution gross expenditure.

The increase in citizen co-payment is mainly due to an increase of the co-payment for the reference price system for off-patent medicines (+2.8%), while a reduction was reported of the per prescription/package citizen co-payment (-3.7%), compared to 2016.

The amount of packages supplied according to standard distribution showed a slight decrement (-0.7%), whereas an increase was recorded of citizen Class A packages purchased by citizens, compared to 2016 (+2.8%).

During 2017 (Table 1.13), an average of 972.7 daily doses of NHS reimbursed Class A medicines per 1,000 inhabitants (hereinafter called DDD/1000 inhab die) were consumed accounting to over 1 billion packages dispensed (18.3 packs per capita). This item amounted to 971.4 DDD in 2016. The decrease (-1.5%) of standard distribution pharmaceutical expenditure resulted from different components: medicinal product consumption stability (+0.1% of DDD), reduction of average costs (-2.4%, in part due to a lager use of off-patent medicines), and prescription increase of more expensive medicines (mix effect: +1.1%) (Figure 1.1.2).

The citizen expenditure for Class C medications with medical prescription amounted to € 98.0 per capita with a fair variability across the Italian Regions.

Table 1.1.1. NHS oupatient expenditure: comparison 2013-2017

		2013 *million*	2014 *million*	2015 *million*	2016 *million*	2017 *million*	Δ % 14/13	Δ % 15/14	Δ % 16/15	Δ % 17/16
1+2+3+4	Gross outpatient NHS expenditure	11,226	10,988	10,863	10,638	10,495	-2.1	-1.1	-2.1	-1.3
1+2	Citizen co-payment	1,436	1,500	1,521	1,540	1,549	4.5	1.4	1.2	0.6
1	Fixed co-payment (ticket)	558	546	524	518	499	-2.0	-4.1	-1.2	-3.7
2	Reference price share	878	954	997	1,022	1,050	8.6	4.5	2.5	2.8
3	Discount ^	927	889	865	845	829	-4.1	-2.7	-2.4	-1.8
4	Net NHS expenditure	8,863	8,598	8,477	8,254	8,116	-3.0	-1.4	-2.6	-1.7
5	Class A direct and *per conto* distribution°	3,003	3,250	4,921	5,556	4,793	8.2	51.4	12.9	-13.7
4+5	**Outpatient expenditure**	**11,866**	**11,848**	**13,398**	**13,810**	**12,909**	**-0.2**	**13.1**	**3.1**	**-6.5**

^ including the discount per price ranges charged to pharmacies; extra-discounts following AIFA Resolution of June 15, 2012 and art. 15, paragraph 2 of Law 135/2012 and, charged to the industry, both the discount from AIFA Determination December 30, 2005, and the pay-back on the agreement under art. 11, paragraph 6, of Law 122/2010, temporarily modified by Law 135/2012

° direct distribution expenditure and per conto of Class A, including - in the case of Regions with missing data - the value of 40% of unconventional pharmaceutical expenditure recorded through the flow of the "Traceability of medicines", pursuant to Law 222/2007. In 2017 no Region implemented this condition. *Source: OsMed processing on NSIS data*

Table 1.1.2. Comparison of public and private outpatient expenditure (2013-2017)

		2013 *million*	2014 *million*	2015 *million*	2016 *million*	2017 *million*	Δ% 14/13	Δ% 15/14	Δ % 16/15	Δ % 17/16
1	Net NHS expenditure	8,863	8,598	8,477	8,254	8,116	-3.0	-1.4	-2.6	-1.7
2	Class A medicines by Direct and *per conto* distribution	3,003	3,250	4,921	5,556	4,793	8.2	51.4	12.9	-13.7
1+2	Total public expenditure	11,866	11,848	13,398	13,810	12,909	-0.2	13.1	3.1	-6.5
3	Citizen co-payment	1,436	1,500	1,521	1,540	1,549	4.5	1.4	1.2	0.6
4	Class A medicines paid by citizens*	1,468	1,442	1,487	1,309	1,317	-1.8	3.1	-11.9	0.6
5	Class C medicine with prescription	2,985	2,937	2,997	2,642	2,874	-1.6	2.1	-11.8	8.8
6	OTC medicines	2,278	2,269	2,375	2,429	2,732	-0.4	4.7	2.3	12.4
7	Drugstores	-	-	-	301	333	-	-	-	10.8
3+4+5+6+7	Total private expenditure	8,168	8,148	8,380	8,221	8,806	-0.2	2.9	-1.9	7.1
	Total pharmaceutical expenditure	20,035	19,996	21,778	22,030	21,715	-0.2	8.9	1.2	-1.4
	Share (%) borne by the NHS	**59.2**	**59.3**	**61.5**	**62.7**	**59.4**				

* Data concerning private expenditure for medicines reimbursed by the NHS has been estimated on the basis of the historical series 2013-2016.

Source: OsMed processing on data from "Traceability of medicines" flow (for private expenditure data). Elaboration on IMS Health data for the estimate of private expenditure for the years prior to 2016.

Figure 1.1.1. Outpatient pharmaceutical consumption: comparison 2013-2017

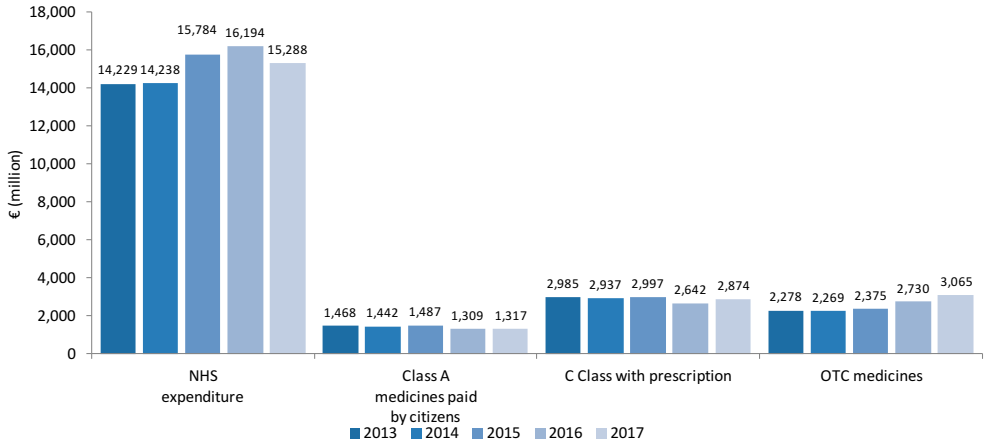


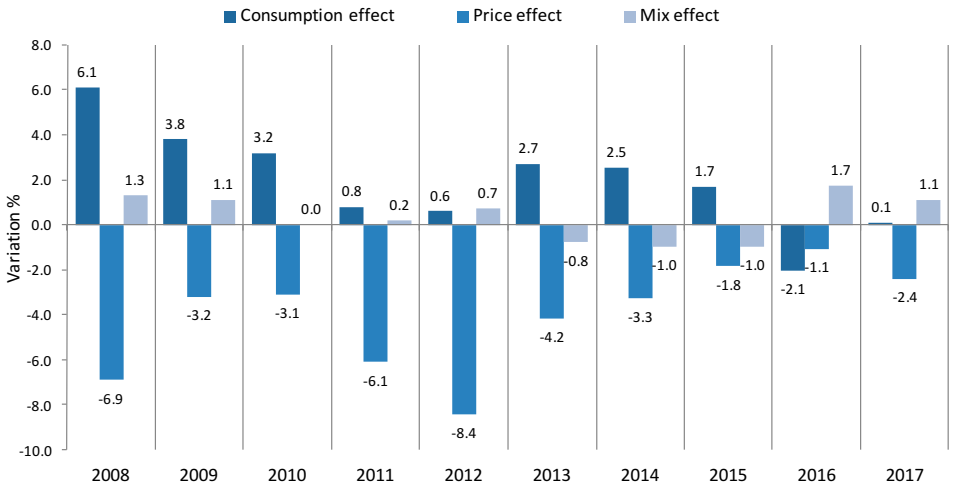
Table 1.1.3. Public and private outpatient pharmaceutical consumption: comparison 2013-2017

		2013	2014	2015	2016	2017	Δ %	Δ %	Δ %	Δ %
		*million^*	*million^*	*million^*	*million^*	*million^*	14/13	15/14	16/15	17/16
	Prescriptions #	608	609	596	587	581	0.2	-2.2	-1.5	-1.1
	N. Packages									
1	NHS consumption	1,116	1,133	1,131	1,117	1,109	1.5	-0.2	-1.2	-0.7
2	Class A medicines paid by citizen *	213	221	225	210	216	3.4	2.1	-6.7	2.8
3	Class A medicines by direct and *per conto* distribution	ND	ND	ND	86	105				21.5
1+2+3	Total class A medicines	1,329	1,354	1,356	1,414	1,430	1.8	0.2	4.2	1.1
4	Class C medicines with prescription	254	250	248	209	226	-1.6	-0.8	-15.6	7.8
5	OTC	287	277	280	259	286	-3.4	0.8	-7.3	10.4
6	Malls	-	-	-	32	35	-	-	-	6.7
4+5+6	Total Class C medicines	541	527	528	501	547	-2.5	0.1	-5.1	9.1
1+2+3 +4+5	Total packages	1,870	1,881	1,884	1,915	1,977	0.6	0.2	1.6	3.2
	DDD/1,000 inhab die #	990.8	983.5	980.0	971.4	972.7	-0.7	-0.4	-0.9	0.1

ND: data not available
related to the consumption of Class A medicines provided under the agreed assistance scheme and to the Class C medicines reimbursed for the holders of an annuity was directly in compliance with Law no. 203 of 19 July 2000.
* The data relating to the private expenditure of medicines reimbursable by the NHS is obtained by the difference between total expenditure (estimated through the data from the "Traceability of medicines" flow) and the expense borne by NHS (obtained from OsMed data).
^ only the number of recipes and packages is expressed in millions of units.
Source: OsMed processing on "Traceability of medicines" flow (for private expenditure data). Elaboration on IMS Health data for the estimate of private expenditure for the years prior to 2016.

The following tables show expenditure and consumption values not including oxygen, unless otherwise indicated

Figure 1.1.2. Trend of Class A reimbursed medicines expenditure: consumption effect, prices effect and mix effect, period 2008-2017



1.2 Medicines purchased by public health facilities

The expenditure for medicines purchased by public health facilities (hospitals, health local units (HLU), IRCCS etc) amounted to approximately € 12.1 billion (€ 194.58 per capita) in 2017. This item of expenditure represented the 40% of the total public and private pharmaceutical expenditure (Table 1.1.a € 4,793 + € 7,267 billion) and it decreased by -0.7% during 2017 compared to 2016. In terms of pharmaceutical consumption, expressed as DDD, a +4.8% increase was registered in 2017, with an average of 158.7 daily doses per 1000 inhabitants. It should be highlighted that, although DDD approach allows a useful parameterization of pharmaceutical consumption at different levels (geographical and temporal), it does not represent the real pharmaceutical dose administered to the patient. Although this assumption is also valid in cases where DDD is used to parametrize the outpatient consumption (e.g. in the pediatric population), it becomes even more in the hospital context, where the dose of a medicine can vary in function of the patient's care needs.

1.3 Pharmaceutical consumption by age and gender

The variability of pharmaceutical expenditure and consumption is primarily due to changes of epidemiological profiles over the time, on variety of healthcare settings and on different prescribing attitudes of physicians. In addition, pharmaceutical consumption is significantly higher in specific population groups, according to age, gender and type of disease. Data for this analysis have been provided by six Italian Regions which are representative of the South, North and Center of the Country, covering over 55% of the entire Italian population. The prevalence of medicine use amounted globally to 66.1% in 2017, with a significant difference between men (61.8%) and women (70.2%). The trend of pharmaceutical expenditure and of average consumption was highly dependent on age (Table 1.3.1). The pharmaceutical expenditure per capita was three times higher in citizens being older than 64 years compared to the national average value. Moreover for each citizens being older than 64 years the NHS pharmaceutical expenditure was six times higher than the average value consumed by citizens belonging to younger age groups. This result is due both to the change in the prevalence of medicines use, which moves from some 50% in children and in adults up to 54 years, to over 95% in the elderly population over the age of 74, and to an increase in consumption ranging from about 400 doses in the age bracket between 40 and 50 years to over 3,000 in the 70-year-old population (Figure 1.3.1 and Table 1.3.1). Gender differences can be seen in the 15-64 age group, in which women show an average prevalence of medicines use higher than men, with an average difference of 10 percentage points (Figure 1.3.1). In particular, the highest levels of prescription concern medicines for the genitourinary system (and specifically contraceptives), antibiotics, antiemetic medicines and medicines for the central nervous system (in particular antidepressants). The population over 64 years absorbs over 60% of the standard distribution expenditure and over 65% of DDD (Table 1.3.1). In terms of consumption, an individual aged 65 to 74 years consumes an average of 2.6 doses per day and an individual over 74 years consumes 3.5 DDD (Table 1.3.1 and Figure 1.3.2). In the pediatric population medicines use prevalence amounts on average to about 50%, which ranges from over 70% in children aged 0 to 4 years and 38.7% in the age range 10-14 years (for more details see section "1.4 Pharmaceutical consumption in pediatric population").

Table 1.3.1. Outpatient pharmaceutical expenditure and consumption by age, year 2017

Age (class)	Gross expenditure (per capita)			Total expenditure		DDD/1000 inhab die			DDD total	
	Men	Women	Total	%	% cum	Men	Women	Total	%	% cum
00-04	32	26	29	0.5	0.5	71	62	67	0.3	0.3
05-09	31	26	29	0.6	1.1	58	49	53	0.3	0.5
10-14	48	29	39	0.8	2.0	63	50	56	0.3	0.8
15-19	43	30	37	0.8	2.7	78	79	79	0.4	1.2
20-24	46	37	42	0.9	3.7	92	110	101	0.5	1.7
25-29	46	47	47	1.1	4.8	108	143	125	0.7	2.4
30-34	54	66	60	1.5	6.3	136	185	160	0.9	3.3
35-39	69	87	78	2.2	8.5	194	234	214	1.4	4.8
40-44	89	105	97	3.3	11.8	298	308	303	2.4	7.2
45-49	119	127	123	4.4	16.2	473	454	464	3.8	11.0
50-54	176	173	174	6.2	22.4	764	695	729	5.9	16.9
55-59	263	235	249	7.5	29.9	1,206	1,032	1,117	7.7	24.7
60-64	378	320	348	9.1	39.0	1,775	1,450	1,606	9.7	34.4
65-69	515	437	474	12.1	51.1	2,450	2,010	2,220	13.1	47.5
70-74	679	573	622	13.2	64.2	3,210	2,672	2,921	14.3	61.8
75-79	783	660	714	14.0	78.2	3,625	3,085	3,323	15.0	76.9
80-84	894	736	799	11.3	89.6	4,031	3,437	3,676	12.1	88.9
85+	909	680	752	10.4	100.0	3,968	3,227	3,460	11.1	100.0
Total	**228**	**230**	**229**			**985**	**994**	**989**		

Figure 1.3.1. Prevalence of use by age and gender in the outpatient setting, year 2017

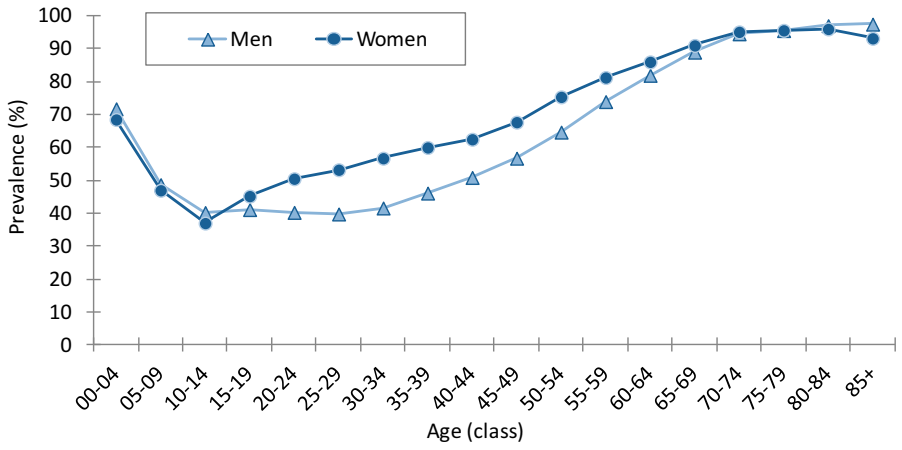
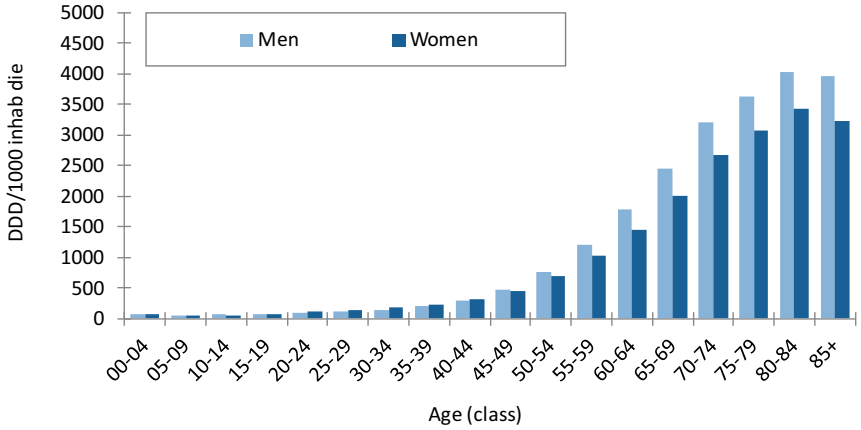


Figure 1.3.2. Outpatient consumption (DDD/1000 inhab die) by age and gender, year 2017



1.4 Pharmaceutical consumption in pediatric population

This section shows the class A pharmaceutical consumption in pediatric population (subjects under 18 years of age). Data for this analysis have been provided by 6 Italian Regions representative of the Northern (Lombardy and Veneto), Center (Lazio and Tuscany) and Southern (Campania and Apulia) Italy and accounting for 34.5 millions of inhabitants, of which more than 5.8 millions are pediatric subjects.

Each subject received an average of 2.1 medical prescriptions and 2.2 packages of medical products in one year. There was a slight difference between males and females: 2.2 vs 2.0 medical prescriptions and 2.3 vs 2.1 packages in the two groups, respectively (Table 1.4.1).

In line with international data, the highest rate of prescription was registered in the 1st year of life, after which the prescription rate decreases gradually with the increasing age of the subjects (Figure 1.4.1). In all age groups a higher prevalence was recorded of prescriptions in males compared to females (50.7% vs 48.9%) (Table 1.4.1).

The medicine consumption analysis sorted by therapeutical category (ATC I level) shows that the antiinfective for systemic use ranks 1st (46.1%), followed by medicines for the respiratory system (26.7%), hormones, with the exception of the sexual ones (7.4%), medicines for alimentary tract and metabolism (7.1%) and medicines for central nervous system (6.6%) (Figure 1.4.2). The medicine consumption analysis sorted by therapeutical category and gender globally shows a higher consumption in males compared to females with the exception of three categories (medicines for genitourinary system and sex hormones, antineoplastic and immunomodulating agents and antiparasitic products), which are most prescribed in the female gender (Figure 1.4.2).

Antiinfectives for systemic use are the most prescribed therapeuthical category (prevalence of 392.5 every 1000 inhabitants); amoxicillin/clavulanate is the most prescribed product of this category (211.1 every 1000 inhabitants) and it is also the most prescribed among first thirty active ingredients consumed in pediatric population during

2017 (Table 1.4.3 e Table 1.4.4). Medicines for the respiratory system ranks below with a prevalence of 224.5 every 1000 inhabitants. In particular beclometasone is the most prescribed medical product of this category (109.5 every 1000 inhabitants) and ranks second among the first thirty active ingredients consumed in pediatric population.
Hormones, with the exclusion of sexual ones, have a prevalence of utilization amounting to 81,9 every 1000 inhabitants; betametasone (69.4 every 1000 inhabitants) is the most prescribed medicine in this category. Medicines for alimentary tract and metabolism and medicines for central nervous system have a prevalence of use that amounts to respectively 50.7 and 9.0 every 1000 inhabitants (Table 1.4.3 and Table 1.4.4).
The respiratory system category accounts for nearly a third of the first thirty active ingredients consumed in pediatric population during 2017 (11 active ingredients), antiinfectives for systemic use (8 antibiotics and 1 antiviral medicine), hormones, with the exception of sexual ones (4 actives ingredients) and medicines for central nervous system (3 antiepileptic medicines) rank below (Table 1.4.4).
The analysis of prescriptions of respiratory system medicines shows that 22.8% of children received, on average, one package during the reporting year, for a total of 3,4 millions of prescriptions amounting to 27.5% of total medicines consumption in pediatric population (Table 1.4.5). As already stated, the highest prescription prevalence is registered in the 1st year of life, then it decreases with the increasing age of children (Figure 1.4.1).
The inhaled corticosteroids are the therapeutic class with the highest prescription rate (16.5%) and beclometasone is the most prescribed active ingredient (12.7%). The oral steroids rank below (7.6%) and betametasone is the most prescribed active ingredient (8.2%). Following are SABAs (Short-Acting Beta Agonists) (6.5%), which include salbutamol among the most prescribed active ingredients (7.5%) (Table 1.4.6).
The analysis of prescriptions, sorted by therapeutical subgroup and age group, shows that the highest prevalence of use is up to the age of 6 years for all medicines, with the exception of Beta2 in association with Laba and of injective steroids. After this age only a single prescription during the year is usually observed. Most probably this finding suggests a need-based use of this type of medicines (Table 1.4.7).
The analysis of the utilization rate, sorted by therapeutical category and age group, inhaled steroids showed the highest rate of utilization in all age groups, in particular in the 2-3-year-old age group. After this age the utilization rate decreases gradually with the increasing age of the subject.
The oral steroids show a stable utilization trend, with the exception of two peak periods: 4-7 year-old and 12-17 year-old age groups. SABAs in combination are more prescribed in the first year of life compared to the following years when the prescription declines with the age increase. SABAs non in combination have an utilization trend more or less stable in all age groups, while a slight decrease is present only during the 1st year of age and after 12 years of age (Figure 1.4.5).
The analysis of antibiotics prescription shows that, during 2017, 38.3% of children received on average 2.6 packages accounting to 5.4 millions of prescriptions, that is 44.7% of total medicines consumption in the pediatric population. The highest peak is registered in the 2-3 year-old age group (Figure 1.4.6).
As alredy reported, combinations of penicillins, including beta-lactamase inhibitors, are the most prescribed therapeutic class (prevalence of 21.1%), followed by macrolides and

lincosamides (11.6%) with claritromicine the most prescribed active ingredient of this group (7.1%), and then by oral cephalosporins (10.2%); cefixime is the most prescribed active ingredient in this last class (8.4%) (Table 1.4.9).
The analysis of consumption rate, sorted by therapeutical category and age group, shows that penicillins combinations are most prescribed in all age groups with a slight peak in the 4-7 years of age. Furthermore, their consumption shows a gradual decrease after 7 years of age. Macrolides and lincosamides have their peak of consumption in children aged between 4-7 years and 12-17 years. Oral cephalosporins are mostly used in children being 2-11 years old, while their prescriptions are smaller in the extreme age groups (0-1 and 12-17 years age groups). Penicillins with extended spectrum show their highest level of consumption in the first year of life and a progressive decline of their prescription is observed with age increase (Figure 1.4.7).

Table 1.4.1. General prescribing data in the pediatric population (2017)

	Male	Female	Total
Users	1,506,732	1,370,696	2,877,428
prevalence (%)	50.7	48.9	49.9
Prescriptions	6,611,587	5,558,325	12,169,912
per capita	2.2	2.0	2.1
Packages	6,969,050	5,844,815	12,813,865
per capita	2.3	2.1	2.2
Expenditure (€)	114,819,095	76,749,931	191,569,026
per capita	38.7	27.4	33.2
per user	76.20	55.99	66.58

Figure 1.4.1. Prescription trends in the pediatric population by age and gender (2017)

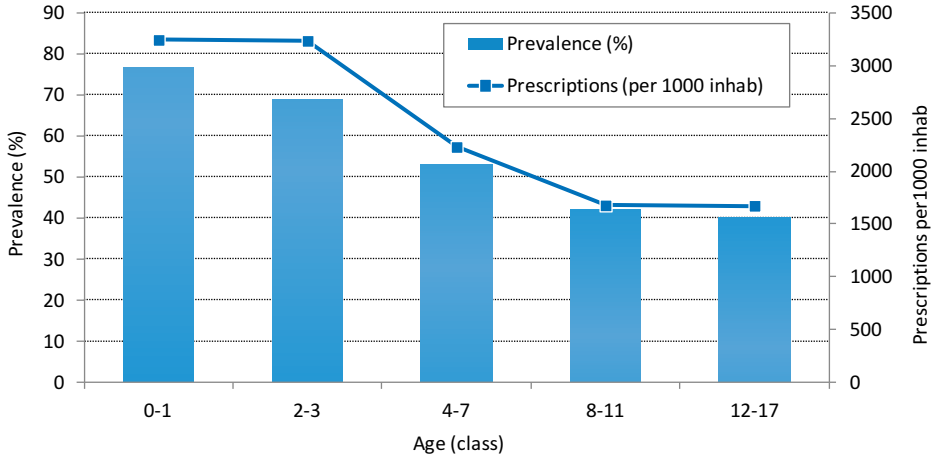


Table 1.4.2. Age and gender distribution of pediatric consumption in 2017 (packages)

Age class	Packs per capita		
	Male	Female	Total
<1	3.8	3.1	3.5
1-5	3.2	2.9	3.0
6-11	2.0	1.7	1.8
12-17	1.9	1.7	1.8
Total	**2.3**	**2.1**	**2.2**

Figure 1.4.2. Distribution of consumption (packages) in the pediatric age for the ATC level in 2017

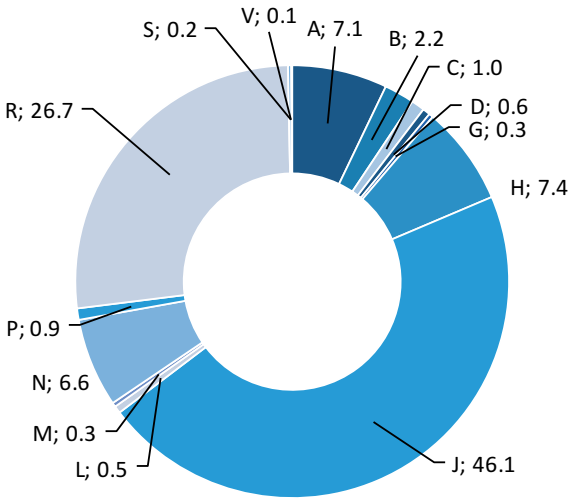


Figure 1.4.3. Percentage distribution of consumption (packages) for ATC level and gender (2017)

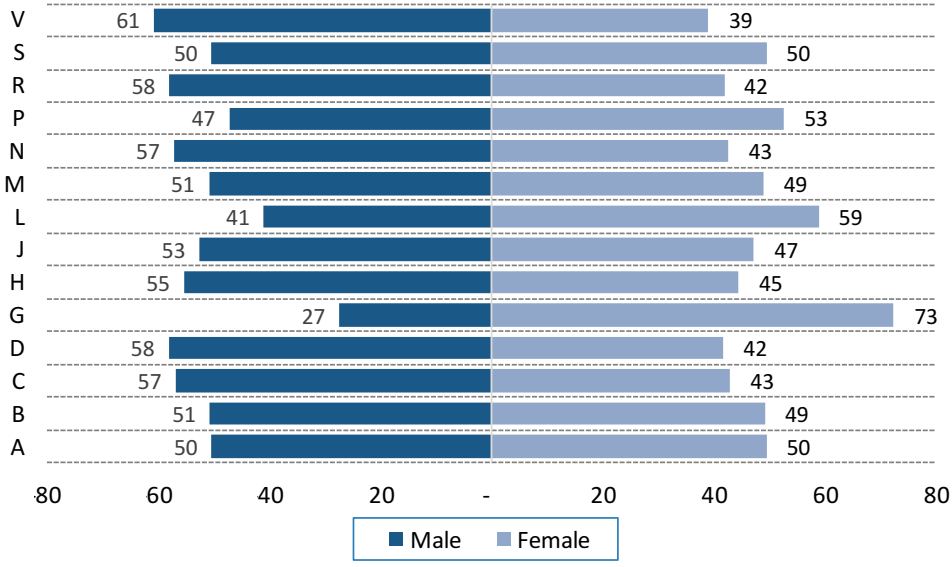


Table 1.4.3. Most prescribed active ingredients by therapeutic category (75% of prescriptions) (2017)

Therapeutic category/active ingredient	Prescriptions (x 1000 ab.)	Prevalence (x 1000 inhab.)	Ratio M/F
J - Antiinfectives for systemic use	**975.6**	**392.5**	**1.03**
amoxicillin / clavulanic acid	385.1	211.1	1.07
amoxicillin	121.6	66.7	1.03
cefixime	101.8	66.6	0.98
azitromycin	94.1	62.7	1.06
clarithromycin	84.6	59.2	1.09
R – Respiratory system	**581.3**	**224.5**	**1.16**
beclomethasone	149.9	109.5	1.10
salbutamol	93.2	64.5	1.34
cetirizine	66.6	34.7	1.26
budesonide	55.8	39.4	1.18
fluticasone	43.5	25.9	1.43
montelukast	40.8	12.9	1.54
H - Hormones *(excluding sexual ones)*	**154.8**	**81.9**	**1.17**
betamethasone	100.2	69.4	1.19
somatropin	14.2	0.7	1.42
levothyroxine	13.9	2.4	0.53
prednisone	12.8	6.1	1.21
desmopressin	6.9	1.2	2.14
A - Alimentary tract and metabolism	**146.6**	**50.7**	**0.95**
colecalciferol	64.9	29.1	0.95
lansoprazole	9.1	2.1	0.94
omeprazole	6.8	1.9	0.86
esomeprazole	6.0	1.8	0.91
nystatine	5.1	4.1	0.97
rifaximin	5.0	3.4	1.24
insulin lispro	4.5	0.7	1.15
insulin aspart	4.4	0.5	0.95
ursodeoxycholic acid	4.3	0.4	0.92
N – Nervous system	**130.1**	**9.0**	**1.14**
valproic acid	53.9	2.8	1.54
carbamazepine	12.4	0.7	1.15
levetiracetam	12.4	1.1	0.81
lamotrigine	6.1	0.4	0.66
topiramate	3.8	0.4	0.72
phenobarbital	3.5	0.3	1.26
aripiprazole	3.5	0.5	1.32
sertraline	3.2	0.6	0.77

Table 1.4.4. First thirty active ingredients for consumption in the pediatric age in 2017

ATC	Active ingredient	Packs (per 1000 inhab)	Consumption (%)*	
			Male	Female
J	amoxicillin/clavulanic acid	401.9	53.6	46.4
R	beclomethasone	151.0	54.4	45.6
J	amoxicillin	127.5	52.4	47.6
J	cefixime	104.7	51.1	48.9
H	betamethasone	101.7	56.7	43.3
J	azitromycin	96.5	53.2	46.8
R	salbutamol	94.1	60.0	40.0
J	clarithromycin	86.7	53.9	46.1
A	colecalciferol	68.6	49.5	50.5
R	cetirizine	68.6	59.4	40.6
N	valproic acid	58.4	62.4	37.6
R	budesonide	56.3	56.2	43.8
R	fluticasone	44.4	61.4	38.6
J	cefpodoxime	43.9	52.8	47.2
R	montelukast	42.6	63.2	36.8
J	ceftriaxone	37.7	53.7	46.3
R	salbutamol/ipratropium	36.1	55.1	44.9
J	cefaclor	26.1	50.5	49.5
H	somatropin	18.5	62.1	37.9
J	acyclovir	17.3	51.2	48.8
R	flunisolide	17.0	54.5	45.5
R	levocetirizine	17.0	63.3	36.7
H	levothyroxine	14.9	37.0	63.0
N	carbamazepine	13.6	55.0	45.0
H	prednisone	13.6	53.6	46.4
N	levetiracetam	13.3	46.3	53.7
R	salmeterol/fluticasone	13.0	66.2	33.8
P	mebendazole	12.5	47.6	52.4
R	desloratadine	11.7	61.2	38.8
B	sodium chloride	11.2	54.3	45.7

* calculated compared to total consumption in the pediatric age

Prescription of respiratory system medicines in the pediatric population

Table 1.4.5. Prescription of respiratory medicines in the pediatric population (2017)

	Total
Prescriptions	3,349,868
For 1000 children	580.3
% share of total consumption	27.5
Packages	3,405,153
By prescription	1.0
Users	1,315,691
Prevalence (%)	22.8

Figure 1.4.4 Prescription development of respiratory system medicines by age (2017)

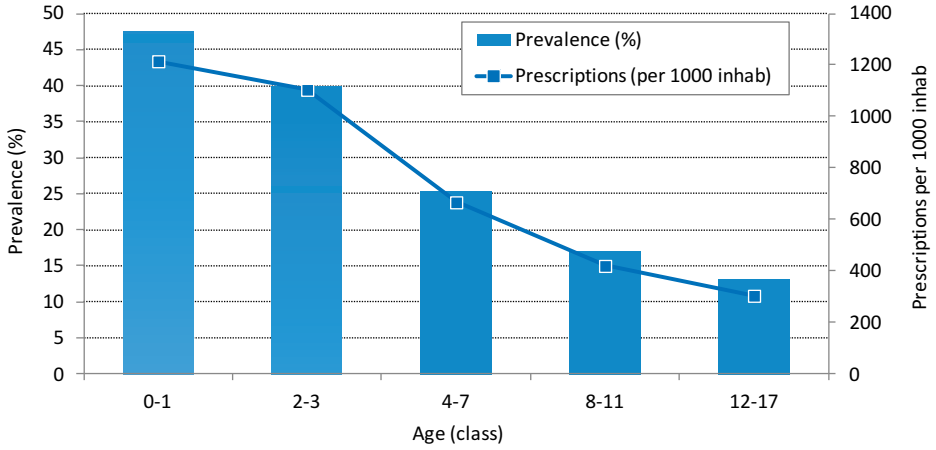


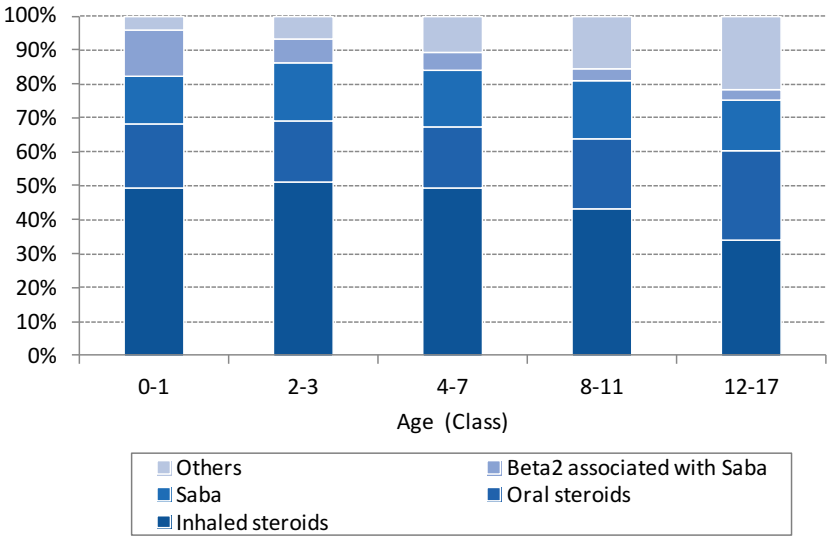
Table 1.4.6. Prescription of respiratory medicines in the pediatric population by therapeutic category and by active ingredient (2017)

Categories and active ingredients	Prevalence (%)	Prescriptions for 1000 inhabitants
Inhaled steroids	16.5	266.4
Oral steroids	7.6	116.0
Saba	6.5	93.2
Beta2 associated with saba	3.1	38.0
Anti-leukotrienics	1.3	40.8
Beta2 associated with laba	0.8	19.4
Anticholinergic	0.2	2.9
Injective steroids	0.1	2.1
Cromoglycate	0.1	0.8
Theophyllinics	0.0	0.3
Laba	0.0	0.3
Other antiasthmatic	0.0	0.1
Total	**22.2**	**542.2**
beclomethasone	12.7	149.9
betamethasone	8.2	100.2
salbutamol	7.5	93.2
budesonide	4.6	55.8
fluticasone	3.2	43.5
montelukast	2.3	40.8
salbutamol/ipratropium	3.2	36.0
flunisolide	1.5	16.9
prednisone	0.9	12.8
salmeterol/fluticasone	0.8	12.5

Table 1.4.7. Respiratory medicine users by number of prescriptions received during the year by therapeutic subgroup and age class (2017)

Subgroup	0-6 years					7-17 years				
	Prevalence %	Users for no. prescriptions (%)				Prevalence %	Users for no. prescriptions (%)			
		1	2	3	>3		1	2	3	>3
Inhaled steroids	28.4	63.1	21.2	8.1	7.7	9.8	73.5	17.1	4.8	4.5
Oral steroids	11.6	70.9	18.9	5.7	4.5	5.4	73.5	18.2	3.9	4.4
Saba	11.1	75.6	16.3	4.8	3.3	3.8	71.5	18.1	5.0	5.4
Beta2 associated with Saba	6.7	83.2	12.8	2.7	1.2	1.1	88.3	9.3	1.5	0.9
Anti leukotrienics	1.9	35.7	22.6	11.7	30.0	1.0	30.2	24.6	10.2	35.0
Beta2 associated with Laba	0.3	54.3	20.6	9.7	15.5	1.1	47.7	22.8	9.4	20.1
Anticholinergic	0.3	71.8	17.4	5.0	5.9	0.1	72.5	18.2	3.9	5.5
Injective steroids	0.1	82.5	13.0	2.4	2.1	0.2	74.1	19.8	2.8	3.3
Cromoglycate	0.1	75.6	15.2	4.9	4.3	0.1	75.3	16.3	2.9	5.6
Theophyllinics	0.0	81.1	14.6	3.4	0.9	0.0	80.4	12.2	3.7	3.8
Laba	0.0	73.4	16.4	4.5	5.6	0.0	65.2	19.5	5.9	9.4

Figure 1.4.5. Percentage distribution of respiratory medicine consumption by therapeutic category and age class (2017)



Antibiotics prescription in the pediatric population

Table 1.4.8. Prescription of antibiotics in the pediatric population (2017)

	Total
Prescriptions	5,435,212
For 1000 children	941.6
% share of total consumption	44.7
Packs	5,697,259
For prescription	1.0
Users	2,212,551
Prevalence (%)	38.3

Figure 1.4.6. Prescription development of antibiotics by age (2017)

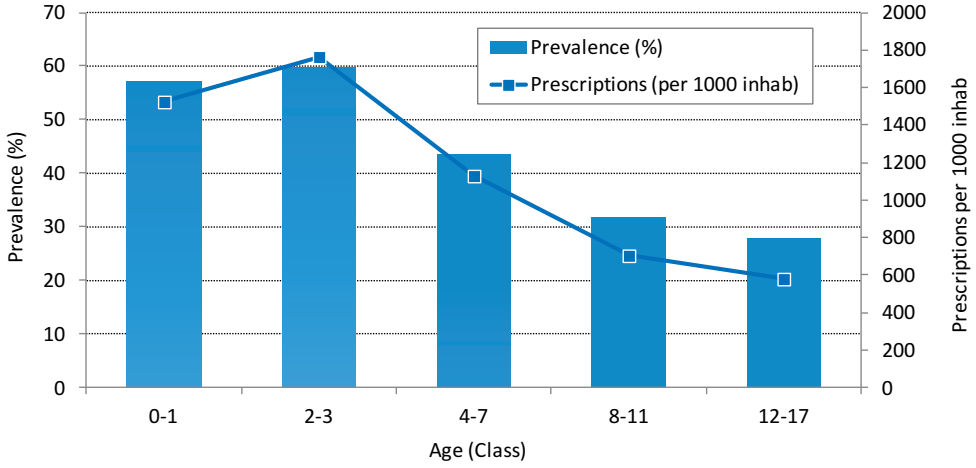
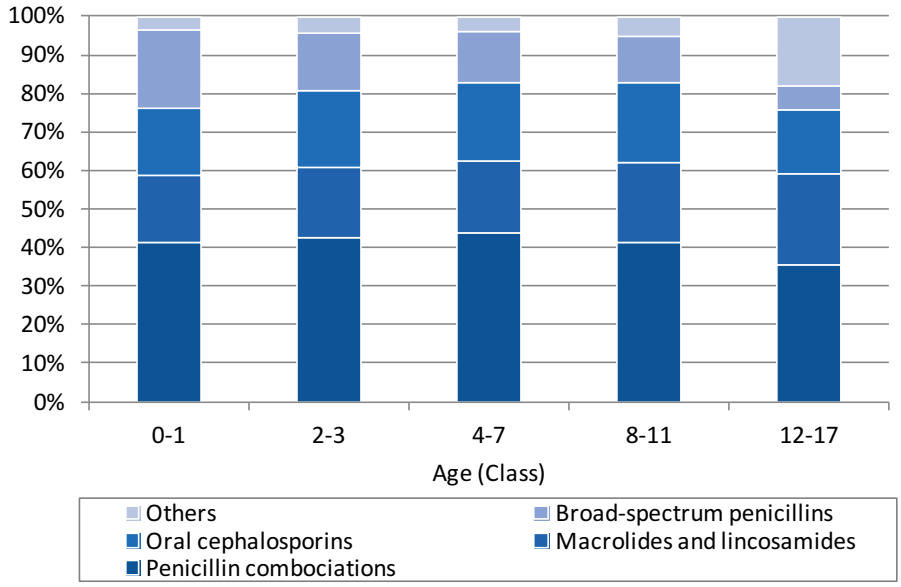


Table 1.4.9. Prescription of antibiotics in the pediatric population by therapeutic category and active ingredient (2017)

Categories and active ingredients	Prevalence (%)	Prescriptions for 1000 inhabitants
Penicillin combinations (including beta lactamase inhibitors)	21.1	385.6
Macrolides and lincosamides	11.6	186.9
Oral cephalosporins	10.2	179.0
Broad-spectrum penicillins and penicillins sensitive to beta lactamases	6.7	122.6
Cephalosporine im/ev III-IV gen	0.7	36.9
Quinolones	0.5	8.5
Tetracyclines	0.3	8.2
Sulfonamides and trimetropim	0.3	4.3
Cephalosporine im/ev II gen	0.2	4.6
Aminoglycosides	0.1	4.3
Cephalosporine im/ev I gen	0.0	0.5
Total	**37.3**	**900.8**
amoxicillin/clavulanic acid	29.1	385.1
amoxicillin	9.3	121.6
cefixime	8.4	101.8
azithromycin	7.7	94.1
clarithromycin	7.1	84.6
cefpodoxime	3.1	41.1
ceftriaxone	1.8	31.6
cefaclor	1.9	24.9
ceftibuten	0.8	9.9
fosfomycin	0.8	7.9

Figure 1.4.7. Percentage distribution of antibiotics consumption by therapeutic category and age class (2017)



List of therapeutic cathegories

Antibiotics	
Aminoglycosides	amikacin, gentamicin, netilmicin, tobramycin
Antibiotics vs resistant germs	linezolid
Penicillin combinations (including beta lactamase inhibitors)	amoxicillin/clavulanic acid, ampicillin/sulbactam, flucloxacillin, oxacillin sodium, piperacillin/tazobactam
Cephalosporine im/ev I gen	cefazolin, cefonicid, cefoxitin, cefuroxime
Cephalosporine im/ev III-IV gen	cefepime, cefodizima, cefotaxima, ceftazidime, ceftriaxone
Oral cephalosporins	cefaclor, cefalexin, cefditoren, cefixime, cefpodoxime, cefprozil, ceftibuten
Quinolones	pipemidic acid, ciprofloxacin, levofloxacin, lomefloxacin, moxifloxacin, norfloxacin, pefloxacin, prulifloxacin, rufloxacin
Glycopeptides	teicoplanina
Macrolides and lincosamides	azithromycin, clarithromycin, clindamycin, erythromycin, josamycin, lincomycin, myocamycin, roxithromycin, spiramycin, telithromycin
Broad-spectrum penicillins and penicillins sensitive to beta lactamases	amoxicillin, ampicillin, bacampicillin, benzylpenicillin benzatinic, piperacillin
Polymyxins	colistimethate
Sulfonamides and trimetropim	trimethoprim/sulfamethoxazole
Tetracyclines	doxycycline, limecicline (tetracycline-levo-methylenlysine), methacrycline, minocycline, tetracycline
Respiratory System	
Other antiasthmatic	omalizumab, roflumilast
Anticholinergic	aclidinium, glycopyrronium, ipratropium, oxitropio bromide, tiotropium, umeclidinium
Anti leukotrienics	montelukast, zafirlukast
Beta2 in combination with laba	aclidinium/formoterol, beclometasone/formoterol, budesonide formoterol, fenoterol/ipratropium bromide, fluticasone formoterol, fluticasone/vilanterol, indacaterol/glycopyrronium, salmeterol fluticasone
Beta2 in combination with saba	beclomethasone/salbutamol, salbutamol/flunisolide, salbutamol ipratropium
Cromoglycate	nedocromile sodium
Laba	formoterol, indacaterol, olodaterol, salmeterol
Lama – laba	tiotropium/olodaterol, umeclidinium/vilanterol
Saba	fenoterol, salbutamol, terbutaline
Inhaled steroids	beclometasone, budesonide, ciclesonide, flunisolide, fluticasone, mometasone
Injective steroids	betamethasone, dexamethasone, hydrocortisone, methylprednisolone, triamcinolone
Oral steroids	betamethasone, cortisone acetate, deflazacort, dexamethasone, methylprednisolone, prednisolone, prednisone
Theophylline	ambroxol, doxofillina, theophylline

1.5. Pharmaceutical consumption in the elderly population

This section shows the Class A pharmaceutical consumption in the elderly population (subjects aged 65 years and older). Data for the analysis are related to 6 Italian Regions representative of Northern (Lombardy and Veneto), Center (Lazio and Tuscany) and Southern (Campania and Apulia) Italy, accounting for 34.5 millions inhabitants, 7.4 millions of which are elderly population.

In this population group, the average expenditure amounts to € 690 per user (€ 754 in males and € 640 in females) (Table 1.5.1). Medicines consumption is higher in men than in women: 3,488 vs 2,992 DDD/1000 users per day, respectively. For this analysis all subjects were considered with at least one prescription during 2017, that is 94% of the sample, without differences of use prevalence according to sex.

In the elderly population, the number of doses (consumption) and expenditure increases with age, up to the 80-84 years age group, then a slight decrease is reported in the age group over 85 years (Figure 1.5.1). The 80-84 years age group and the one over 85 years are those with the highest consumptions (3,816 and 3,663 DDD/1000 users per day) that account for 830 and 796 euros respectively. Differences between genders are in all age groups: men show a higher consumption and expenditure compared to women.

The analysis of the average number of active ingredients prescribed per user was used as a proxy of polytherapy in the elderly population. In both genders and in all age groups an average number is reported of 9.7 different active ingredients per user, with differences among different age groups. The lowest value is registered in the 65-69 years age group (7.7 active ingredients per user), while the highest value is registered in subjects aged 85 years or older (11.8 active ingredients per user).

A gradual increase of the number of active ingredients per user is detectable in both genders varying in men from the mean value of 7.6 active ingredients registered in the age group 65-69 years and the value of 12.1 registered in the age group 85 years or over. A similar trend is observed also in women: 7.8 different active ingredients consumed in the age group 65-69 years and 11,6 in the age group 85 or over (Table 1.5.2). After that, more than 64% of elderly received at least 5 different active active ingredients during 2017, and 21.6% received 10 different active ingredients. These findings suggest that polytherapy is frequent in the geriatric population (Figure 1.5.2).

Cardiovascular system medicines, antithrombotic agents for systemic use, gastrointestinal tract and metabolism medicines are the most prescribed therapeutic classes.

In terms of medicine use prevalence, agents for peptic ulcer and gastro-oesophageal reflux disease are the most prescribed (48.3%; 47.0% in men and 49.2% in women), followed, in decreasing order by: antithrombotic agents (41.5%; 45.2% in men and 38.6% in women), lipid lowering medicines (34.4%; 36.9% in men and 32.6% in women) and anti-inflammatory and antirheumatic products (32.8%; 28,6% in men and 35.9% in women).

The differences observed in use prevalence between men and women reflect the different prevalences of diseases for which these medical products are intended. Vitamins A and D (37.4% vs 10.7% in men), thyroid hormones (9.9% vs 3.3% in males) and antidepressants (17.8% vs 9.7% in men) are the classes of medicinal products for which a higher prevalence of prescription is observed in women. The use of products for prostatic hypertrophy instead is exclusively found in men (Table 1.5.3).

Table 1.5.1. Age and gender distribution of the pharmaceutical prescription in the population aged ≥65 (2017)

Age (class)	Expenditure for user			DDD/1000 users die			Prevalence of use (%)		
	M	W	Tot	M	W	Tot	M	W	Tot
65-69	579	480	527	2,756	2,211	2,468	89	91	90
70-74	719	602	656	3,398	2,811	3,082	94	95	95
75-79	820	691	748	3,798	3,230	3,481	95	96	95
80-84	922	767	830	4,158	3,583	3,816	97	96	96
≥85	933	731	796	4,074	3,467	3,663	97	93	94
Total	**754**	**640**	**690**	**3,488**	**2,992**	**3,206**	**94**	**94**	**94**

Figure 1.5.1. Prescription in the population aged ≥65 (DDD/1000 users and user expense) (2017)

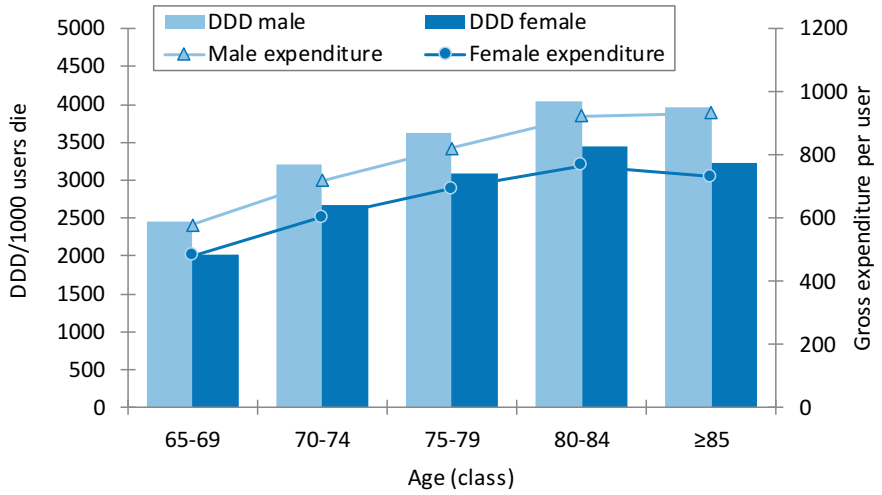


Table 1.5.2. Average number of active ingredients by age and gender (2017)

Age class	Average number of active ingredients		
	Men	Women	Total
65-69	7.6	7.8	7.7
70-74	9.1	9.3	9.2
75-79	10.1	10.3	10.2
80-84	11.4	11.4	11.4
≥85	12.1	11.6	11.8
Total	**9.6**	**9.9**	**9.7**

Figure 1.5.2. Distribution of users in the population aged ≥65 years by number of different active ingredient (2017)

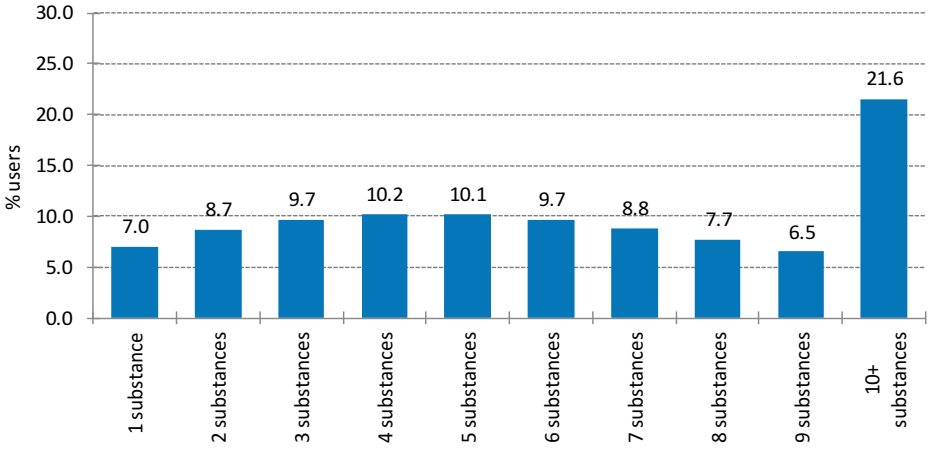


Table 1.5.3. Exposure to medicines in the population aged ≥65 years for ATC at level III (2017)

ATC III level	Category	Prevalence of use (%)		
		Men	Women	Total
A02B	Peptic antiulcer and gastroesof reflux disease (Gord)	47.0	49.2	48.3
B01A	Antithrombotic	45.2	38.6	41.5
C10A	Active ingredients that modify lipids, not associated	36.9	32.6	34.4
M01A	Non-steroidal anti-inflammatory and anti-rheumatic drugs	28.6	35.9	32.8
C07A	Beta blockers	29.3	29.7	29.5
A11C	Vitamins A and D, including their associations	10.7	37.4	25.9
J01C	Beta-lactam antibacterials, penicillins	23.9	23.2	23.5
J01M	Quinolone antibacterials	22.8	20.4	21.4
C09A	ACE inhibitors not associated	21.8	16.8	18.9
C08C	Selective calcium channel blockers with prevailing vascular effect	19.3	17.3	18.2
C09D	Angiotensin II antagonists, associations	15.1	17.8	16.6
H02A	Systemic corticosteroids, not associated	15.5	17.3	16.5
C03C	Diuretics with greater diuretic action	15.5	17.1	16.4
A10B	Hypoglycemic agents, excluding insulins	17.8	13.5	15.4
C09C	Angiotensin II antagonists, not associated	15.0	15.1	15.1
N06A	Antidepressants	9.7	17.8	14.3
J01D	Other beta-lactam antibacterials	14.2	14.0	14.1
R03B	Other drugs for obstructive airway disorders for aerosols	14.9	13.2	13.9
C09B	ACE inhibitors, associations	13.9	13.8	13.8
G04C	Medicines used in benign prostatic hypertrophy	29.9	0.2	13.0
N02A	Opioids	9.0	14.5	12.2
J01F	Macrolides, lincosamides and streptogramins	11.7	12.3	12.1
R03A	Adrenergics for aerosols	12.0	10.4	11.1
A07A	Intestinal antiinfectives	7.9	10.3	9.3
M04A	Antigout	11.8	7.3	9.2
H03A	Thyroid preparations	3.4	11.4	7.9
J01X	Other antibacterials	3.3	9.9	7.1
N03A	Antiepileptic	6.1	7.3	6.8
S01E	Antiglaucoma and miotics preparations	6.7	6.7	6.7
B03B	Vitamin B12 and folic acid	6.1	6.5	6.3

1.6 Pharmaceutical consumption on a monthly basis

Figure 1.6.1 shows consumption trend of Class A reimbursed medicines (consumption is expressed as DDD) according to the period 2004-2017. Over the last fourteen years, pharmaceutical consumption has registered a persistent upward trend and has increased from 736.8 DDD/1000 inhabitants per day in 2004 up to 972.7 DDD/1000 inhabitants per day in 2017. This results in a +27.4% increase. In addition to the increased trend, pharmaceutical consumption is associated to seasonal variations as proved by peaks in medicine consumption detectable on a monthly basis (see Figure 1.6.1). As a result of this periodicity, consumption levels registered in the first half of 2017 are higher than the annual average of +2.0%, in contrast to the second half of the year, where the consumption is below -2.0%. In particular, the pharmaceutical consumptions registered in August are -11.3% lower than the average consumption of the same year. Generally, systemic antimicrobial medicines and respiratory medicines are the therapeutic categories on which seasonality of consumption has the highest impact.
Figure 1.6.2 shows consumption trend of Class C medicines with prescription since January 2004. This trend could have been affected by regulatory decisions whereby over time granting or not of the status of reimbursed medicine was determined. Starting from 2004, a downward trend in consumption of Class C medicines was observed; indeed, the tendency varied from 236.5 DDD/1000 inhabitants per day in 2004 up to 183.3 DDD/1000 inhabitants per day in 2017 (-22% lower than the 2014 value). The highest average consumption was recorded in September (207.3 DDD/1000 inhabitants per day) and October (201.0 DDD/1000 inhabitants per day), while the lowest levels of consumption are observed in August (156.2 DDD/1000 inhabitants per day). Peaks corresponding to the first months of the year are attributed to higher consumption of doses of respiratory system medicines in such period than in summer months. Figure 1.6.3 shows consumption trend of medicines purchased by public health facilities in the period 2006-2017. In detail, an overall growing trend in consumption is recorded, increasing from 100.6 DDD/1000 inhabitants per day during 2006 up to 158.7 DDD/1000 inhabitants per day in 2017 (+58% higher than the 2014 value). During 2017 the lowest level in consumption is observed in August (-30.6%) and December (-28.5%), while January (+23.6%) and June (+18.2%) registered the highest levels in consumption.
For a correct interpretation of monthly consumption trends (consumption expressed as DDD/1000 inhabitants per day) regarding medicines purchased by public health facilities compared to annual consumption trends, it should be noted that these trends are influenced by purchasing procedures carried out by the public health facilities themselves. Therefore, such trends cannot be strictly interpreted in terms of monthly patient consumption. This clarification is confirmed by irregularities in the volume of monthly purchases by public health facilities that were registered in the last six years.

Figure 1.6.1. Consumption trend of Class A medicines reimbursed by the NHS (DDD/1000 inhab die), years 2004-2017

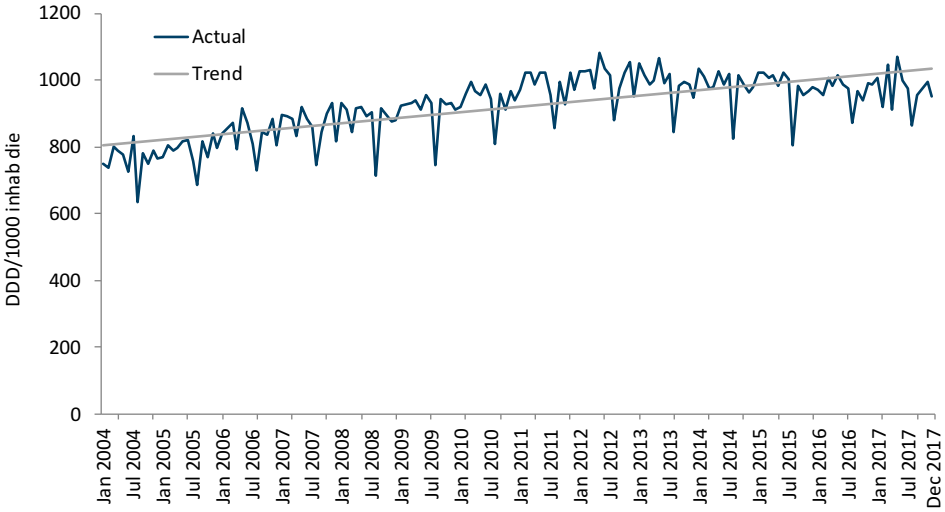


Figure 1.6.2. Consumption trend of Class C medicines with prescription (DDD/1000 inhab die), years 2004-2017

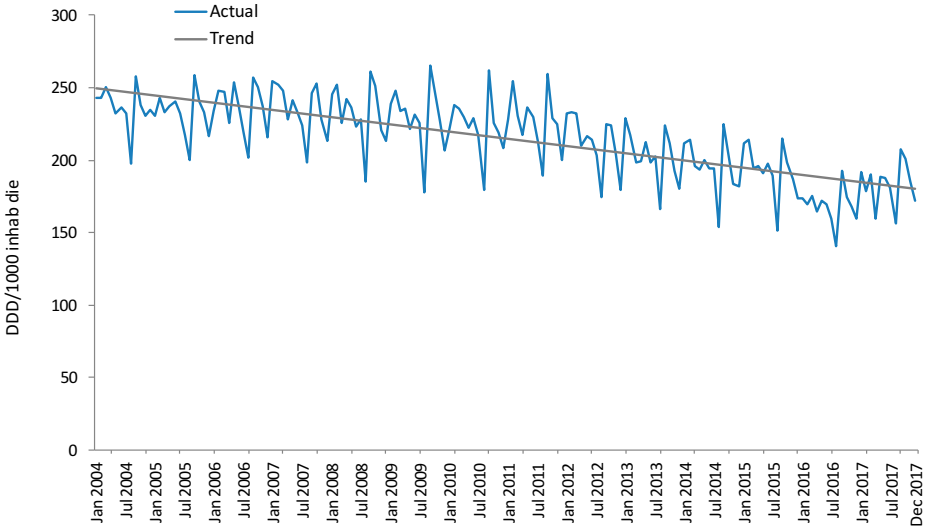
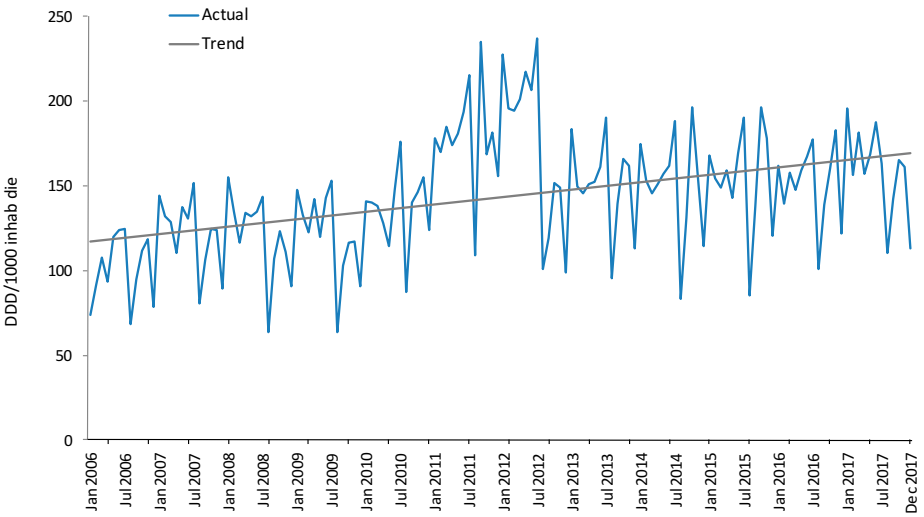


Figure 1.6.3. Consumption trend of medicines purchased by public health facilities (DDD/1000 inhab die), years 2006-2017



1.7 Trend of pharmaceutical prices

Data shown in Figure 1.7.1 represent the average price, weighed per package and per DDD, of Class A medicines reimbursed by the NHS in the period between January 2004 and December 2017. The time series show a decreasing trend for both prices, especially since 2005 and in the period 2011-2012. This decline was mostly driven by measures of price reduction, which were implemented at National level at the beginning of 2004, and by the economic effect resulting from AIFA Resolution of 8 April 2011. These procedures resulted in a reduction of the reference prices of medicinal products included in the Transparency List (*Liste di trasparenza)* on the basis of a comparison carried out between the prices of generic medicines in Italy and the same pharmaceutical packages marketed in Germany, UK, France and Spain.

Figure 1.7.2 shows the average price trend, weighed per package and per DDD, of Class C medicines requiring a medical prescription (not-reimbursed by the NHS), regarding the period between 2004 and 2017. Looking at the monthly time series data, trends of the two indexes reveal a steady growth, rising from € 10.13 per package (and € 0.61 per DDD) during 2004 up to € 12.73 per package (and € 0.71 per DDD) during 2017, resulting in an increase of +25.7% of average price and of +15.2% of price per DDD, compared to 2004.

Figure 1.7.3 shows the average price trend, weighed per package and per DDD, of Class C medicines with prescription in the period 2006-2017. Average prices increased from 2006 to 2010; they remained stable in the period between 2011 and 2012, later to increase again in the period 2013-2017. As abovementioned, the average price of medicines purchased by public health facilities is mainly influenced by both purchasing procedures and by the average price of mixed medicines purchased from time to time.

Figure 1.7.1. Average price trend of Class A medicines reimbursed by the NHS, years 2004-2017

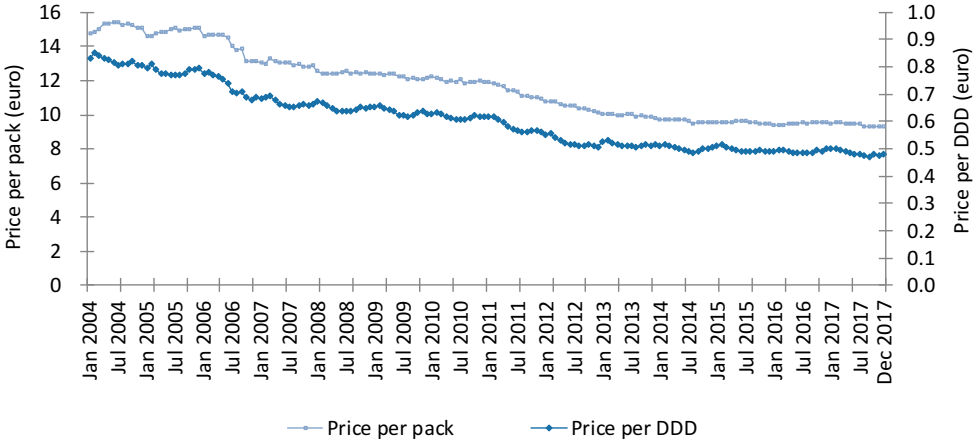


Figure 1.7.2. Average price trend of Class C medicines requiring a medical prescription, 2004-2017

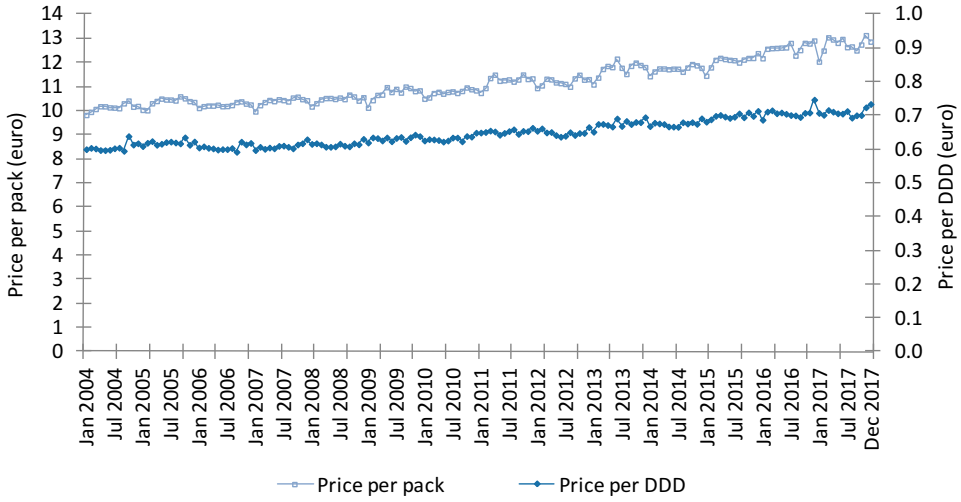


Figure 1.7.3. Average price trend of medicines purchased by health public facilities, 2006-2017

Section 2

Consumption and expenditure by therapeutic class

Therapeutic categories and active ingredients

In this section main data on individual therapeutic categories will be presented.

Table 2.1. NHS expenditure per capita by I ATC level in descending order of expenditure: comparison 2017-2016

I level ATC	Per capita outpatient NHS expenditure Class A (a)	Δ% 17-16	Per capita inpatient NHS expenditure (b)	Δ% 17-16	NHS expenditure (a+b)	Δ% 17-16
L	3.93	0.0	79.64	12.9	83.57	12.2
C	53.63	-2.9	4.93	8.2	58.56	-2.1
J	13.14	-2.4	44.39	-25.1	57.54	-20.9
A	32.80	2.0	12.58	2.8	45.38	2.2
B	8.08	-2.6	26.05	3.7	34.13	2.2
N	22.43	-0.1	8.37	17.8	30.80	4.2
R	16.36	-1.9	2.04	30.2	18.40	0.9
G	6.60	-7.6	1.90	-10.3	8.50	-8.2
H	3.79	15.6	4.59	-4.2	8.38	3.9
M	6.08	-7.7	1.51	35.2	7.58	-1.5
S	3.81	-0.3	3.06	35.0	6.87	12.9
V	0.14	-0.2	5.17	6.1	5.31	5.9
D	0.95	6.4	0.36	10.7	1.30	7.5
P	0.21	2.1	0.03	19.0	0.24	3.7
Total	**171.96**	**-1.3**	**194.61**	**-0.7**	**366.57**	**-1.0**

A	Alimentary tract and metabolism	H	Systemic hormonal preparations, excl. sex hormones and insulins	M	Musculo-skeletal system
B	Blood and blood forming organs	J	Antiinfectives for systemic use	N	Nervous system
C	Cardiovascular system	L	Antineoplastic and immunomodulating agents	P	Pesticides
D	Dermatologicals			R	Respiratory system
G	Genito-urinary system and sex hormones			S	Sensory organs
				V	Various

Table 2.2. NHS consumption (DDD/1000 inhabitants die) for I ATC level in descending order of consumption: comparison 2017-2016

I level ATC	DDD/1000 inhab die outpatient NHS expenditure (a)	Δ% 17-16	DDD/1000 inhab die inpatient NHS expenditure (b)	Δ% 17-16	DDD/1000 inhab die NHS (a+b)	Δ% 17-16
C	466.8	0.3	17.4	-2.5	484.2	0.2
A	152.0	0.1	31.0	3.3	183.0	0.6
B	86.4	0.8	39.0	7.7	125.4	2.9
N	63.3	1.8	22.7	-2.3	86.0	0.7
R	41.2	-2.2	2.4	-0.5	43.6	-2.1
G	39.5	-3.3	2.4	6.5	41.9	-2.8
M	37.6	-1.4	4.3	7.9	41.9	-0.5
H	34.4	1.4	5.5	-3.4	39.9	0.7
J	20.7	-2.2	6.5	-1.9	27.2	-2.1
S	20.0	-0.1	2.6	13.5	22.6	1.3
D	4.1	18.0	12.8	29.5	16.9	26.5
L	5.8	2.5	9.0	6.7	14.8	5.0
V	0.1	3.3	3.1	20.4	3.1	19.8
P	0.9	4.1	0.0	2.5	0.9	4.0
Total	**972.7**	**0.1**	**158.7**	**4.8**	**1131.4**	**0.8**

Table 2.3. Composition of pharmaceutical expenditure 2017 for I ATC level and reimbursement class (decreasing order for total expenditure)

I level ATC	Class A medicines reimbursed by the NHS^		Class A medicines privately purchased by the citizens		Class C with medical prescription		Self-medication SOP and OTC medicines		Medicines purchased by Public Health Facilities		Total
	€°	%*	€°	%*	€°	%*	€°	%*	€°	%*	€°
L	238	4.7	24	0.5	13	0.3	-	0.0	4,825	94.6	5,101
C	3,250	81.3	234	5.8	42	1.0	175	4.4	299	7.5	3,999
A	1,987	51.6	254	6.6	212	5.5	635	16.5	762	19.8	3,851
J	796	21.4	148	4.0	81	2.2	-	0.0	2,690	72.4	3,716
N	1,359	41.7	153	4.7	969	29.7	270	8.3	507	15.6	3,259
R	991	40.7	126	5.2	150	6.2	1,044	42.9	124	5.1	2,435
B	490	21.8	93	4.1	79	3.5	4	0.2	1,578	70.3	2,244
M	368	28.4	151	11.6	202	15.6	485	37.4	91	7.0	1,297
G	400	32.1	35	2.8	624	50.1	73	5.9	115	9.2	1,247
S	231	32.4	18	2.5	191	26.7	89	12.5	185	26.0	713
D	57	9.1	24	3.8	244	38.6	286	45.2	22	3.4	632
H	230	38.8	51	8.5	34	5.7	-	0.0	278	46.9	592
V	9	2.4	4	1.2	31	8.7	0	0.1	311	87.6	356
P	13	56.1	4	15.4	3	11.2	2	10.1	2	7.2	23
Total	**10,419**	**35.4**	**1,317**	**4.5**	**2,874**	**9.8**	**3,065**	**10.4**	**11,789**	**40.0**	**29,465**

^ Expenditure for Class A net of Class C reimbursed for war pension holders of direct life annuity pursuant to Law n. 203 of 19 July 2000 (24 million euros); ° Gross in millions of euros; * Calculated on the category.

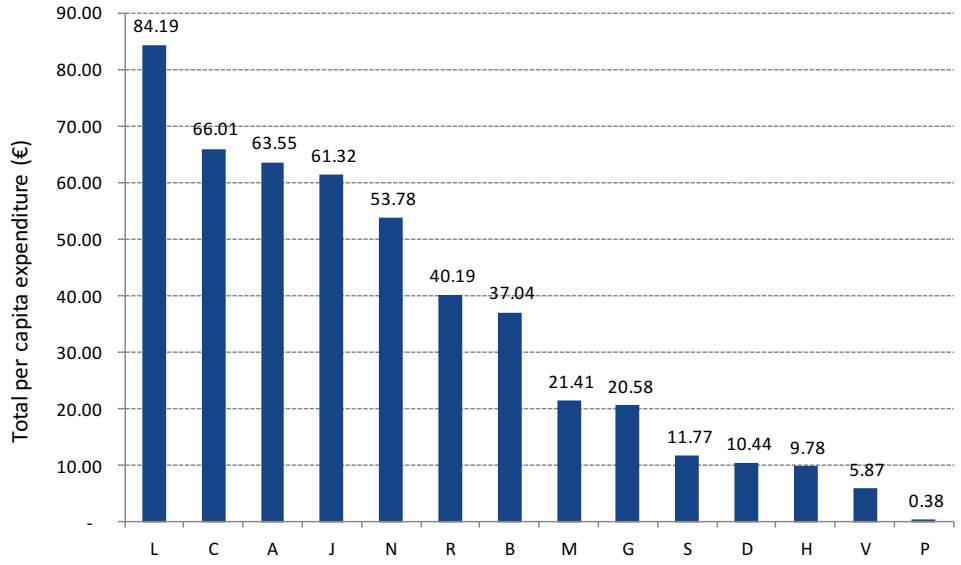
Source: OsMed, Traceability of the drug

Table 2.4. Composition of consumption (in terms of DDD/1000 inhabitants die) 2017, for I ATC level and reimbursement class (decreasing order for total expenditure)

I level ATC	Class A medicines reimbursed by the NHS^		Class A medicines privately purchased by the citizens		Class C with medical prescription		Self-medication SOP and OTC medicines		Medicines purchased by Public Health Facilities		Total
	DDD	%*	DDD	%*	DDD	%*	DDD	%*	DDD	%*	DDD
L	5.8	38.8	0.1	0.7	0.1	0.5	-	0.0	9.0	60.0	15.0
C	466.8	86.8	42.6	7.9	1.5	0.3	9.2	1.7	17.4	3.2	537.5
A	152.0	55.7	47.8	17.5	7.2	2.6	35.0	12.8	31.0	11.4	273.0
J	20.7	57.5	6.1	16.9	2.8	7.8	-	0.0	6.5	17.9	36.1
N	63.2	38.3	10.5	6.4	61.7	37.4	6.9	4.2	22.7	13.8	165.2
R	41.2	35.6	12.4	10.8	11.7	10.1	48.0	41.4	2.4	2.1	115.7
B	86.4	36.8	75.4	32.2	33.6	14.3	0.1	0.1	39.0	16.6	234.5
M	37.6	41.6	22.2	24.6	3.3	3.7	23.1	25.5	4.3	4.7	90.6
G	39.5	49.4	4.1	5.1	31.6	39.5	2.4	3.0	2.4	3.0	80.0
S	20.0	43.3	1.4	3.1	10.8	23.4	11.4	24.7	2.6	5.5	46.2
D	4.1	7.5	2.8	5.2	16.7	30.8	17.7	32.7	12.8	23.7	54.1
H	34.4	62.7	13.7	25.0	1.3	2.4	-	0.0	5.5	10.0	54.9
V	0.1	2.3	0.2	3.8	0.9	21.8	0.0	0.5	3.0	71.5	4.3
P	0.9	73.8	0.2	20.1	0.0	2.6	0.0	1.0	0.0	2.6	1.2
Total	**972.7**	**56.9**	**239.7**	**14.0**	**183.3**	**10.7**	**153.8**	**9.0**	**158.7**	**9.3**	**1,708.2**

* Calculated on the category
Source: OsMed and Traceability of the drug

Figure 2.1. Per capita total pharmaceutical expenditure by I ATC level (sorted for total per capita expenditure in 2017)

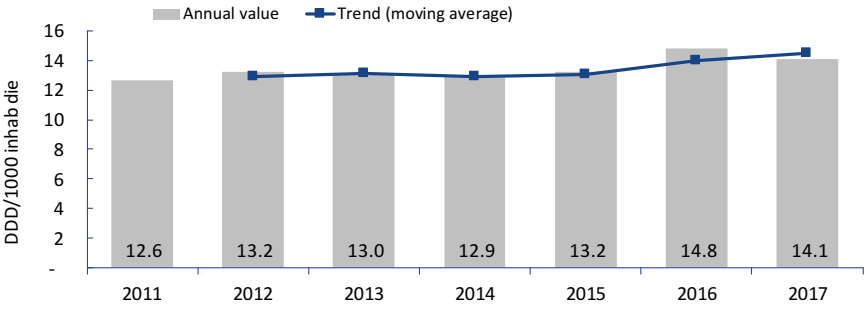


2.1 Antineoplastic and immunomodulating agents

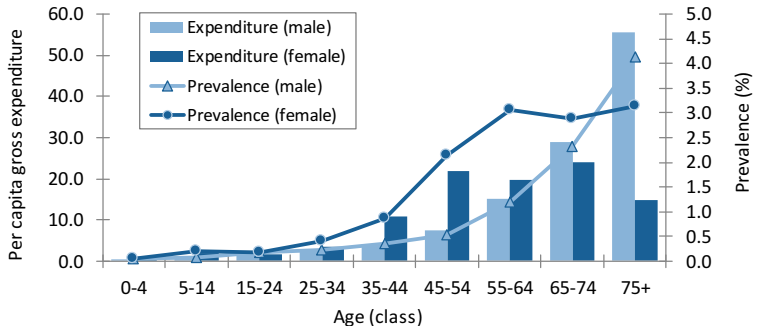
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Antineoplastic and immunomodulating agents

NHS expenditure, million €* (% on the total)	**5,063.5**	**(22.8)**
Δ % 2017/2016		12.0
Per capita gross expenditure, range among Regions:	59.2	102.2
DDD/1000 inhab die* (% on the total)	**14.8**	**(1.3)**
Δ % 2017/2016		5.0
DDD/1000 inhab die, range among Regions:	11.2	17.2

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



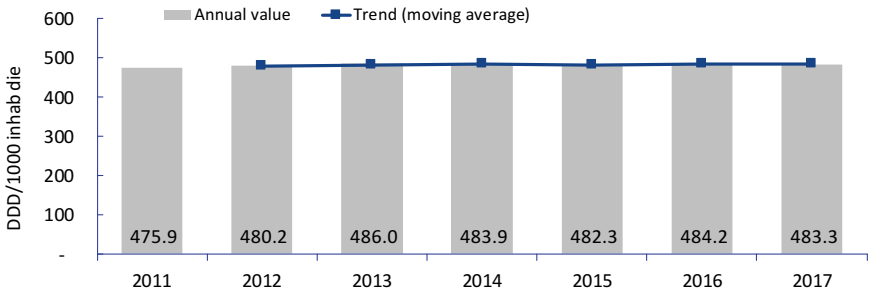
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	0.5	0.4	0.4	0.1	0.2	0.1
5-14	0.9	2.1	1.5	0.4	1.0	0.7
15-24	1.7	1.6	1.6	0.6	0.7	0.6
25-34	2.9	3.6	3.2	0.9	1.5	1.2
35-44	4.1	11.0	7.5	1.4	5.9	3.7
45-54	7.5	21.8	14.7	2.6	15.6	9.2
55-64	15.2	19.9	17.6	5.5	17.3	11.6
65-74	28.9	24.0	26.3	11.6	22.7	17.5
75+	55.5	14.9	30.8	29.5	17.7	22.4

2.2 Cardiovascular system

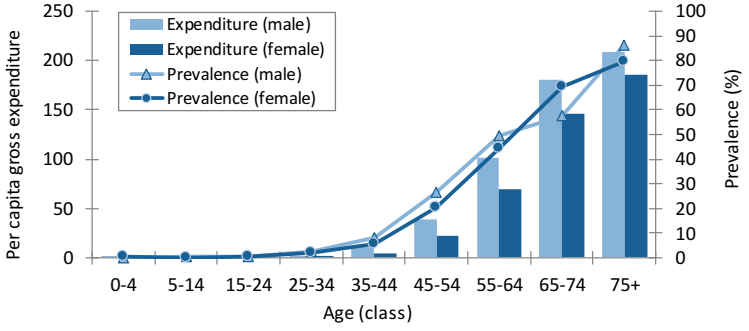
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Cardiovascular system

NHS expenditure, million €* (% on the total)	**3,548.3**	**(16.0)**
Δ % 2017/2016		-2.2
Per capita gross expenditure, range among Regions:	42.7	68.9
DDD/1000 inhab die* (% on the total)	**484.2**	**(42.8)**
Δ % 2017/2016		0.2
DDD/1000 inhab die, range among Regions:	370.8	580.2

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



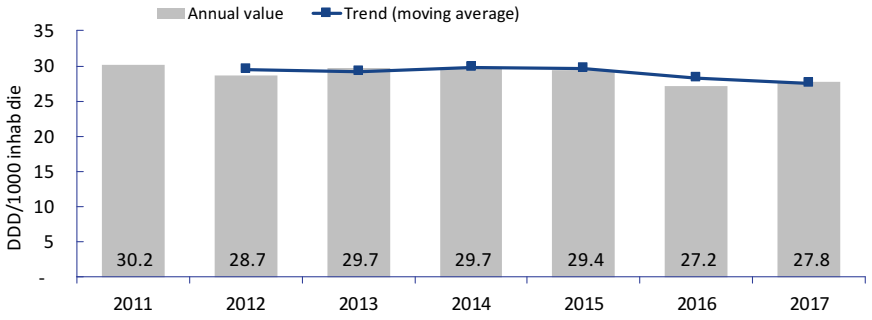
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	0.1	0.2	0.2	0.5	0.5	0.5
5-14	0.1	0.1	0.1	1.1	0.8	1.0
15-24	0.5	0.4	0.4	4.2	2.5	3.4
25-34	2.0	1.1	1.5	16.6	8.5	12.6
35-44	10.5	4.9	7.7	86.8	42.6	64.7
45-54	39.4	22.4	30.8	320.9	192.1	255.7
55-64	101.8	70.0	85.4	812.5	560.1	682.0
65-74	180.4	146.1	162.2	1441.1	1142.9	1283.1
75+	208.5	185.1	194.3	1807.4	1605.1	1684.6

2.3 Anti-infectives for sistemic use

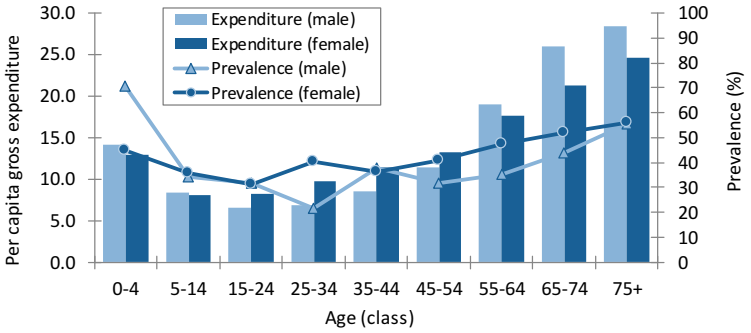
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Anti-infectives for sistemic use

NHS expenditure, million €* (% on the total)	**3,486.2**	**(15.7)**
Δ % 2017/2016		-21.0
Per capita gross expenditure, range among Regions:	34.1	73.4
DDD/1000 inhab die* (% on the total)	**27.2**	**(2.4)**
Δ % 2017/2016		-2.1
DDD/1000 inhab die, range among Regions:	16.9	34.2

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



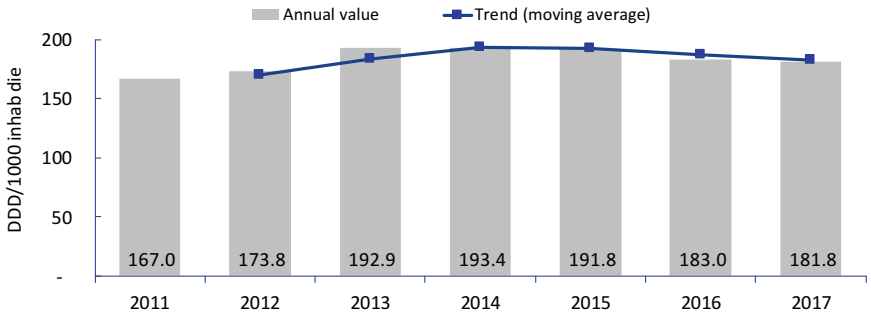
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	14.2	12.9	13.5	25.1	22.6	23.9
5-14	8.4	8.1	8.2	16.0	15.1	15.6
15-24	6.6	8.2	7.3	13.0	14.7	13.8
25-34	6.9	9.7	8.3	12.0	16.8	14.4
35-44	8.6	11.4	10.0	14.2	19.2	16.7
45-54	11.3	13.3	12.3	16.2	21.1	18.7
55-64	19.1	17.6	18.3	22.3	26.0	24.2
65-74	26.0	21.2	23.5	30.0	29.5	29.7
75+	28.3	24.6	26.0	33.7	29.6	31.3

2.4 Alimentary Tract and metabolism

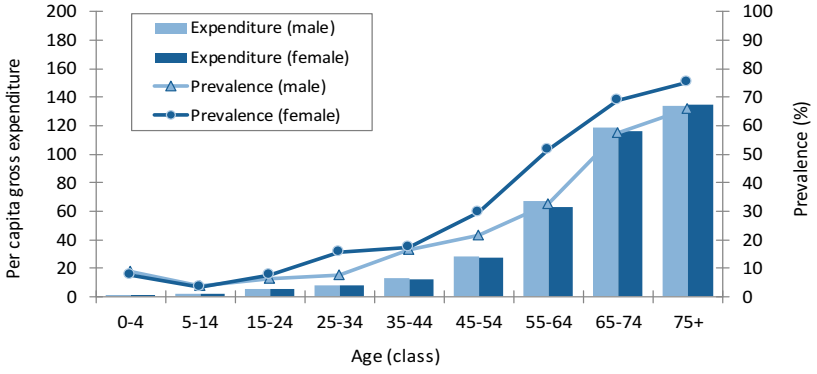
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Alimentary tract and metabolism

NHS expenditure, million €* (% on the total)	**2,749.5**	**(12.4)**
Δ % 2017/2016		2.1
Per capita gross expenditure, range among Regions:	29.1	59.1
DDD/1000 inhab die* (% on the total)	**183.0**	**(16.2)**
Δ % 2017/2016		0.6
DDD/1000 inhab die, range among Regions:	137.0	208.9

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



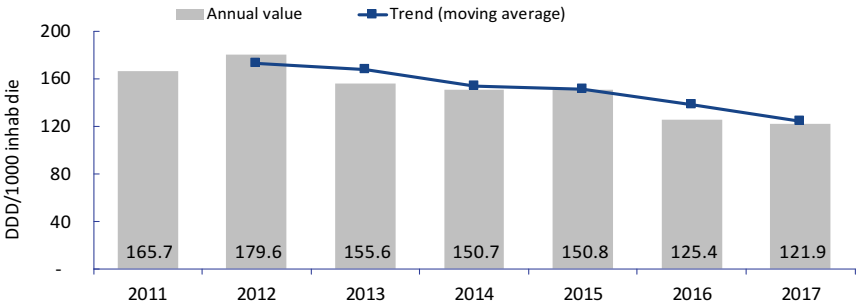
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	1.3	1.2	1.3	4.9	4.7	4.8
5-14	2.1	2.0	2.1	4.6	4.7	4.7
15-24	5.2	5.1	5.1	12.6	13.7	13.2
25-34	7.6	7.7	7.6	21.7	24.0	22.9
35-44	13.2	12.4	12.8	42.8	43.5	43.1
45-54	28.4	27.7	28.1	95.6	98.6	97.1
55-64	67.3	62.9	65.0	230.8	225.9	228.3
65-74	118.9	116.2	117.5	440.2	436.6	438.2
75+	133.6	134.9	134.4	544.3	552.0	549.0

2.5 Blood and blood forming organs

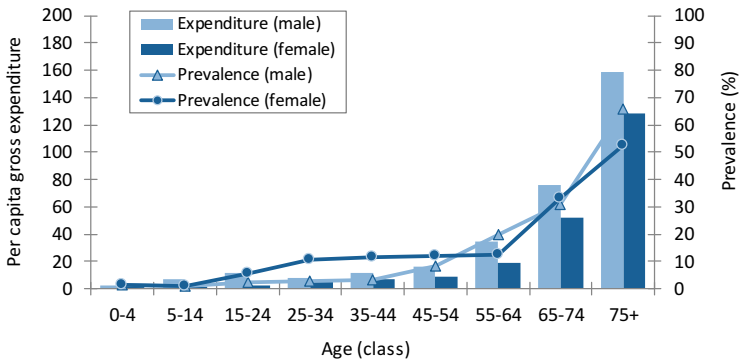
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Blood and blood forming organs

NHS expenditure, million €* (% on the total)	**2,068.1**	**(9.3)**
Δ % 2017/2016		2.0
Per capita gross expenditure, range among Regions:	23.1	47.3
DDD/1000 inhab die* (% on the total)	**125.4**	**(11.1)**
Δ % 2017/2016		2.9
DDD/1000 inhab die, range among Regions:	93.4	160.4

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



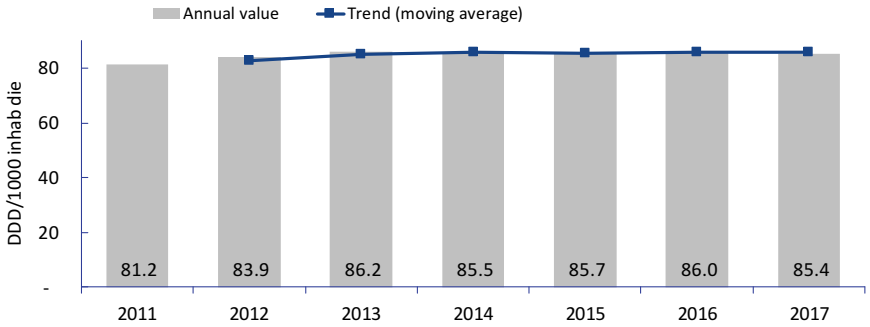
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	2.6	0.3	1.5	1.5	1.5	1.5
5-14	7.3	0.4	4.0	1.4	1.3	1.4
15-24	11.2	1.9	6.7	3.6	9.2	6.3
25-34	8.1	5.4	6.8	4.9	25.3	15.0
35-44	11.8	7.0	9.4	12.0	26.4	19.2
45-54	15.7	9.1	12.4	39.8	31.6	35.7
55-64	34.5	18.6	26.3	124.9	69.2	96.1
65-74	76.2	51.9	63.3	290.6	190.0	237.3
75+	158.7	128.4	140.3	485.4	399.5	433.2

2.6 Nervous system

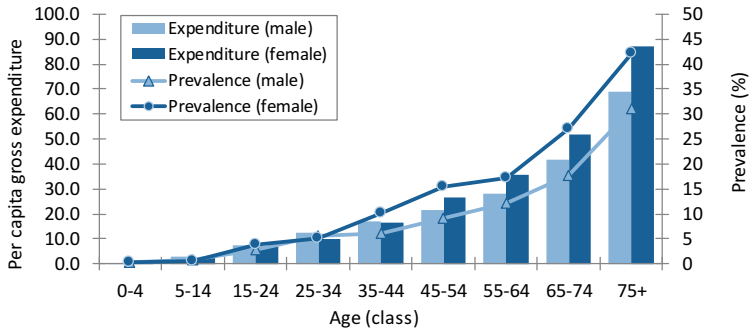
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Nervous system

NHS expenditure, million €* (% on the total)	**1,865.9**	**(8.4)**
Δ % 2017/2016		4.1
Per capita gross expenditure, range among Regions:	27.2	37.3
DDD/1000 inhab die* (% on the total)	**86.0**	**(7.6)**
Δ % 2017/2016		0.7
DDD/1000 inhab die, range among Regions:	71.5	109.4

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



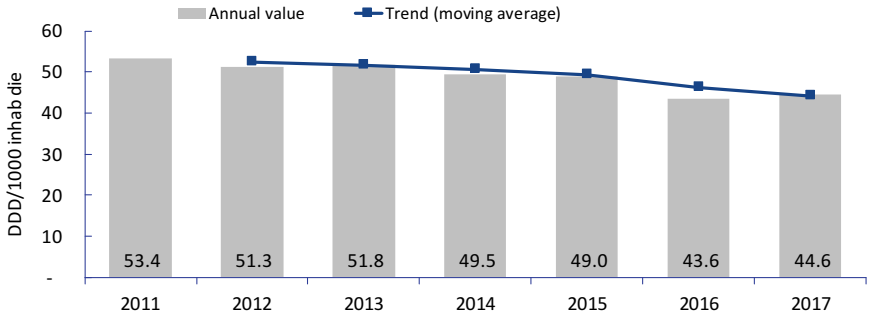
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	0.5	0.5	0.5	0.7	0.6	0.6
5-14	2.7	2.1	2.4	4.0	2.9	3.5
15-24	7.5	6.7	7.1	15.2	14.1	14.7
25-34	12.2	10.0	11.1	28.2	25.2	26.7
35-44	16.8	16.5	16.6	40.4	45.0	42.7
45-54	21.6	26.7	24.2	52.8	75.0	64.0
55-64	27.8	35.6	31.9	65.4	102.9	84.8
65-74	41.8	51.6	47.0	91.9	140.9	117.9
75+	69.1	87.1	80.0	153.0	213.6	189.8

2.7 Respiratory system

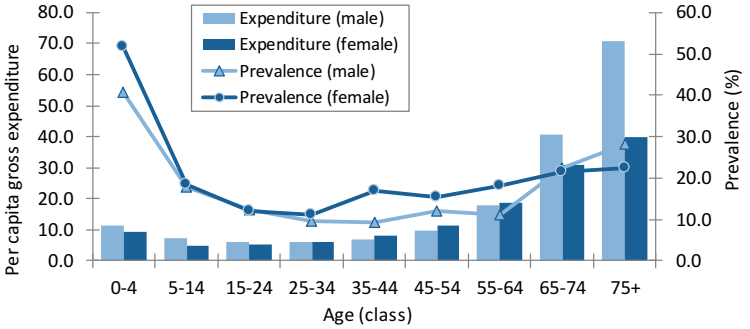
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Respiratory system

NHS expenditure, million €* (% on the total)	**1,114.9**	**(5.0)**
Δ % 2017/2016		0.7
Per capita gross expenditure, range among Regions:	14.3	23.6
DDD/1000 inhab die* (% on the total)	**43.6**	**(3.9)**
Δ % 2017/2016		-2.1
DDD/1000 inhab die, range among Regions:	32.3	59.0

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



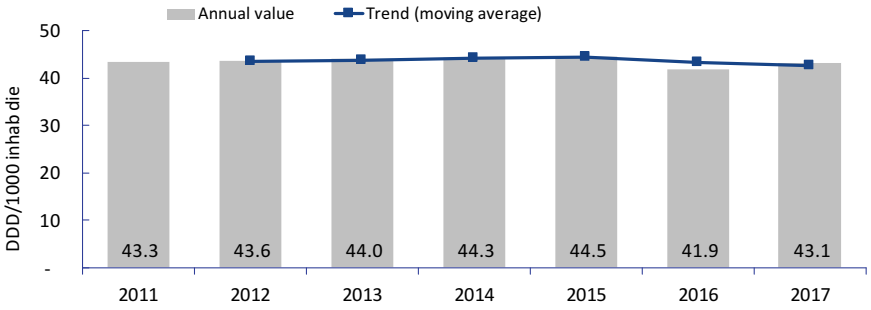
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	11.4	9.4	10.4	34.3	28.0	31.2
5-14	7.5	5.1	6.3	26.9	18.1	22.6
15-24	6.0	5.2	5.6	24.3	20.8	22.6
25-34	5.9	6.0	6.0	20.0	20.6	20.3
35-44	7.1	8.2	7.6	21.3	25.9	23.6
45-54	9.8	11.5	10.7	26.5	34.4	30.5
55-64	17.9	18.6	18.3	41.8	48.0	45.0
65-74	40.6	30.9	35.4	84.1	71.6	77.5
75+	70.7	39.9	52.0	142.8	88.8	110.0

2.8 Genito-urinary system and sex hormones

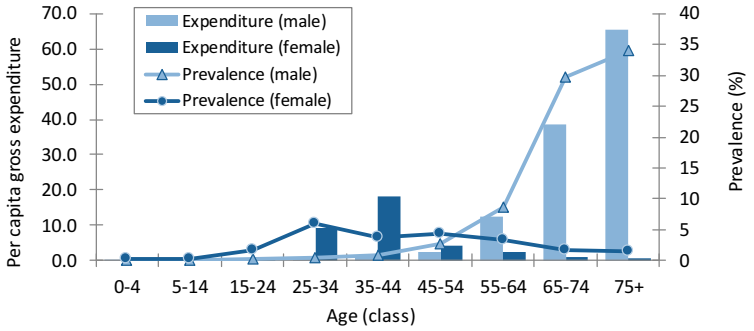
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Genito-urinary system and sex hormones

NHS expenditure, million €* (% on the total)	**515.0**	**(2.3)**
Δ % 2017/2016		-8.3
Per capita gross expenditure, range among Regions:	7.0	10.1
DDD/1000 inhab die* (% on the total)	**41.9**	**(3.7)**
Δ % 2017/2016		-2.8
DDD/1000 inhab die, range among Regions:	32.6	48.7

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	0.0	0.0	0.0	0.0	0.1	0.1
5-14	0.0	0.0	0.0	0.1	0.2	0.2
15-24	0.3	0.9	0.6	0.5	5.3	2.8
25-34	1.0	9.3	5.1	1.2	15.0	8.1
35-44	1.4	18.1	9.8	2.4	17.0	9.7
45-54	2.3	4.2	3.3	11.8	17.4	14.6
55-64	12.5	2.2	7.2	71.8	15.5	42.7
65-74	38.7	1.0	18.7	226.8	8.2	111.0
75+	65.5	0.5	26.0	379.3	3.7	151.3

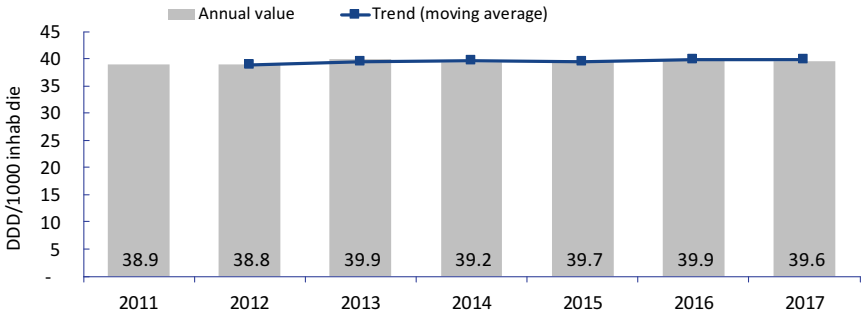
2.9 Systemic hormonal preparations, excluding sex hormones and insulins

MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE

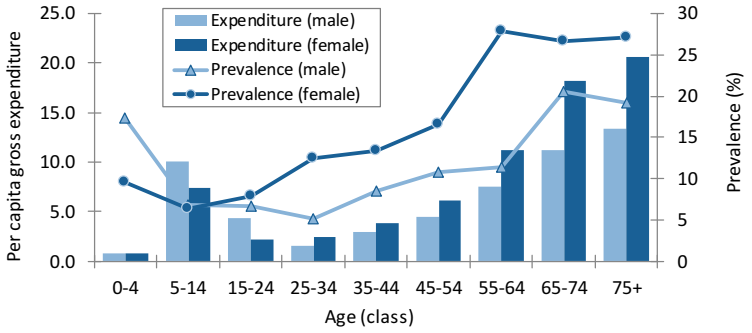
Systemic hormonal preparations, excluding sex hormones and insulins

NHS expenditure, million €* (% on the total)	**507.9**	**(2.3)**
Δ % 2017/2016		3.7
Per capita gross expenditure, range among Regions:	6.5	10.8
DDD/1000 inhab die* (% on the total)	**39.9**	**(3.5)**
Δ % 2017/2016		0.7
DDD/1000 inhab die, range among Regions:	27.8	48.9

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



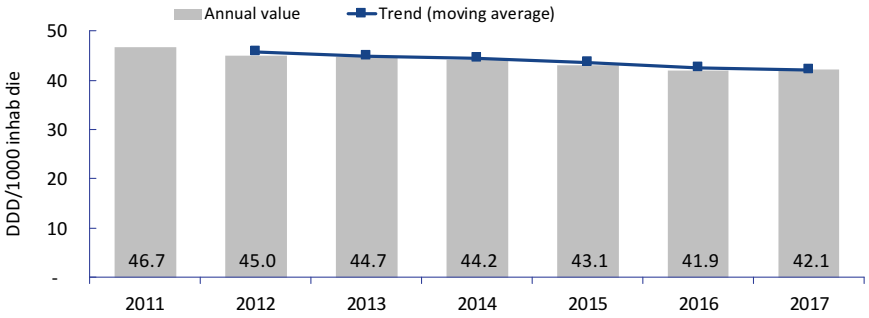
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	0.8	0.8	0.8	3.2	2.7	3.0
5-14	10.0	7.4	8.7	4.4	3.7	4.1
15-24	4.4	2.2	3.3	5.8	8.8	7.3
25-34	1.5	2.4	2.0	7.9	19.0	13.4
35-44	2.9	3.9	3.4	11.8	32.2	22.0
45-54	4.5	6.1	5.3	18.0	49.9	34.2
55-64	7.6	11.2	9.4	28.2	71.6	50.7
65-74	11.2	18.2	14.9	42.3	89.4	67.3
75+	13.4	20.6	17.7	52.5	82.6	70.8

2.10 Musculo-skeletal system

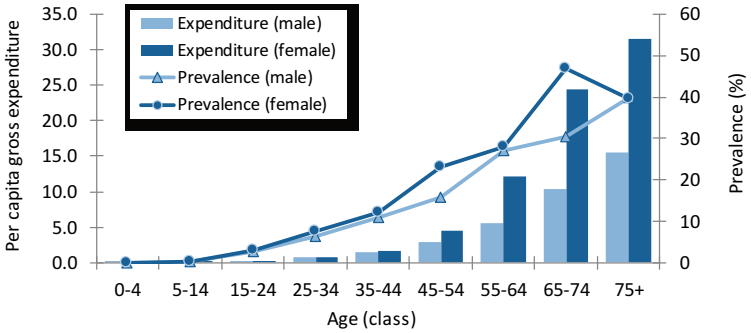
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Musculo-skeletal system

NHS expenditure, million €* (% on the total)	**459.6**	**(2.1)**
Δ % 2017/2016		-1.6
Per capita gross expenditure, range among Regions:	5.5	11.5
DDD/1000 inhab die* (% on the total)	**41.9**	**(3.7)**
Δ % 2017/2016		-0.5
DDD/1000 inhab die, range among Regions:	31.2	63.5

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



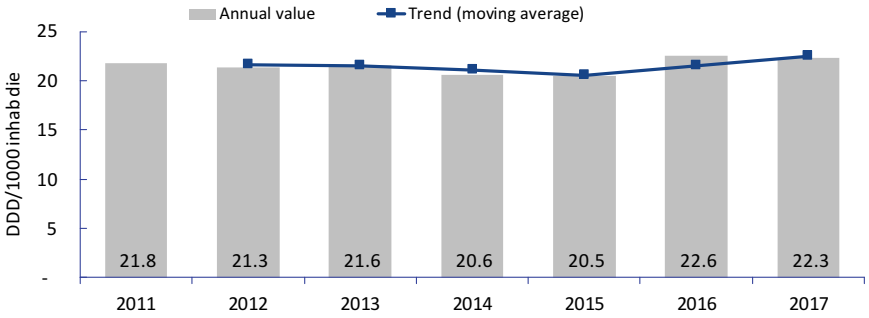
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	0.0	0.0	0.0	0.0	0.1	0.0
5-14	0.0	0.0	0.0	0.2	0.2	0.2
15-24	0.3	0.3	0.3	2.1	2.0	2.0
25-34	0.7	0.7	0.7	4.8	5.1	4.9
35-44	1.4	1.7	1.6	10.0	11.2	10.6
45-54	2.9	4.4	3.6	19.7	26.7	23.2
55-64	5.6	12.1	9.0	38.8	63.3	51.5
65-74	10.4	24.4	17.8	70.4	121.0	97.2
75+	15.5	31.5	25.2	100.7	156.4	134.5

2.11 Sensory organs

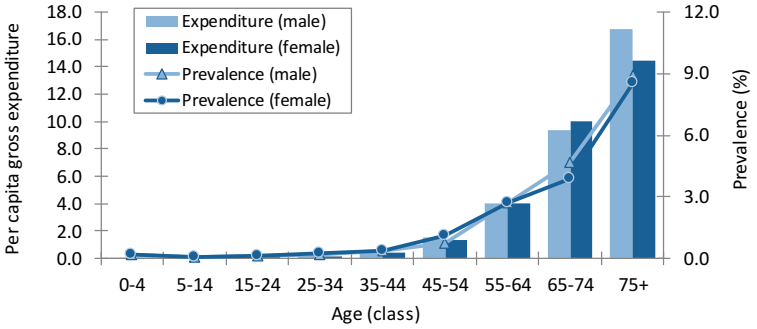
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Sensory organs

NHS expenditure, million €* (% on the total)	**416.0**	**(1.9)**
Δ % 2017/2016		12.7
Per capita gross expenditure, range among Regions:	5.1	26.6
DDD/1000 inhab die* (% on the total)	**22.6**	**(2.0)**
Δ % 2017/2016		1.3
DDD/1000 inhab die, range among Regions:	17.6	30.9

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



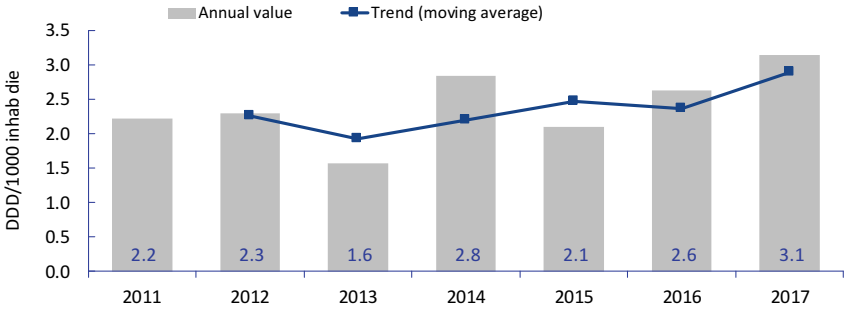
Age (class)	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	0.0	0.0	0.0	0.3	0.3	0.3
5-14	0.0	0.1	0.1	0.2	0.3	0.3
15-24	0.1	0.1	0.1	0.6	0.6	0.6
25-34	0.2	0.2	0.2	1.2	1.0	1.1
35-44	0.6	0.4	0.5	2.9	2.2	2.6
45-54	1.5	1.4	1.5	8.0	7.2	7.6
55-64	4.0	4.1	4.0	20.6	21.1	20.9
65-74	9.4	10.0	9.7	48.4	51.9	50.3
75+	16.8	14.5	15.4	87.0	76.9	80.9

2.12 Various

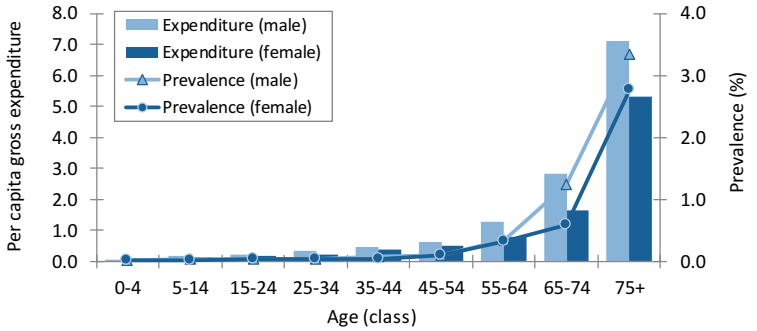
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Various

NHS expenditure, million €* (% on the total)	**322.0**	**(1.4)**
Δ % 2017/2016		5.8
Per capita gross expenditure, range among Regions:	3.6	10.4
DDD/1000 inhab die* (% on the total)	**3.1**	**(0.3)**
Δ % 2017/2016		19.8
DDD/1000 inhab die, range among Regions:	1.5	5.7

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



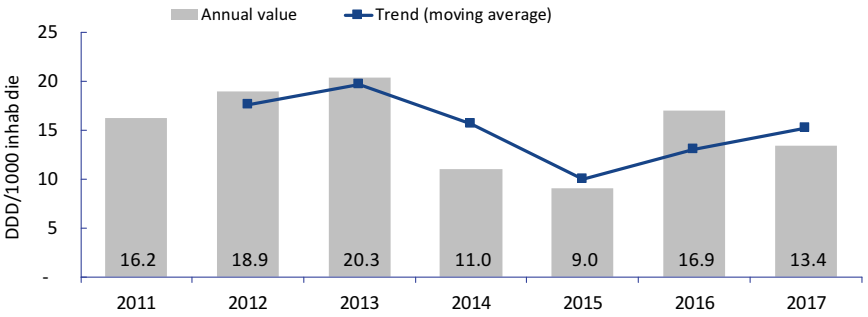
Age	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	0.1	0.0	0.0	0.0	0.0	0.0
5-14	0.2	0.1	0.2	0.1	0.0	0.1
15-24	0.2	0.2	0.2	0.1	0.1	0.1
25-34	0.3	0.2	0.3	0.1	0.1	0.1
35-44	0.5	0.4	0.4	0.1	0.1	0.1
45-54	0.6	0.5	0.6	0.2	0.1	0.2
55-64	1.3	0.8	1.0	0.4	0.2	0.3
65-74	2.8	1.7	2.2	0.7	0.3	0.5
75+	7.1	5.3	6.0	0.9	0.4	0.6

2.13 Dermatologicals

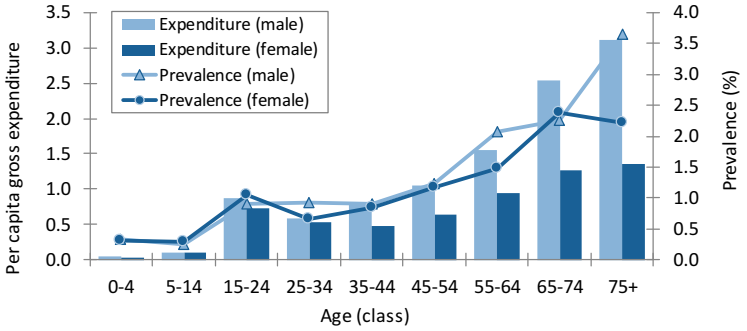
MAIN MEASURES CONCERNING EXPENDITURE, CONSUMPTION AND EXPOSURE
Dermatologicals

NHS expenditure, million €* (% on the total)	**79.0**	**(0.4)**
Δ % 2017/2016		7.4
Per capita gross expenditure, range among Regions:	1.0	1.5
DDD/1000 inhab die* (% on the total)	**16.9**	**(1.5)**
Δ % 2017/2016		26.5
DDD/1000 inhab die, range among Regions:	7.4	36.3

** Includes outpatient and inpatient NHS expenditure*



Distribution of expenditure by age and gender, prevalence of use and consumption for outpatient NHS expenditure 2017 (Chart and Table)



Age groups	Gross expenditure per capita			DDD/1000 inhab die		
	Male	Female	Total	Male	Female	Total
0-4	0.0	0.0	0.0	0.4	0.3	0.3
5-14	0.1	0.1	0.1	0.5	0.5	0.5
15-24	0.9	0.7	0.8	2.5	2.2	2.4
25-34	0.6	0.5	0.6	2.5	2.1	2.3
35-44	0.8	0.5	0.6	3.6	2.2	2.9
45-54	1.0	0.6	0.8	4.8	3.0	3.9
55-64	1.6	0.9	1.2	6.9	4.4	5.6
65-74	2.5	1.3	1.9	10.1	6.1	8.0
75+	3.1	1.3	2.0	11.0	6.0	8.0

Table 2.5. Consumption, price and mix effects on outpatient Class A NHS pharmaceutical expenditure variation: comparison 2017-2016

(for each ATC category the therapeutic subgroups were included in decreasing order of expenditure, up to the per capita expenditure value of 0.10 euro)

ATC I level Subgroups	Per capita gross expenditure	DDD/ 1000 inhab die	Δ% 17-16				Δ% DDD average cost
			Exp	DDD	Prices	Mix	
Italy	**171.96**	**972.7**	**-1.5**	**0.1**	**-2.4**	**1.1**	**-1.21**
C – Cardiovascular system	**53.63**	**466.8**	**-3.1**	**-0.1**	**-4.1**	**1.2**	**-2.97**
HMG CoA reductase inhibitors	10.50	72.4	0.8	3.6	0.0	-2.7	-2.71
Angiotensin II antagonists, plain	4.75	55.7	-19.0	-0.2	-18.0	-1.0	-18.83
Angiotensin II antagonists and diuretics	4.69	36.7	-19.9	-3.1	-16.5	-1.0	-17.33
Dihydropyridine derivatives	4.32	50.0	-2.8	-2.3	-0.1	-0.4	-0.46
Beta-blocking agents, selective	4.17	37.1	3.7	1.4	-0.1	2.3	2.24
ACE inhibitors, plain	3.94	84.8	-2.4	-1.5	0.0	-0.9	-0.85
Other lipid modifying agents	3.73	6.9	14.7	13.9	0.0	0.7	0.68
HMG CoA reductase inhibitors in combination with other lipid modifying agents	3.08	4.1	6.4	6.4	0.0	0.0	0.02
ACE inhibitors and diuretics	2.83	22.0	-6.3	-4.4	-1.7	-0.3	-1.96
ACE inhibitors and calcium channel blockers	1.73	10.5	-1.0	9.3	-5.0	-4.6	-9.40
Angiotensin II antagonists and calcium channel blockers	1.53	4.8	8.3	12.9	-4.0	0.0	-4.07
Alpha-adrenoreceptor antagonists	1.22	7.4	-1.7	-1.6	0.0	0.0	-0.04
Organic nitrates	0.99	9.5	-13.9	-14.0	0.0	0.1	0.02
Antiarrhythmics, class IC	0.95	4.6	3.7	0.9	0.0	2.8	2.80
Sulphonamides, plain	0.94	27.1	-1.2	-1.0	0.1	-0.3	-0.23
Alpha and beta blocking agents	0.62	3.4	-6.0	-5.4	0.0	-0.6	-0.62
Beta blocking agents, selective, and thiazides	0.61	5.2	-0.9	6.7	-6.4	-0.8	-7.11
Aldosterone antagonists	0.49	3.2	14.0	15.3	-0.3	-0.9	-1.15
Fibrates	0.37	2.6	0.8	1.6	0.0	-0.8	-0.75
ACE inhibitors, other associations	0.33	1.6	195.4	201.5	-1.0	-1.0	-2.02
Antiarrhythmics, class III	0.27	2.9	-2.2	-1.1	0.0	-1.1	-1.09
Imidazoline receptor agonists	0.23	1.7	-6.3	-6.3	0.0	0.0	0.00
Benzothiazepine derivatives	0.22	1.3	-8.9	-8.7	0.0	-0.2	-0.21
Phenylalkyl derivatives	0.17	1.4	-8.3	-8.5	0.0	0.2	0.22
Beta blocking agents, selective, and other diuretics	0.15	2.1	-6.7	-6.6	0.0	-0.2	-0.15
Beta blocking agents, non-selective	0.14	1.6	-3.4	-2.3	0.0	-1.2	-1.20
Low-ceiling diuretics and potassium-sparing agents	0.14	2.5	-5.9	-5.6	0.0	-0.3	-0.30
Other cardiac preparations	0.14	0.1	-5.2	-3.2	0.0	-2.1	-2.06
High-ceiling diuretics and potassium-sparing agents	0.12	0.6	-3.1	-1.7	0.0	-1.5	-1.47
A – Alimentary tract and metabolism	**32.80**	**152.0**	**1.9**	**-0.3**	**0.0**	**2.2**	**2.17**
Proton pump inhibitors	13.15	67.5	-2.9	-2.0	0.0	-0.8	-0.89
Vitamin D and analogs	4.28	12.3	23.3	21.4	0.0	1.6	1.56
Insulins and analogues, fast-acting	3.85	7.7	1.4	1.1	0.0	0.3	0.32

ATC I level Subgroups	Per capita gross expenditure	DDD/ 1000 inhabdie	Δ% 17-16				Δ% DDD average cost
			Exp	DDD	Prices	Mix	
Aminosalicylic acid and similar agents	1.80	4.6	3.5	3.7	0.0	-0.2	-0.18
Antibiotics	1.50	2.0	0.8	0.8	0.0	0.0	-0.02
Biguanides	1.45	21.1	5.2	2.7	0.0	2.5	2.47
Other drugs for peptic ulcer and gastrooesophageal reflux disease (GORD)	0.85	4.0	-1.0	-1.4	0.0	0.4	0.36
Bile acids preparations	0.66	2.2	3.1	2.9	0.0	0.3	0.25
Insulins and analogues, long acting	0.57	0.6	14.3	16.5	-0.3	-1.6	-1.89
Sulphonamides, urea derivatives	0.57	9.7	0.1	-5.4	0.0	5.8	5.78
Biguanides-sulphonamides association	0.46	2.8	-6.0	-17.7	0.0	14.2	14.19
Calcium, combinations with other drugs	0.45	4.8	-3.6	-4.5	0.0	0.9	0.91
Combinations and complexes of aluminum, calcium and magnesium compounds	0.41	1.8	0.4	0.0	0.0	0.4	0.40
Other blood glucose lowering drugs	0.40	2.9	-10.0	-10.6	0.0	0.7	0.67
H2-receptor antagonists	0.32	2.1	0.1	-1.4	0.0	1.6	1.57
Corticosteroids acting locally	0.29	0.4	2.4	-1.6	0.0	4.0	4.02
Insulins and analogues, intermediate or long acting combined with fast-acting	0.23	0.5	-19.3	-19.5	0.0	0.2	0.16
Serotonin (5HT3) antagonists	0.21	0.0	3.0	-0.8	1.0	2.7	3.73
Enzyme preparations	0.20	0.5	3.2	3.2	0.0	0.0	0.00
Glucagon-like peptide-1 receptor agonists	0.19	0.1	49.9	61.8	0.0	-7.3	-7.34
Dipeptil peptidase 4 (DPP-4) inhibitors	0.18	0.2	17.5	16.5	-0.2	1.0	0.81
Alpha glucosidase inhibitors	0.18	0.6	-2.5	-2.7	0.0	0.2	0.23
Osmotically acting laxatives	0.12	1.1	-2.0	-3.7	0.0	1.8	1.79
Sodium glucose co-transporter 2 (SGLT2) inhibitors	0.11	0.1	27.7	27.4	4.3	-3.9	0.22
Calcium	0.11	1.3	-0.4	-1.2	0.0	0.8	0.77
N – Nervous system	**22.43**	**63.3**	**-0.2**	**1.4**	**-3.8**	**2.3**	**-1.58**
Other antiepileptics	4.56	5.2	-7.8	4.9	-10.2	-2.1	-12.10
Selective serotonin reuptake inhibitors	3.25	27.9	-1.6	-0.7	-0.2	-0.7	-0.97
Other antidepressants	2.61	9.5	9.6	7.5	-0.5	2.4	1.88
Other opioids	1.35	1.1	11.2	3.2	0.0	7.7	7.74
Natural opium alkaloids	1.33	0.6	6.3	5.2	0.0	1.0	1.00
Phenylpiperidine derivatives	1.26	0.5	4.9	1.8	0.0	3.0	3.07
Dopamine agonists	1.21	1.2	1.6	-0.1	0.0	1.7	1.69
Selective serotonin (5HT1) agonists	0.98	0.8	-1.6	-0.3	-1.0	-0.2	-1.21
Fatty acid derivatives	0.92	2.2	1.0	0.7	0.0	0.3	0.28
Diazepines, oxazepines, thiazepines and oxepines	0.83	1.1	5.9	5.4	0.0	0.4	0.44
Dopa and dopa derivates	0.70	2.0	1.6	2.3	0.0	-0.7	-0.72
Monoamine oxidase B inhibitors	0.63	1.4	-23.3	9.3	-36.1	9.9	-29.80
Opioids in combination with non-opioid analgesics	0.55	1.5	-2.6	-3.1	0.0	0.4	0.44
Carboxamide derivatives	0.50	1.9	-2.1	-1.8	0.0	-0.3	-0.25
Amides	0.34	0.3	18.3	18.3	0.0	0.0	0.00
Anticholinesterases	0.26	0.7	-1.1	0.1	0.0	-1.2	-1.18
Other antipsychotics	0.22	0.3	11.3	14.8	-4.0	1.0	-3.08

ATC I level Subgroups	Per capita gross expenditure	DDD/ 1000 inhabdie	Δ% 17-16				Δ% DDD average cost
			Exp	DDD	Prices	Mix	
Non-selective monoamine reuptake inhibitors	0.17	1.0	-6.0	-6.3	0.0	0.3	0.33
Oripavine derivatives	0.10	0.1	-3.0	-2.9	0.0	-0.1	-0.07
R – Respiratory system	**16.36**	**41.2**	**-2.0**	**-2.6**	**-0.6**	**1.2**	**0.60**
Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics	7.76	11.5	0.4	0.8	0.8	-1.2	-0.38
Anticholinergics	3.07	5.8	-7.8	-2.8	-3.5	-1.7	-5.16
Glucocorticoids	2.24	5.9	-6.2	-6.3	0.0	0.1	0.09
Selective beta-2-adrenoreceptor agonists	0.85	4.4	-13.5	-10.5	0.4	-3.8	-3.44
Adrenergics in combination with anticholinergics	0.85	1.6	54.1	29.7	0.5	18.3	18.86
Other antihistamines for systemic use	0.64	5.6	-11.4	-4.0	-6.9	-0.9	-7.72
Leukotriene receptor antagonists	0.48	2.0	-3.9	-2.1	0.0	-1.9	-1.87
Piperazine derivates	0.37	3.7	-3.9	-3.1	0.0	-0.8	-0.78
J – Antiinfectives for systemic use	**13.14**	**20.7**	**-2.5**	**-2.6**	**-0.1**	**0.1**	**0.08**
Combination of penicillins, incl. beta-lactamase inhibitors	2.98	8.6	-1.1	-0.6	-0.1	-0.4	-0.47
Third-generation cephalosporins	2.93	1.8	-3.0	-1.7	0.0	-1.3	-1.31
Fluoroquinolones	2.09	2.7	-4.5	-4.0	0.0	-0.5	-0.54
Macrolides	1.52	3.5	-5.0	-4.6	0.0	-0.5	-0.51
Triazole derivatives	1.05	0.6	-4.1	-5.1	0.0	1.1	1.06
Nucleosides and nucleotides excl.reverse transcriptase inhibitors	0.60	0.2	-0.8	2.3	-0.8	-2.3	-3.08
Other antibacterials	0.59	0.4	1.9	2.2	0.0	-0.2	-0.22
Specific immunoglobulins	0.54	0.0	22.0	-19.7	0.0	51.9	51.88
Penicillins with extended spectrum	0.27	1.8	-9.2	-7.4	0.0	-1.9	-1.92
Second-generation cephalosporins	0.11	0.2	-10.4	-9.5	0.0	-1.1	-1.07
B – Blood and blood forming organs	**8.08**	**86.4**	**-2.7**	**0.4**	**-0.2**	**-2.9**	**-3.11**
Heparin group	3.01	3.1	-10.8	-11.1	0.0	0.3	0.33
Platelet aggregation inhibitors excl.Heparin	2.99	60.9	-2.1	-1.0	0.0	-1.1	-1.06
Folic acid and derivatives	0.44	5.2	6.1	9.3	-2.4	-0.5	-2.93
Iron bivalent, oral preparations	0.35	2.8	1.7	0.8	1.2	-0.3	0.89
Direct factor Xa inhibitors	0.27	0.2	175.1	173.2	0.0	0.7	0.71
Blood substitutes and plasma protein fractions	0.21	0.0	21.0	23.7	-0.2	-2.0	-2.19
Blood substitutes and plasma protein fractions	0.20	4.9	-9.2	-9.2	0.0	0.0	-0.03
Solutions affecting the electrolyte balance	0.16	0.3	4.5	4.0	0.0	0.5	0.47
G – Genito urinary system and sex hormones	**6.60**	**39.5**	**-7.7**	**-3.7**	**-6.2**	**-1.3**	**-4.09**
Alpha-adrenoreceptor antagonists	2.90	24.1	2.7	2.3	0.0	0.4	0.43
Testosterone-5-alpha reductase inhibitors	2.61	9.9	-17.0	1.2	-14.0	-4.7	-18.03
Prolactine inhibitors	0.15	0.1	-0.6	-2.4	0.0	1.9	1.85
Gonadotropins	0.12	0.0	20.2	-63.7	0.3	230.6	231.42
Pregnen (4) derivatives	0.12	1.0	-3.4	-7.0	0.0	3.8	3.80
Other estrogens	0.11	0.7	-1.6	-1.0	0.0	-0.6	-0.60
Progestogens and estrogens	0.11	0.6	0.2	0.3	0.0	-0.1	-0.09

ATC I level Subgroups	Per capita gross expenditure	DDD/ 1000 inhabdie	Δ% 17-16				Δ% DDD average cost
			Exp	DDD	Prices	Mix	
M – Musculo-skeletal system	**6.08**	**37.6**	**-7.8**	**-1.8**	**-5.3**	**-0.8**	**-6.09**
Bisphosphonates	1.32	6.6	0.0	1.4	0.0	-1.4	-1.42
Preparations inhibiting uric acid production	1.16	9.1	12.8	4.7	-0.1	7.8	7.68
Coxibs	0.93	3.8	-21.6	-7.4	-13.4	-2.2	-15.32
Acetic acid derivatives and related active ingredients	0.80	4.9	-1.8	-0.2	0.0	-1.6	-1.63
Propionic acid derivatives	0.78	6.4	-6.2	-5.0	0.0	-1.2	-1.25
Bisphosphonates, combinations	0.64	2.7	-32.0	-12.0	-20.0	-3.3	-22.67
Other antiinflammatory and antirheumatic agents, non-steroids	0.18	2.2	-3.1	-4.8	0.0	1.8	1.79
Oxicams	0.13	1.0	-8.0	-8.2	0.0	0.3	0.28
L – Antineoplastic and immunomodulating agents	**3.93**	**5.8**	**-0.2**	**2.1**	**-1.9**	**-0.3**	**-2.16**
Aromatase inhibitors	1.73	2.4	6.4	6.4	0.0	0.0	-0.02
Calcineurin inhibitors	0.70	0.2	-4.3	-1.4	0.0	-2.9	-2.90
Other immunosuppressants	0.67	1.5	-5.4	2.6	-10.3	2.8	-7.73
Anti-androgens	0.16	0.3	-12.0	-11.3	-0.8	0.1	-0.71
Other antineoplastic agents	0.15	0.3	3.4	3.3	1.9	-1.7	0.10
Folic acid analogues	0.12	0.1	-7.5	-7.4	0.0	-0.1	-0.11
S – Sensory organs	**3.81**	**20.0**	**-0.4**	**-0.5**	**-1.8**	**2.0**	**0.13**
Beta blocking agents	2.18	11.3	3.1	-0.1	-0.7	3.9	3.20
Prostaglandin analogues	1.28	5.5	-6.0	-2.4	-4.0	0.3	-3.71
Carbonic anhydrase inhibitors	0.22	1.4	-2.0	-1.6	0.0	-0.3	-0.34
H – Systemic hormonal preparations, excl. sex hormones and insulins	**3.79**	**34.4**	**15.5**	**1.0**	**0.0**	**14.3**	**14.33**
Glucocorticoids	1.38	12.9	0.8	0.6	0.6	-0.4	0.18
Parathyroid hormones and analogues	1.16	0.2	60.9	61.9	-0.7	0.0	-0.65
Thyroid hormones	0.93	19.9	6.9	1.1	0.0	5.7	5.67
Vasopressin and analogues	0.14	0.1	0.2	-0.2	0.0	0.4	0.38
D – Dermatologicals	**0.95**	**4.1**	**6.2**	**17.5**	**0.2**	**-9.8**	**-9.59**
Other antipsoriatics for topical use	0.52	1.7	-5.0	-4.7	0.0	-0.3	-0.33
P – Antiparasitic products, insecticides and repellents	**0.21**	**0.9**	**1.9**	**3.7**	**0.0**	**-1.7**	**-1.68**
Aminoquinolines	0.14	0.7	3.6	3.3	0.0	0.2	0.24
V – Various	**0.14**	**0.1**	**-0.3**	**2.9**	**0.2**	**-3.3**	**-3.12**
Drugs for treatment of hyperkalemia and hyperphosphatemia	0.12	0.1	2.8	2.4	0.1	0.2	0.38

Table 2.6. Expenditure and consumption in 2017 of medicines purchased by public health facilities by I ATC level

(for each ATC category at 1st level the therapeutic subgroups were included in decreasing order of expenditure, up to the per capita expenditure value of 0.1 euro)

ATC I level Subgroups	Per capita NHS expenditure	%	Δ% 17-16	DDD/ 1000 inhabdie	%	Δ% 17-16
L – Antineoplastic and immunomodulating agents	**79.64**		**12.9**	**9.0**		**6.7**
Monoclonal antibodies	20.36	25.6	21.7	1.0	11.6	13.5
Protein kinase inhibitors	12.85	16.1	5.2	0.4	4.0	17.2
Tumor necrosis factor alpha (TNF-) inhibitors	10.94	13.7	2.4	1.1	12.4	7.1
Selective immunosuppressants	8.71	10.9	19.2	0.8	9.2	15.4
Others Selective immunosuppressants	4.72	5.9	10.4	0.2	2.4	9.7
Interleukin inhibitors	3.51	4.4	57.0	0.3	3.4	59.2
Other antineoplastic agents	3.21	4.0	30.6	0.2	2.2	4.6
Interferons	2.64	3.3	41.2	0.6	6.1	7.8
Other hormone antagonists and related agents	1.74	2.2	-4.6	0.1	1.2	5.1
Gonadotropin releasing hormone analogues	1.72	2.2	-3.3	0.9	10.5	0.6
Other cytokines and immunomodulators	1.38	1.7	3.4	0.1	1.3	5.7
Pyrimidine analogues	1.16	1.5	-0.9	0.4	4.7	-1.3
Folic acid analogues	1.08	1.4	-7.4	0.1	1.0	-13.8
Colony stimulating factors	0.89	1.1	-8.3	0.1	1.0	6.9
Anti-androgens	0.88	1.1	55.9	0.7	8.2	-1.4
Calcineurin inhibitors	0.83	1.0	6.2	0.4	4.0	9.2
Taxanes	0.68	0.9	1.8	0.2	2.0	11.4
Anti-estrogens	0.57	0.7	13.3	0.3	2.9	7.1
Antracyclines and relate active ingredients	0.47	0.6	-5.3	0.1	1.2	-7.2
Other plant alkaloids and natural products	0.31	0.4	1.1	0.0	0.0	1.6
Vinca alkaloids and analogues	0.23	0.3	-1.7	0.0	0.5	-0.7
Nitrogen mustard analogues	0.19	0.2	-52.7	0.1	0.8	-32.3
J – Antiinfectives for systemic use	**44.39**		**-25.1**	**6.5**		**-1.9**
Antivirals for the treatment of HCV infections	15.61	35.2	-52.3	0.3	3.9	-21.7
Antivirals for treatment of HIV infections, combinations	7.14	16.1	14.7	1.2	19.0	15.7
Meningococcal vaccines	2.71	6.1	105.2	0.2	2.4	61.7
Nucleoside reverse transcriptase inhibitors	2.26	5.1	-1.9	0.8	11.7	4.5
Other antivirals	1.76	4.0	-0.9	0.3	4.8	0.5
Pneumococcal vaccines	1.66	3.7	8.7	0.1	1.5	9.6
Immunoglobulins, normal human	1.54	3.5	18.8	0.0	0.3	9.1
Bacterial and viral vaccines, combined	1.26	2.9	5.0	0.1	1.4	2.4
Other antimycotics for systemic use	1.24	2.8	-0.1	0.0	0.2	14.5
Protease inhibitors	1.20	2.7	-40.4	0.2	3.7	-40.5
Influenza vaccines	0.78	1.8	16.7	0.4	6.9	-37.6
Other antibacterials	0.67	1.5	-1.3	0.1	0.8	43.0
Measles vaccines	0.59	1.3	66.2	0.1	0.9	25.1
Glycopeptide antibacterials	0.57	1.3	-10.2	0.1	0.9	-0.7
Triazole derivatives	0.57	1.3	-16.1	0.1	1.7	5.0
Specific immunoglobulins	0.51	1.2	-24.2	0.0	0.2	-4.1
Antibiotics	0.47	1.1	-2.5	0.1	1.1	-5.4
Tetracyclines	0.44	1.0	11.5	0.0	0.5	2.5
Non-nucleoside reverse transcriptase inhibitors	0.41	0.9	-17.0	0.2	3.1	-12.4

ATC I level Subgroups	Per capita NHS expenditure	%	Δ% 17-16	DDD/ 1000 inhab die	%	Δ% 17-16
Combinations of penicillins, incl. beta-lactamase inhibitors	0.41	0.9	2.6	0.7	11.1	7.1
Papillomavirus vaccines	0.38	0.9	17.4	0.0	0.4	-4.7
Carbapenems	0.25	0.6	3.2	0.0	0.7	6.9
Polymyxins	0.22	0.5	-4.9	0.0	0.5	1.6
Nucleosides and nucleotides excl. reverse transcriptase inhibitors	0.18	0.4	3.1	0.1	1.3	11.6
Varicella zoster vaccines	0.17	0.4	16.9	0.0	0.2	-7.4
B – Blood and blood forming organs	**26.05**		**3.7**	**39.0**		**7.7**
Blood coagulation factors	8.03	30.8	6.5	0.1	0.1	6.0
Direct inhibitors Xa factor	4.39	16.9	37.5	5.4	13.8	38.9
Other antianemic preparations	3.57	13.7	-7.7	3.2	8.2	15.0
Platelet aggregation inhibitors excl. heparin	2.13	8.2	1.8	8.7	22.4	9.2
Heparin group	2.09	8.0	-0.9	6.5	16.8	1.0
Direct thrombin inhibitors	1.58	6.1	21.7	1.8	4.5	26.7
Other systemic hemostatics	0.76	2.9	20.9	0.0	0.1	27.8
Solutions affecting the electrolyte balance	0.73	2.8	-11.4	5.2	13.4	-2.7
Solutions for parenteral nutrition	0.56	2.1	-34.6	0.7	1.7	7.6
Drugs used in hereditary angioedema	0.35	1.3	19.8	0.0	0.0	23.3
Blood substitutes and plasma protein fractions	0.33	1.3	-1.9	0.1	0.2	4.3
Other antithrombotic agents	0.26	1.0	-13.5	0.5	1.2	7.1
Enzymes	0.25	1.0	7.7	0.0	0.0	20.0
Local hemostatics	0.22	0.8	-31.2	0.0	0.0	-37.8
Hypertonic solutions	0.19	0.7	-61.1	0.1	0.2	-50.6
Proteinase inhibitors	0.18	0.7	9.0	0.0	0.0	-8.8
A – Alimentary tract and metabolism	**12.58**		**2.8**	**31.0**		**3.3**
Enzymes	4.38	34.8	6.2	0.0	0.0	7.4
Insulins and analogues for injection, long-acting	2.29	18.2	-7.7	5.7	18.2	4.4
Combinations of Biguanides and Sulfonamid	1.69	13.4	-2.9	4.2	13.5	9.1
GLP-1 receptors analogues	1.13	9.0	21.0	1.2	4.0	30.7
Dipeptidyl peptidase 4 (DPP-4) inhibitors	0.95	7.6	-5.1	2.1	6.7	9.3
Various alimentary tract and metabolism products	0.31	2.5	4.6	0.0	0.0	-2.8
SGLT-2 co-carrier inhibitors	0.30	2.4	72.1	0.6	2.0	73.1
Insulins and analogues for injection, fast-acting	0.23	1.8	7.3	0.9	2.8	6.2
Proton pump inhibitors	0.20	1.6	-3.4	3.9	12.7	0.3
N – Nervous system	**8.37**		**17.8**	**22.7**		**-2.3**
Other antipsychotics	2.32	27.7	3.5	2.1	9.4	9.0
Other nervous system drugs	1.92	22.9	772.1	0.2	0.9	204.5
Diazepines, oxazepines, thiazepines and oxepines	0.56	6.7	-23.0	3.4	14.9	1.0
Drugs used in opioid dependence	0.54	6.4	2.3	3.3	14.6	3.7
Dopa and dopa derivatives	0.52	6.2	-15.6	0.3	1.5	-6.7
Other antiepileptics	0.44	5.2	-4.1	0.9	3.8	6.1
Anticholinesterases	0.21	2.5	-23.0	1.1	4.7	-0.5
Amides	0.21	2.5	-14.0	1.4	6.1	-29.5
V – Various	**5.14**		**6.3**	**3.1**		**20.4**
Iron chelating agents	1.27	24.8	5.7	0.1	2.0	-7.3
Watersoluble, nephrotropic, low osmolar X-ray contrast media	1.08	21.1	0.7	0.1	2.0	-3.3
Antidotes	0.60	11.6	33.0	0.1	3.9	37.2

ATC I level Subgroups	Per capita NHS expenditure	%	Δ% 17-16	DDD/ 1000 inhabdie	%	Δ% 17-16
Paramagnetic contrast media	0.34	6.6	-0.6	0.0	0.7	0.1
Drugs for treatment of hyperkalemia and hyperphosphatemia	0.31	6.1	-8.9	0.2	7.6	0.5
Other diagnostic radiopharmaceuticals for tumour detection	0.29	5.6	19.2	0.0	0.1	16.0
Detoxifying agents for antineoplastic treatment	0.18	3.5	12.7	0.2	7.4	-4.1
C – Cardiovascular system	**4.93**		**8.2**	**17.4**		**-2.5**
Other antihypertensives	2.17	44.1	-2.5	0.1	0.4	7.5
Other cardiac preparations	1.73	35.1	16.8	2.4	13.8	11.9
Other lipid modifying agents	0.23	4.8	91.3	0.2	1.2	32.0
H – Systemic hormonal preparations, excl. sex hormones and insulins	**4.59**		**-4.2**	**5.5**		**-3.4**
Somatostatin and analogues	1.45	31.6	7.0	0.2	3.5	4.8
Somatropin and somatropin agonists	1.40	30.5	-5.6	0.3	4.8	5.2
Other anti-parathyroid agents	0.65	14.2	-13.4	0.3	5.3	4.5
Other anterior pituitary lobe hormones and analogues	0.40	8.7	5.8	0.0	0.3	4.9
Glucocorticoids	0.37	8.0	4.2	4.2	76.3	-4.4
Parathyroid hormones and analogues	0.25	5.5	-37.2	0.1	1.0	-36.7
S – Sensory organs	**3.06**		**35.0**	**2.6**		**13.5**
Antineovascularisation agents	1.95	63.8	7.9	0.3	12.5	18.5
Other antibacterials	0.59	19.2	6677.9	0.0	0.3	-35.3
Corticosteroids, plain	0.35	11.4	11.7	0.2	8.5	12.4
R – Respiratory system	**2.04**		**30.2**	**2.4**		**-0.5**
Other respiratory system products	0.81	39.8	43.6	0.0	0.2	82.6
Other systemic drugs for obstructive airway diseases	0.61	29.7	18.5	0.1	3.1	21.5
Mucolytics	0.18	9.0	9.9	0.2	9.8	-6.0
G – Genito urinary system and sex hormones	**1.90**		**-10.3**	**2.4**		**6.5**
Gonadotropins	1.04	55.1	-13.4	0.1	5.7	-7.1
Drugs used in erectile dysfunction	0.39	20.3	4.6	0.2	8.0	25.4
M – Musculo-skeletal system	**1.51**		**35.2**	**4.3**		**7.9**
Other drugs acting on mineralization	0.72	47.5	18.5	2.4	55.9	16.5
Other drugs affecting bone structure	0.29	19.4	1148.3	0.0	1.0	-5.0
Other muscle relaxants, peripherally acting agents	0.23	15.0	7.5	0.0	0.1	10.0
D – Dermatologicals	**0.36**		**10.7**	**12.8**		**29.5**

Table 2.7. Outpatient NHS consumption and expenditure for the year 2017: most frequently prescribed active ingredients by I ATC level categories (up to 75% of expenditure within the therapeutic category)

Therapeutic category	Per capita gross expenditure	%*	Δ % 17-16	DDD/1000 inhab die	%*	Δ % 17-16	Average cost DDD
C – Cardiovascular system	**53.63**		**-2.9**	**466.8**		**0.3**	**0.31**
rosuvastatin	4.04	7.5	-3.3	12.0	2.6	-2.6	0.93
atorvastatin	3.87	7.2	7.8	41.1	8.8	9.3	0.26
ezetimibe/simvastatin	3.08	5.7	6.5	4.1	0.9	6.8	2.07
bisoprolol	2.15	4.0	7.3	9.9	2.1	7.1	0.60
ramipril	2.02	3.8	0.2	61.4	13.2	0.5	0.09
ezetimibe	1.88	3.5	25.3	2.9	0.6	25.7	1.76
omega 3	1.85	3.5	5.9	3.9	0.8	7.2	1.29
simvastatin	1.71	3.2	-2.7	14.3	3.1	-2.4	0.33
amlodipin	1.55	2.9	-1.4	26.4	5.6	-1.0	0.16
olmesartan/amlodipin	1.53	2.9	8.4	4.8	1.0	13.4	0.88
nebivolol	1.37	2.6	1.9	14.6	3.1	2.7	0.26
olmesartan	1.36	2.5	-43.3	8.6	1.8	7.0	0.43
doxazosin	1.21	2.3	-1.5	7.4	1.6	-1.2	0.45
olmesartan/hydrochlorothiazide	1.18	2.2	-45.5	7.2	1.6	2.1	0.45
valsartan/hydrochlorothiazide	1.08	2.0	-4.2	10.1	2.2	-3.7	0.29
valsartan	0.91	1.7	-0.1	14.6	3.1	0.1	0.17
barnidipin	0.87	1.6	-0.9	4.7	1.0	-0.1	0.50
perindopril/amlodipin	0.84	1.6	-10.2	5.0	1.1	0.3	0.47
nitroglycerine	0.82	1.5	-13.9	6.9	1.5	-13.9	0.33
losartan	0.80	1.5	-2.5	7.5	1.6	-1.6	0.29
lercanidipin	0.76	1.4	-1.2	9.2	2.0	-0.7	0.23
furosemide	0.73	1.4	-0.5	24.5	5.3	-0.3	0.08
irbesartan/hydrochlorothiazide	0.70	1.3	-5.3	5.9	1.3	-4.4	0.32
hydrochlorothiazide	0.69	1.3	7.9	2.2	0.5	10.2	0.85
irbesartan	0.67	1.3	-3.4	8.2	1.8	-2.7	0.22
ramipril/hydrochlorothiazide	0.64	1.2	-3.9	7.2	1.5	-2.9	0.24
zofenopril/hydrochlorothiazide	0.63	1.2	-5.6	4.0	0.8	1.6	0.44
carvedilol	0.61	1.1	-5.9	3.4	0.7	-5.1	0.49
enalapril/lercanidipin	0.60	1.1	-1.8	3.2	0.7	2.8	0.51
losartan/hydrochlorothiazide	0.58	1.1	-5.7	5.1	1.1	-5.1	0.31
A – Alimentary tract and metabolism	**32.80**		**2.0**	**152.0**		**0.1**	**0.59**
pantoprazole	4.59	14.0	0.7	20.4	13.4	1.8	0.62
colecalciferol	3.86	11.8	26.0	10.5	6.9	25.6	1.00
lansoprazole	2.98	9.1	-7.2	15.4	10.1	-6.5	0.53
omeprazole	2.70	8.2	-4.6	17.0	11.2	-3.5	0.44
esomeprazole	2.46	7.5	-0.9	12.6	8.3	2.7	0.54
mesalazine	1.72	5.2	3.8	4.3	2.8	4.3	1.10
insulin lispro	1.71	5.2	6.4	3.4	2.2	6.7	1.40
insulin aspart	1.48	4.5	-2.2	2.9	1.9	-1.9	1.40
metformin	1.45	4.4	5.3	21.1	13.9	3.1	0.19
rifaximin	1.39	4.2	1.2	1.8	1.2	1.4	2.08
sodium alginate/potassium bicarbonate	0.81	2.5	-0.6	3.8	2.5	-0.6	0.58
N – Nervous system	**22.43**		**-0.1**	**63.2**		**1.8**	**0.97**
pregabalin	1.67	7.5	-22.0	1.7	2.8	5.4	2.63
levetiracetam	1.42	6.3	6.7	1.8	2.9	7.6	2.10

Therapeutic category	Per capita gross expenditure	%*	Δ % 17-16	DDD/1000 inhab die	%*	Δ % 17-16	Average cost DDD
fentanil	1.26	5.6	5.1	0.5	0.8	2.2	6.80
naloxone/ossicodone	1.06	4.7	9.1	0.4	0.6	9.9	7.25
tapentadol	1.06	4.7	16.8	0.5	0.7	17.2	6.30
paroxetine	1.03	4.6	-2.1	7.7	12.1	0.0	0.37
escitalopram	0.93	4.1	-2.5	7.1	11.2	-1.3	0.36
valproic acid	0.89	4.0	1.3	2.1	3.4	1.2	1.14
venlafaxine	0.75	3.4	-0.4	3.3	5.2	0.1	0.63
rotigotine	0.69	3.1	1.1	0.4	0.6	1.6	5.39
duloxetine	0.69	3.1	-0.9	2.7	4.3	2.9	0.70
sertraline	0.67	3.0	2.6	7.3	11.6	2.4	0.25
quetiapine	0.47	2.1	6.7	0.4	0.6	5.3	3.27
citalopram	0.42	1.9	-3.6	4.0	6.4	-2.8	0.28
lamotrigine	0.39	1.8	2.9	0.6	1.0	3.9	1.78
pramipexole	0.38	1.7	7.8	0.5	0.7	8.8	2.26
lacosamide	0.38	1.7	13.8	0.2	0.3	14.1	5.73
trazodone	0.35	1.6	6.1	1.0	1.6	6.5	0.98
lidocaine	0.34	1.5	18.5	0.3	0.4	18.8	3.61
vortioxetine	0.32	1.4	237.9	0.8	1.2	238.8	1.14
gabapentin	0.31	1.4	1.2	0.4	0.6	1.5	2.14
mirtazapine	0.31	1.4	1.6	1.5	2.3	2.3	0.57
paracetamol/codeine	0.30	1.3	-3.7	1.1	1.8	-3.2	0.71
levodopa/benserazide	0.30	1.3	3.6	0.9	1.4	2.9	0.93
tramadol	0.29	1.3	-5.0	0.6	1.0	-4.6	1.28
topiramate	0.29	1.3	-1.8	0.3	0.5	-1.0	2.43
R – Respiratory system	**13.36**		**-1.9**	**41.2**		**-2.2**	**1.09**
salmeterol/fluticasone	2.66	16.3	-14.4	3.6	8.7	-13.9	2.03
beclomethasone/formoterol	2.05	12.5	6.8	3.1	7.6	7.2	1.79
fluticasone/vilanterol	1.59	9.7	30.8	2.5	6.1	25.1	1.73
tiotropium	1.59	9.7	-18.1	2.7	6.7	-13.3	1.59
beclomethasone	1.18	7.2	-9.7	3.1	7.5	-8.6	1.05
budesonide/formoterol	1.02	6.3	1.7	1.3	3.1	4.9	2.18
aclidinium	0.68	4.1	4.7	1.2	2.8	5.0	1.61
glycopyrronium	0.58	3.5	-3.7	1.0	2.5	-2.1	1.51
montelukast	0.48	2.9	-2.5	2.0	4.8	-1.1	0.66
fluticasone	0.41	2.5	-1.0	0.9	2.2	-2.2	1.25
J – Antiinfectives for systemic use	**13.14**		**-2.4**	**20.7**		**-2.2**	**1.74**
amoxicillin/clavulanic acid	2.87	21.8	-1.0	8.6	41.6	-0.2	0.91
ceftriaxone	1.27	9.7	-9.9	0.3	1.4	-9.7	11.73
ciprofloxacin	0.97	7.4	-4.4	1.0	4.8	-3.5	2.70
cefixime	0.85	6.5	-0.8	1.0	4.8	-0.9	2.34
fluconazole	0.82	6.2	-3.3	0.4	1.9	-2.7	5.60
levofloxacin	0.80	6.1	-3.3	1.5	7.1	-2.9	1.48
clarithromycin	0.76	5.7	-7.6	2.2	10.4	-5.7	0.96
azithromycin	0.66	5.0	-1.3	1.2	5.9	-0.9	1.48
fosfomycin	0.59	4.5	1.9	0.4	1.7	2.6	4.58
human immunoglobulin against hepatitis B	0.52	3.9	30.7	0.0	0.0	29.1	316.27
B – Blood and blood forming organs	**8.08**		**-2.6**	**86.4**		**0.8**	**0.26**
enoxaparin sodium	2.05	25.3	-13.3	2.2	2.6	-12.8	2.54
acetylsalicylic acid	1.14	14.2	0.0	43.3	50.1	0.8	0.07

Therapeutic category	Per capita gross expenditure	%*	Δ % 17-16	DDD/1000 inhab die	%*	Δ % 17-16	Average cost DDD
clopidogrel	0.98	12.1	0.8	4.7	5.5	2.4	0.57
calcium nadroparin	0.66	8.2	-1.1	0.6	0.7	-1.1	2.93
folic acid	0.44	5.4	6.3	5.2	6.0	9.8	0.23
ticlopidine	0.27	3.3	-14.0	2.9	3.4	-13.9	0.25
ferrous sulphate	0.24	3.0	3.4	2.2	2.5	1.8	0.31
clopidogrel/acetylsalicylic acid	0.23	2.9	0.5	0.7	0.9	0.8	0.86
parnaparin	0.23	2.9	-4.8	0.2	0.2	-4.6	3.02
G – Genito-urinary system and sex hormones	**6.60**		**-7.6**	**39.5**		**-3.3**	**0.46**
dutasteride	2.03	30.8	-20.9	7.3	18.4	1.7	0.76
tamsulosin	1.02	15.4	1.3	9.6	24.4	1.9	0.29
silodosin	0.91	13.7	8.1	4.8	12.3	8.4	0.51
alfuzosin	0.76	11.5	1.6	8.0	20.2	2.1	0.26
finasteride	0.57	8.7	1.0	2.6	6.6	1.5	0.60
M – Musculo-skeletal system	**6.08**		**-7.7**	**37.6**		**-1.4**	**0.44**
febuxostat	0.86	14.1	17.4	1.8	4.7	17.6	1.32
etoricoxib	0.79	13.0	-23.1	3.0	7.8	-6.4	0.74
alendronic acid	0.68	11.2	6.9	3.4	9.1	8.0	0.54
alendronic acid/colecalciferol	0.64	10.6	-31.9	2.7	7.0	-11.7	0.66
diclofenac	0.57	9.5	1.5	4.0	10.5	2.9	0.40
risedronate	0.42	6.9	-5.7	2.3	6.1	-2.8	0.50
ketoprofen	0.35	5.7	-6.2	3.3	8.8	-4.7	0.29
allopurinol	0.31	5.0	2.0	7.3	19.5	2.5	0.11
L – Antineoplastic and immunomodulating agents	**3.93**		**0.0**	**5.8**		**2.5**	**1.85**
letrozole	1.03	26.1	8.4	1.2	21.1	9.5	2.29
cyclosporine	0.65	16.6	-6.6	0.2	3.7	-3.1	8.40
methotrexate	0.56	14.2	-5.8	1.1	19.5	4.6	1.35
anastrozole	0.42	10.6	-1.8	0.8	13.9	0.3	1.41
exemestane	0.29	7.4	13.5	0.4	6.0	14.6	2.26
bicalutamide	0.16	4.0	-11.8	0.3	5.3	-10.9	1.38
S – Sensory organs	**3.81**		**-0.3**	**20.0**		**-0.1**	**0.52**
bimatoprost	0.46	11.9	1.8	1.8	9.2	2.5	0.68
timolol/bimatoprost	0.42	11.0	3.8	1.3	6.7	3.5	0.86
brinzolamide/timolol	0.40	10.5	4.2	1.5	7.7	4.5	0.71
tafluprost	0.37	9.8	0.6	1.2	5.9	0.9	0.86
timolol	0.31	8.2	0.0	3.0	15.0	-6.9	0.29
timolol/travoprost	0.30	7.7	-10.4	0.9	4.3	-5.9	0.94
dorzolamide /timolol	0.27	7.1	11.5	1.9	9.4	10.9	0.39
latanoprost	0.23	6.0	-7.5	1.6	7.9	-6.3	0.40
travoprost	0.22	5.9	-24.5	0.9	4.7	-6.3	0.66
H – Systemic hormonal preparations, excl. sex hormones and insulins	**3.79**		**15.6**	**34.4**		**1.4**	**0.30**
teriparatide	1.16	30.6	61.1	0.2	0.5	62.6	18.90
levothyroxine	0.90	23.7	7.2	19.9	57.7	1.5	0.12
prednisone	0.63	16.5	1.2	5.9	17.1	1.8	0.29
betamethasone	0.31	8.2	-1.7	2.0	5.9	-1.2	0.42
methylprednisolone	0.22	5.8	-0.2	3.5	10.1	0.5	0.17

Therapeutic category	Per capita gross expenditure	%*	Δ % 17-16	DDD/1000 inhab die	%*	Δ % 17-16	Average cost DDD
D – Dermatologicals	**0.95**		**6.4**	**4.1**		**18.0**	**0.64**
calcipotriol/betamethasone	0.42	43.8	-2.3	1.4	33.2	-2.1	0.84
isotretinoin	0.07	7.4	1.4	0.1	3.3	1.8	1.43
clobetasol	0.07	7.2	49.5	1.1	27.2	56.9	0.17
terbinafine	0.06	6.5	-4.1	0.1	2.9	-3.8	1.41
diclofenac	0.06	5.9	0.0	0.1	1.7	0.0	2.16
tacalcitol	0.05	5.2	-2.3	0.1	2.8	-1.0	1.17
P – Antiparasitic products, insecticides and repellents	**0.21**		**2.1**	**0.9**		**4.1**	**0.66**
hydroxychloroquine	0.14	63.6	3.9	0.7	80.8	4.2	0.52
mefloquine	0.03	14.7	2.1	0.0	0.7	2.3	13.27
mebendazole	0.02	9.8	12.6	0.1	10.7	13.9	0.61
metronidazole	0.01	4.7	2.7	0.0	3.1	3.0	1.03
tinidazole	0.01	2.7	-19.9	0.0	0.7	-19.7	2.71
V – Various	**0.14**		**-0.2**	**0.1**		**3.3**	**3.87**
sevelamer	0.04	31.6	-6.6	0.0	19.7	3.6	6.21
sodium polystyrenesulfonate	0.03	21.5	1.4	0.0	28.8	1.7	2.88
sucroferric hydroxide	0.01	10.1	74.0	0.0	4.4	66.5	8.84
calcium polystyrenesulfonate	0.01	8.7	13.4	0.0	12.9	13.7	2.62
deferoxamine	0.01	7.5	-37.1	0.0	1.2	-34.5	24.90

* the percentages of expenses and DDD are calculated on the total of the ATC category

Table 2.8 First thirty active ingredients in terms of outpatient NHS expenditure: comparison 2017-2016

ATC	Active ingredient	Exp *(million)*	%*	Per capita expenditure	Rank 2017	Rank 2016
A	pantoprazole	277.9	2.7	4.59	1	1
C	rosuvastatin	244.8	2.3	4.04	2	2
C	atorvastatin	234.5	2.3	3.87	3	3
A	colecalciferol	233.9	2.2	3.86	4	6
C	ezetimibe/simvastatin	186.8	1.8	3.08	5	8
A	lansoprazole	180.4	1.7	2.98	6	4
J	amoxicillin/clavulanic acid	173.7	1.7	2.87	7	7
A	omeprazole	163.5	1.6	2.70	8	9
R	salmeterol/fluticasone	161.3	1.5	2.66	9	5
A	esomeprazole	149.2	1.4	2.46	10	11
C	bisoprolol	130.3	1.3	2.15	11	17
R	beclomethasone/formoterol	124.0	1.2	2.05	12	19
B	enoxaparin sodium	124.0	1.2	2.05	13	13
G	dutasteride	123.1	1.2	2.03	14	10
C	ramipril	122.4	1.2	2.02	15	16
C	ezetimibe	113.8	1.1	1.88	16	26
C	omega 3	112.3	1.1	1.85	17	21
A	mesalamine	104.3	1.0	1.72	18	22
A	insulin lispro	103.9	1.0	1.71	19	23
C	simvastatin	103.8	1.0	1.71	20	20
N	pregabalin	101.5	1.0	1.67	21	15
R	fluticasone/vilanterol	96.6	0.9	1.59	22	35
R	tiotropium	96.4	0.9	1.59	23	18
C	amlodipine	93.7	0.9	1.55	24	24
C	olmesartan/amlodipine	92.6	0.9	1.53	25	28
A	insulin aspart	89.6	0.9	1.48	26	25
A	metformin	87.8	0.8	1.45	27	29
N	levetiracetam	85.9	0.8	1.42	28	32
A	rifaximin	84.2	0.8	1.39	29	30
C	nebivolol	83.0	0.8	1.37	30	31
	Total	**4,079.0**	**39.1**			
	Total expenditure Class A	**10,418.9**				

*calculated on the total of outpatient expenditure

Table 2.9. First thirty active ingredients* with greater variation of outpatient expenditure compared to the previous year: comparison 2017-2016

ATC	Active ingredient	Per capita expenditure	Δ% 17-16	DDD/1000 inhab die	Δ% 17-16
H	teriparatide	1.16	61.1	0.2	62.6
R	fluticasone/vilanterol	1.59	30.8	2.5	25.1
J	human immunoglobulin against hepatitis b	0.52	30.7	0.0	29.1
A	colecalciferol	3.86	26.0	10.5	25.6
C	ezetimibe	1.88	25.3	2.9	25.7
M	febuxostat	0.86	17.4	1.8	17.6
N	tapentadol	1.06	16.8	0.5	17.2
N	naloxone/oxyicodone	1.06	9.1	0.4	9.9
C	olmesartan/amlodipine	1.53	8.4	4.8	13.4
L	letrozole	1.03	8.4	1.2	9.5
G	silodosin	0.91	8.1	4.8	8.4
C	flecainide acetate	0.69	7.9	2.2	10.2
C	atorvastatin	3.87	7.8	41.1	9.3
C	bisoprolol	2.15	7.3	9.9	7.1
H	levothyroxine	0.90	7.2	19.9	1.5
M	alendronic acid	0.68	6.9	3.4	8.0
R	beclomethasone/formoterol	2.05	6.8	3.1	7.2
N	levetiracetam	1.42	6.7	1.8	7.6
C	ezetimibe/simvastatin	3.08	6.5	4.1	6.8
A	insulin lispro	1.71	6.4	3.4	6.7
C	omega 3	1.85	5.9	3.9	7.2
A	metformin	1.45	5.3	21.1	3.1
N	fentanyl	1.26	5.1	0.5	2.2
R	aclidinium	0.68	4.7	1.2	5.0
A	mesalamine	1.72	3.8	4.3	4.3
A	ursodeoxycholic acid	0.63	3.1	2.1	3.2
C	zofenopril	0.58	2.7	3.9	2.7
N	sertraline	0.67	2.6	7.3	2.4
C	nebivolol	1.37	1.9	14.6	2.7
J	fosfomycin	0.59	1.9	0.4	2.6

* selected among the top 100 active ingredients at the highest per capita expenditure

Table 2.10. First thirty active ingredients in terms of outpatient NHS consumption: comparison 2017-2016

ATC	Active ingredient	DDD/1000 inhab die	%*	Rank 2017	Rank 2016
C	ramipril	61.4	6.3	1	1
B	acetylsalicylic acid	43.3	4.4	2	2
C	atorvastatin	41.1	4.2	3	3
C	amlodipine	26.4	2.7	4	4
C	furosemide	24.5	2.5	5	5
A	metformin	21.1	2.2	6	6
A	pantoprazole	20.4	2.1	7	7
H	levothyroxine	19.9	2.0	8	8
A	omeprazole	17.0	1.7	9	9
A	lansoprazole	15.4	1.6	10	10
C	nebivolol	14.6	1.5	11	13
C	valsartan	14.6	1.5	12	12
C	simvastatin	14.3	1.5	13	11
A	esomeprazole	12.6	1.3	14	15
C	rosuvastatin	12.0	1.2	15	14
A	colecalciferol	10.5	1.1	16	25
C	valsartan/hydrochlorothiazide	10.1	1.0	17	17
C	bisoprolol	9.9	1.0	18	20
C	enalapril	9.8	1.0	19	16
G	tamsulosin	9.6	1.0	20	18
C	lercanidipine	9.2	0.9	21	19
C	atenolol	8.8	0.9	22	21
C	telmisartan	8.7	0.9	23	22
J	amoxicillin/clavulanic acid	8.6	0.9	24	23
C	olmesartan	8.6	0.9	25	26
C	irbesartan	8.2	0.8	26	24
C	candesartan	8.1	0.8	27	28
G	alfuzosin	8.0	0.8	28	29
N	paroxetine	7.7	0.8	29	30
C	losartan	7.5	0.8	30	31
	Total	**491.7**	**50.6**		
	Total DDD Class A	**972.7**			

* calculated on the total of outpatient expenditure

Table 2.11. Inpatient NHS consumption and expenditure for the year 2017 of medicines purchased by public health facilities: most frequently prescribed active ingredients by ATC I level categories (up to 75% of expenditure within the therapeutic category)

ATC I level	Per capita expenditure	%*	Δ % 17-16	DDD/1000 inhab die	%*	Δ % 17-16
L – Antineoplastic and immunomodulating agents	**79.64**		**12.9**	**9.0**		**6.7**
adalimumab	4.70	5.9	7.9	0.4	4.3	7.8
trastuzumab	4.62	5.8	1.9	0.2	2.3	7.3
bevacizumab	3.68	4.6	1.7	0.1	1.4	5.4
lenalidomide	3.35	4.2	10.0	0.1	0.8	29.2
rituximab	3.07	3.9	-1.8	0.6	6.1	7.0
etanercept	3.02	3.8	-5.0	0.3	3.1	2.2
nivolumab	3.00	3.8	193.6	0.0	0.5	253.8
fingolimod	2.07	2.6	13.2	0.1	1.2	15.0
interferon beta 1a	1.93	2.4	30.6	0.5	5.0	3.6
imatinib	1.73	2.2	-36.9	0.1	1.1	-3.4
eculizumab	1.73	2.2	12.3	0.0	0.1	15.2
pertuzumab	1.67	2.1	29.6	0.0	0.4	28.9
abiraterone	1.63	2.0	-5.4	0.0	0.5	0.8
infliximab	1.50	1.9	-3.0	0.3	3.3	9.4
natalizumab	1.35	1.7	7.9	0.1	0.7	8.2
ibrutinib	1.34	1.7	113.1	0.0	0.3	113.5
ustekinumab	1.33	1.7	19.5	0.1	1.6	20.8
bortezomib	1.25	1.6	-4.7	0.1	1.2	-4.4
golimumab	1.22	1.5	4.5	0.1	1.2	7.7
dasatinib	1.19	1.5	5.1	0.0	0.3	5.3
glatiramer	1.12	1.4	4.9	0.1	1.2	5.5
nilotinib	1.11	1.4	3.5	0.0	0.3	4.1
pemetrexed	1.06	1.3	-7.1	0.0	0.3	-2.5
pembrolizumab	1.01	1.3	451.2	0.0	0.2	937.3
leuprorelina	0.98	1.2	-3.4	0.2	2.1	0.3
abatacept	0.95	1.2	17.7	0.1	0.6	16.9
ruxolitinib	0.94	1.2	37.6	0.0	0.2	38.6
sunitinib maleate	0.91	1.1	-1.8	0.0	0.1	-1.0
trastuzumab emtansine	0.90	1.1	-4.8	0.0	0.1	-2.8
tocilizumab	0.83	1.0	15.8	0.1	0.8	22.9
secukinumab	0.83	1.0	975.0	0.1	0.8	969.0
enzalutamide	0.82	1.0	71.5	0.0	0.3	73.4
azacytidine	0.82	1.0	-0.8	0.0	0.1	-0.6
everolimus	0.76	1.0	-9.3	0.0	0.2	-9.7
tacrolimus	0.73	0.9	8.6	0.3	3.4	12.4
triptorelin	0.71	0.9	-2.7	0.7	8.1	1.3
J – Antiinfectives for systemic use	**44.39**		**-25.1**	**6.5**		**-1.9**
ledipasvir/sofosbuvir	4.81	10.8	-68.9	0.0	0.4	-68.9
sofosbuvir	4.35	9.8	-61.8	0.0	0.4	-61.7
sofosbuvir/velpatasvir	2.59	5.8	0.0	0.1	1.0	0.0
meningococcal vaccine group B	1.96	4.4	102.3	0.1	1.3	96.1
pneumococcal vaccine	1.64	3.7	8.5	0.1	1.4	9.6
entecavir	1.46	3.3	5.8	0.3	5.1	11.0
elbasvir/grazoprevir	1.45	3.3	0.0	0.0	0.5	0.0
emtricitabine/rilpivirine/tenofovir	1.28	2.9	-0.8	0.2	2.7	-0.5

ATC I level	Per capita expenditure	%*	Δ % 17-16	DDD/1000 inhab die	%*	Δ % 17-16
emtricitabine/tenofovir	1.17	2.6	-29.3	0.2	3.4	-29.1
diphtheria-hemophilus influenzae B-pertussis-poliomyelitis-tetanushepatitis B	1.06	2.4	1.7	0.1	1.0	-2.3
dolutegravir/abacavir/lamivudine	1.03	2.3	204.3	0.1	2.1	193.8
ombitasvir/paritaprevir/ritonavir	0.95	2.1	-60.6	0.0	0.4	-20.6
daclatasvir	0.94	2.1	-69.9	0.0	0.3	-52.9
dolutegravir	0.80	1.8	19.7	0.1	2.1	17.5
raltegravir	0.79	1.8	-12.3	0.2	2.4	-9.7
immunoglobulins, normal human, for intravascular adm.	0.77	1.7	22.8	0.0	0.1	1.0
human immunoglobulin intravenous use	0.76	1.7	15.0	0.0	0.1	19.6
caspofungin	0.69	1.6	-7.2	0.0	0.1	19.1
efavirenz/emtricitabine/tenofovir disoproxil	0.67	1.5	-26.2	0.1	1.4	-26.0
tenofovir	0.67	1.5	-11.2	0.2	3.4	-0.4
darunavir	0.64	1.5	-40.8	0.1	1.6	-40.7
darunavir/cobicistat	0.58	1.3	296.3	0.1	2.0	297.3
elvitegravir/cobicistat/emtricitabine/ tenofovir alafenamide fumarate	0.54	1.2	0.0	0.1	0.9	0.0
teicoplanin	0.51	1.2	-15.6	0.0	0.6	0.0
emtricitabine/tenofovir/elvitegravir/cobicistat	0.50	1.1	-24.2	0.1	0.8	-24.0
B – Blood and blood forming organs	**26.05**		**3.7**	**39.0**		**7.7**
coagulation factor VIII	5.05	19.4	2.3	0.0	0.1	5.2
apixaban	2.24	8.6	43.6	2.3	5.8	43.2
rivaroxaban	1.89	7.3	17.0	2.8	7.1	21.7
dabigatran	1.57	6.0	22.3	1.8	4.5	26.7
epoetin alpha	1.52	5.8	1.4	1.7	4.4	46.9
enoxaparin	1.50	5.8	-2.2	5.1	13.1	-0.6
darbepoetin alpha	1.34	5.1	-10.3	0.6	1.5	-8.5
eptacog alpha activated (recombinant DNA coagulation factor VII)	1.01	3.9	18.8	0.0	0.0	20.8
ticagrelor	0.72	2.8	8.5	0.8	2.1	13.3
treprostinil	0.61	2.3	5.9	0.0	0.0	6.2
sodio chloride	0.60	2.3	-5.8	4.6	11.9	-1.7
nonacog alpha (coagulation factor IX, recombinant)	0.57	2.2	-13.4	0.0	0.0	-12.4
human coagulation factor VIII/Von Willebrand factor	0.46	1.8	-2.4	0.0	0.0	-7.8
eltrombopag olamina	0.46	1.8	31.8	0.0	0.0	44.7
A – Alimentary tract and metabolism	**12.58**		**2.8**	**31.0**		**3.3**
insulin glargine	1.54	12.2	-6.8	4.1	13.3	5.1
recombinant human acid alglucosidase	1.05	8.3	4.2	0.0	0.0	4.5
imiglucerase	0.88	7.0	4.7	0.0	0.0	4.9
agalsidase alpha	0.83	6.6	7.1	0.0	0.0	7.3
liraglutide	0.59	4.7	3.5	0.7	2.2	6.5
sitagliptin/metformin	0.55	4.4	-14.0	1.3	4.2	4.2
idursulfase	0.50	4.0	2.8	0.0	0.0	3.0
insulin degludec	0.49	3.9	-6.3	1.0	3.1	17.9
agalsidase beta	0.45	3.6	14.4	0.0	0.0	14.7
sitagliptin	0.43	3.4	-16.6	0.9	2.9	0.6
dulaglutide	0.33	2.6	156.0	0.4	1.2	205.5
linagliptin	0.32	2.6	29.8	0.7	2.3	33.0

ATC I level	Per capita expenditure	%*	Δ % 17-16	DDD/1000 inhab die	%*	Δ % 17-16
pioglitazone/metformin	0.32	2.5	-9.6	0.9	2.8	-8.9
vildagliptin/metformin	0.28	2.2	-26.0	0.7	2.2	-2.3
insulin detemir	0.26	2.0	-15.5	0.6	1.8	-15.5
velaglucerase alpha	0.25	1.9	2.4	0.0	0.0	2.7
elosulfase alpha	0.21	1.6	24.4	0.0	0.0	24.8
exenatide	0.18	1.5	-5.7	0.2	0.5	-6.1
N – Nervous system	**8.37**		**17.8**	**22.7**		**-2.3**
dimethylfumarate	1.66	19.9	0.0	0.1	0.6	0.0
paliperidone	1.21	14.4	13.0	0.6	2.6	11.4
aripiprazole	0.66	7.9	-1.2	0.8	3.7	13.6
risperidone	0.45	5.4	-10.4	0.7	3.2	2.3
levodopa/carbidopa	0.43	5.2	-1.4	0.1	0.5	6.1
quetiapine	0.32	3.8	-29.0	1.4	6.2	3.5
metadone	0.31	3.7	2.5	2.4	10.7	3.7
levetiracetam	0.19	2.3	2.6	0.4	1.7	8.9
buprenorphine/naloxone	0.19	2.3	0.9	0.2	0.8	0.6
rivastigmine	0.17	2.1	-23.1	0.5	2.1	-5.1
tafamidis meglumine	0.15	1.8	19.7	0.0	0.0	21.1
sevoflurane	0.14	1.6	-33.2	0.0	0.0	-31.4
olanzapine	0.13	1.5	-8.2	1.5	6.7	-4.6
sodium oxybate	0.11	1.3	9.9	0.1	0.5	9.8
pregabalin	0.11	1.3	-32.5	0.2	0.8	-0.7
paracetamol	0.10	1.2	-10.8	1.0	4.3	-28.7
V – Various	**5.14**		**6.3**	**3.0**		**20.4**
deferasirox	1.12	21.8	7.8	0.0	1.1	-7.5
sugammadex	0.51	9.9	39.9	0.0	0.6	40.3
iomeprol	0.39	7.7	7.3	0.0	0.6	3.2
18f-fluoro-deoxyglucose	0.26	5.1	18.8	0.0	0.1	16.3
iodixanol	0.23	4.5	4.1	0.0	0.3	-1.4
sevelamer	0.17	3.3	-17.4	0.1	4.9	-3.2
iopromide	0.16	3.2	-17.0	0.0	0.3	-14.0
iodine 123	0.15	3.0	5.4	0.0	0.0	7.2
iobitrido	0.13	2.6	0.9	0.0	0.3	-4.1
radio-^{223}ra-dichloride	0.13	2.6	30.1	0.0	0.0	27.7
gadobutrol	0.13	2.5	3.7	0.0	0.2	5.8
lanthanum carbonato hydrate	0.12	2.4	-3.7	0.1	1.7	-3.4
deferiprone	0.11	2.2	-4.6	0.0	0.6	-4.4
thyrotropin	0.11	2.1	-11.6	0.0	0.0	-7.1
sodium pertechnetate (^{99m}tc)	0.09	1.8	-4.7	0.0	0.0	-2.2
rasburicase	0.09	1.7	21.8	0.0	0.0	18.4
C – Cardiovascular system	**4.93**		**8.2**	**17.4**		**-2.5**
bosentan	1.13	22.9	-20.8	0.0	0.2	-7.6
ranolazine	0.95	19.3	29.4	0.9	5.2	29.5
ivabradine	0.72	14.5	3.2	1.4	8.2	3.1
macitentan	0.69	14.1	39.5	0.0	0.1	39.2
ambrisentan	0.26	5.2	4.5	0.0	0.1	4.2
H – Systemic hormonal preparations	**4.59**		**-4.2**	**5.5**		**-3.4**
somatropin	1.40	30.4	-5.6	0.3	4.8	5.3
octreotide	0.79	17.2	-1.2	0.1	2.1	0.0
cinacalcet	0.53	11.6	-0.3	0.1	2.1	4.5

ATC I level	Per capita expenditure	%*	Δ % 17-16	DDD/1000 inhab die	%*	Δ % 17-16
lanreotide	0.52	11.3	6.8	0.1	1.3	10.1
pegvisomant	0.40	8.7	5.8	0.0	0.3	4.9
S – Sensory organs	**3.06**		**35.0**	**2.6**		**13.5**
ranibizumab	1.10	35.8	2.9	0.1	4.3	7.0
aflibercept	0.83	27.1	15.8	0.2	8.2	26.4
povidone-iodine	0.59	19.2	6686.4	0.0	0.3	-36.7
dexamethasone	0.34	11.1	10.9	0.2	8.3	11.9
cefuroxime	0.03	0.8	40.0	0.0	0.4	41.7
R – Respiratory system	**2.04**		**30.2**	**2.4**		**-0.5**
omalizumab	0.60	29.4	18.7	0.1	2.6	25.7
ivacaftor	0.48	23.4	-6.5	0.0	0.1	-1.8
lumacaftor/ivacaftor	0.31	15.2	695.0	0.0	0.1	871.3
desossiribonuclease	0.17	8.2	12.5	0.0	0.9	12.6
phospholipid fraction from swine lung	0.09	4.4	1425.6	0.0	0.0	3.5
G – Genito- urinary system and sex hormones	**1.90**		**-10.3**	**2.4**		**6.5**
follitropin alpha from recombinant DNA	0.50	26.1	-24.4	0.1	2.4	-14.5
menotrophin	0.22	11.4	-0.1	0.0	1.8	0.4
tadalafil	0.18	9.7	11.7	0.1	5.6	30.3
sildenafil	0.18	9.5	-6.2	0.0	1.8	-4.2
follitropin beta	0.17	8.8	-0.8	0.0	0.7	-1.2
ulipristal acetate	0.11	5.8	91.9	0.1	3.6	110.2
dinoprostone	0.09	4.9	3.4	0.0	2.0	3.5
M – Musculo-skeletal system	**1.51**		**35.2**	**4.3**		**7.9**
denosumab	0.72	47.5	18.5	2.4	55.9	16.5
botulinum toxin of clostridium botulinum	0.23	14.9	7.5	0.0	0.1	10.0
ataluren	0.14	9.2	0.0	0.0	0.0	0.0
nusinersen	0.13	8.8	0.0	0.0	0.0	0.0
zoledronic acid	0.05	3.3	-4.2	0.0	0.1	-22.6
D – Dermatologicals	**0.36**		**10.7**	**12.8**		**29.5**
povidone-iodine	0.06	15.6	35.0	5.4	42.1	111.1
clorhexidine/benzalkonium	0.05	14.6	31.6	1.4	11.2	14.6
silver sulfadiazine	0.04	12.2	23.5	0.7	5.1	19.8
sodium hypochlorite	0.03	9.7	5.7	2.5	19.8	5.7
hyaluronic acid	0.03	8.1	-1.8	0.2	1.8	1.4
imiquimod	0.02	4.9	-17.9	0.0	0.3	-1.3
watery extract of triticum vulgare	0.02	4.5	-23.6	0.1	0.6	-24.7
silver sulfadiazine/hyaluronic acid	0.01	2.4	-18.7	0.2	1.3	-2.6
clorexidine	0.01	2.2	-13.1	0.4	3.1	-33.1
bromelain	0.01	2.2	238.0	0.0	0.0	250.3
P – Antiparasitic products, insecticides and repellents	**0.03**		**19.0**	**0.0**		**2.5**
atovaquone	0.01	44.3	24.8	0.0	7.2	16.5
permethrin	0.01	25.0	18.7	0.0	7.1	19.2
atovaquone/proguanile	0.00	12.0	37.6	0.0	3.9	13.0
hydroxychloroquine	0.00	5.4	-2.9	0.0	38.5	-1.5
pentamidine isetionate	0.00	4.3	3.4	0.0	1.0	3.6

* the percentages of expenditure and DDD are calculated on the total of the ATC category

Table 2.12. First thirty active ingredients purchased by public health facilities in terms of expenditure: comparison 2017-2016

ATC	Active ingredient	Exp (million)	%*	Per capita expenditure	Rango 2017	Rango 2016
B	coagulation factor VIII	306.0	2.6	5.05	1	3
J	ledipasvir/sofosbuvir	291.6	2.5	4.81	2	1
L	adalimumab	285.0	2.4	4.70	3	5
L	trastuzumab	280.1	2.4	4.62	4	4
J	sofosbuvir	263.3	2.2	4.35	5	2
L	bevacizumab	223.0	1.9	3.68	6	6
L	lenalidomide	202.7	1.7	3.35	7	10
L	rituximab	186.0	1.6	3.07	8	8
L	etanercept	183.0	1.6	3.02	9	7
L	nivolumab	181.7	1.5	3.00	10	45
J	sofosbuvir/velpatasvir	156.7	1.3	2.59	11	0
B	apixaban	136.0	1.2	2.24	12	18
L	fingolimod	125.7	1.1	2.07	13	13
J	meningococcal vaccine group B	118.9	1.0	1.96	14	48
L	interferon beta 1a	117.1	1.0	1.93	15	25
B	rivaroxaban	114.6	1.0	1.89	16	17
L	imatinib	104.8	0.9	1.73	17	11
L	eculizumab	104.8	0.9	1.73	18	20
L	pertuzumab	101.3	0.9	1.67	19	30
N	dimethyl fumarate	100.8	0.9	1.66	20	0
J	pneumococcal vaccine	99.4	0.8	1.64	21	22
L	abiraterone	98.6	0.8	1.63	22	14
B	dabigatran	95.0	0.8	1.57	23	32
A	insulin glargine	93.4	0.8	1.54	24	16
B	epoetin alpha	92.0	0.8	1.52	25	23
L	infliximab	91.1	0.8	1.50	26	19
B	enoxaparin sodium	91.0	0.8	1.50	27	21
J	entecavir	88.3	0.7	1.46	28	28
J	elbasvir/grazoprevir	87.7	0.7	1.45	29	0
H	somatropin	84.6	0.7	1.40	30	26
	Total	**4,504.3**	**38.2**			
	Total inpatient expenditure	**11,789.3**				

*calculated on the total expenditure of medicines purchased by public health facilities
Traceability data for the sofosbuvir/velpatasvir association are net of the credit notes relating to the price/volume agreement in force

Table 2.13. First thirty active ingredients* purchased by public health facilities with greater variation of expenditure compared to previous year: comparison 2017-2016

ATC	Active ingredient	Per capita expenditure	Δ% 17/16	DDD/1000 inhab die	Δ% 17/16
S	povidon-iodine	0.59	>100	0.0	-36.7
L	secukinumab	0.83	>100	0.1	>100
L	pembrolizumab	1.01	>100	0.0	>100
J	darunavir/cobicistat	0.58	>100	0.1	>100
J	dolutegravir/abacavir/lamivudina	1.03	>100	0.1	>100
L	nivolumab	3.00	>100	0.0	>100
L	Ibrutinib	1.34	>100	0.0	>100
J	meningococcal vaccine group B	1.96	>100	0.1	96.1
L	enzalutamide	0.82	71.5	0.0	73.4
B	apixaban	2.24	43.6	2.3	43.2
C	macitentan	0.69	39.5	0.0	39.2
L	ruxolitinib	0.94	37.6	0.0	38.6
L	interferon beta 1a	1.93	30.6	0.5	3.6
L	pertuzumab	1.67	29.6	0.0	28.9
C	ranolazine	0.95	29.4	0.9	29.5
L	teriflunomide	0.59	25.7	0.1	31.9
J	immunoglobulins, normal human, for extravascular adm.	0.77	22.8	0.0	1.0
B	dabigatran	1.57	22.3	1.8	26.7
J	dolutegravir	0.80	19.7	0.1	17.5
L	ustekinumab	1.33	19.5	0.1	20.8
B	activated heptacog alpha (recombinant DNA coagulation factor VII)	1.01	18.8	0.0	20.8
R	omalizumab	0.60	18.7	0.1	25.7
M	denosumab	0.72	18.5	2.4	16.5
L	abatacept	0.95	17.7	0.1	16.9
B	rivaroxaban	1.89	17.0	2.8	21.7
L	tocilizumab	0.83	15.8	0.1	22.9
S	aflibercept	0.83	15.8	0.2	26.4
J	human immunoglobulin intravenous use	0.76	15.0	0.0	19.6
L	fulvestrant	0.57	13.3	0.2	13.3
L	fingolimod	2.07	13.2	0.1	15.0

* selected among the top 100 active ingredients at the highest per capita expenditure

Section 3

Detailed analysis of pharmaceutical expenditure and consumption

National Report
on Medicines
use in Italy
Year 2017

3.2 Therapeutic categories

In the following pages data are reported on the following categories:

- Antineoplastic agents
- Medications for hypertension and heart failure
- Immunosuppressants and immunomodulators
- Lipid-lowering agents
- Antiplatelets and anticoagulants
- Antiasthmatics
- Anti-HCV agents
- Antacid and antiulcer medications
- Antidiabetic agents
- Antibiotics
- Anti-HIV agents
- Medications for multiple sclerosis
- Medications for osteoporosis
- Coagulation factors
- Vaccines
- Pain relief medications
- Medications for eye disorders
- Antidepressants
- Medication for genitourinary disorders
- Antipsychotics
- Parkinson disease medications
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Thyroid disease medications
- Medications for cystic fibrosis
- Antidementia medications

Table 3.2.1. Largest prescription medicine groups in 2017

Group Subgroup	Total Expenditure (in mil)	% on NHS expenditure	Per capita expenditure	Δ% 17/16	DDD/ 1000 inhabdie	Δ% 17/16
Antineoplastic agents	**2,935.1**	**13.2**	**48.44**	**11.4**	**9.5**	**2.8**
Monoclonal antibodies	1,233.6	5.6	20.36	21.7	1.0	13.5
Protein kinase inhibitors	778.5	3.5	12.85	5.2	0.4	17.1
Cytostatic antineoplastics - cytostatic – others	175.5	0.8	2.90	10.2	0.4	1.9
Cytostatic antineoplastics – antimetabolites	148.4	0.7	2.45	-6.1	0.7	-4.8
Endocrine therapy - hormones and GnRH analogs	108.8	0.5	1.80	-3.6	1.0	0.2
Endocrine therapy - aromatase inhibitors	107.4	0.5	1.77	6.9	2.8	6.3
Endocrine therapy - other hormonal antagonists	105.6	0.5	1.74	-4.6	0.1	4.7
Endocrine therapy – antiandrogens	62.9	0.3	1.04	39.5	1.1	-4.5
Cytotoxic antineoplastics - products derived from natural-taxanes	41.3	0.2	0.68	1.8	0.2	11.4
Endocrine therapy - anti-estrogens	40.3	0.2	0.66	10.9	1.1	0.6
Cytotoxic antineoplastics - products of natural derivation – other	33.7	0.2	0.56	-0.1	0.1	2.5
Cytostatic antineoplastics - alkylating agents	30.4	0.1	0.50	-28.4	0.2	-19.8
Antineoplastic – other	29.6	0.1	0.49	>100	<0.05	>100
Cytotoxic antineoplastics - cytotoxic-anthracycline antibiotics and related active ingredients	28.3	0.1	0.47	-5.3	0.1	-7.2
Cytotoxic antineoplastics - cytotoxic antibiotics – other	5.6	0.0	0.09	-3.0	0.1	-9.9
Cytostatic antineoplastics - platinum compounds	5.3	0.0	0.09	-8.9	0.2	3.1
Hypertension and heart failure	**2,031.6**	**9.1**	**33.53**	**-6.1**	**370.5**	**-0.3**
Beta-blocking agents	301.3	1.4	4.97	1.8	43.1	1.3
Calcium channel blockers (diidro.)	262.9	1.2	4.34	-2.6	51.2	-2.1
ACE inhibitors	238.9	1.1	3.94	-2.3	87.4	-1.4
Renin-angiotensin-aldosterone system inhibitors, combinations	212.6	1.0	3.51	-4.7	29.5	-3.9
Renin-angiotensin-aldosterone system inhibitors, combinations, plain	205.4	0.9	3.39	-2.0	47.8	-1.0
ACE inhibitors and diuretics, combinations	171.7	0.8	2.83	-6.2	22.1	-4.1
ACE inhibitors and calcium channel blockers, combinations	104.7	0.5	1.73	-0.9	10.5	9.7
Olmesartan+amlodipine	92.7	0.4	1.53	8.5	4.8	13.4
Olmesartan	82.5	0.4	1.36	-43.3	8.6	7.1
Alpha-adrenoreceptor antagonists	74.5	0.3	1.23	-1.6	7.6	-1.4
Olmesartan+Hydrochlorothiazide	71.7	0.3	1.18	-45.5	7.2	2.1
High-ceiling diuretics and potassium-sparing agents	63.4	0.3	1.05	-0.9	30.5	-0.6
Beta blocking agents and diuretics, combination	46.0	0.2	0.76	-2.0	7.3	2.9
Diuretics and potassium-sparing agents	32.0	0.1	0.53	14.1	3.5	16.5

Group Subgroup	Total Expenditure (in mil)	% on NHS expenditure	Per capita expenditure	Δ% 17/16	DDD/ 1000 inhab die	Δ% 17/16
Calcium channel blockers (not diidro.)	23.7	0.1	0.39	-8.6	2.8	-8.1
ACE inhibitors, combinations	19.7	0.1	0.32	>100	1.6	>100
Thiazides (including combinations)	15.3	0.1	0.25	-3.7	4.7	-4.1
renin-angiotensin-aldosterone system inhibitors and neprilisin inhibitors	7.6	0.0	0.13	0.0	0.1	0.0
Aliskiren	5.1	0.0	0.08	-18.0	0.3	-18.4
Immunosuppressants and immunomodulators	**1,644.2**	**7.4**	**27.14**	**10.8**	**4.5**	**8.7**
Tumor necrosis factor alpha (TNF-) inhibitors	662.7	3.0	10.94	2.4	1.1	7.1
Immunosuppressants and immunomodulators, others	300.9	1.4	4.97	9.7	0.1	21.7
Immunosuppressants selective	267.9	1.2	4.42	23.6	0.6	14.4
Interleukin inhibitors	212.6	1.0	3.51	56.9	0.3	59.1
Calcineurin inhibitors	92.5	0.4	1.53	1.2	0.6	5.0
Growth factors (G-CSF)	57.5	0.3	0.95	-6.9	0.1	7.1
Immunosuppressant	41.6	0.2	0.69	-5.7	1.6	2.7
Interferons	8.4	0.0	0.14	-31.4	0.0	-28.5
Lipid lowering agents	**1,091.1**	**4.9**	**18.01**	**5.2**	**88.8**	**4.8**
Statins	638.2	2.9	10.53	0.9	74.9	3.9
Ezetimibe plain or in combination	305.4	1.4	5.04	13.2	7.2	14.3
Omega 3	112.5	0.5	1.86	5.7	4.1	7.1
Fibrates	22.4	0.1	0.37	0.9	2.6	2.0
PCSK9 inhibitor	6.7	0.0	0.11	>100	<0.05	>100
MTP inhibitors	6.0	0.0	0.10	-5.2	<0.05	5.0
Statins and fibrates	0.0	0.0	0.00	>100	<0.05	>100
Antiplatelet agents and anticoagulants	**1,027.7**	**4.6**	**16.96**	**7.9**	**92.3**	**1.7**
New Oral Anticoagulant (NOA)	378.4	1.7	6.25	36.0	7.3	37.2
Low molecular weight heparins	295.5	1.3	4.88	-6.8	9.2	-2.9
Platelet aggregation inhibitors excluding clopidogrel, prasugrel and ticagrelor	107.7	0.5	1.78	-3.8	57.6	-0.5
Clopidogrel plain or in combination	89.9	0.4	1.48	1.4	11.1	5.7
Antiplatelet agents with vasodilator effect	54.2	0.2	0.89	2.4	0.0	0.8
Ticagrelor	45.3	0.2	0.75	8.0	0.8	12.7
Fondaparinux	17.0	0.1	0.28	4.6	0.5	6.7
Vitamin K antagonists	12.7	0.1	0.21	-9.3	5.1	-8.9
Heparin	10.3	0.0	0.17	-5.6	0.4	-6.7
Prasugrel	6.9	0.0	0.11	-20.5	0.2	-19.9
Glycoprotein IIb/IIIa inhibitors	6.4	0.0	0.11	-16.6	<0.05	-7.3
Antithrombin III	3.3	0.0	0.05	-15.5	<0.05	-5.4
Antiasthmatics	**984.3**	**4.4**	**16.25**	**-0.6**	**33.6**	**-1.8**
Beta2 agonists in combination	528.5	2.4	8.72	4.4	13.5	3.9
Bronchodilators - anticholinergics	192.9	0.9	3.18	-7.8	6.4	-1.7
Anti-inflammatory - cortisone inha.	138.5	0.6	2.29	-5.1	6.2	-5.6
Bronchodilators - beta-2-adrenoreceptor agonists	52.6	0.2	0.87	-13.2	4.7	-9.6
Other antiasthmatic	37.1	0.2	0.61	18.3	0.1	17.6
Antagonists of leukotrienic receptors	29.1	0.1	0.48	-4.0	2.0	-2.0
Bronchodilators - theophylline	4.4	0.0	0.07	-9.5	0.6	-12.0
Anti-inflammatories - chromones	1.2	0.0	0.02	-13.8	0.1	-13.8

Group Subgroup	Total Expenditure (in mil)	% on NHS expenditure	Per capita expenditure	Δ% 17/16	DDD/ 1000 inhab die	Δ% 17/16
Anti-HCV agents	**945.9**	**4.3**	**15.61**	**-52.3**	**0.3**	**-21.7**
Anti-HCV anti-viral in combination	619.9	2.8	10.23	-42.8	0.2	41.6
Other antiviral HCV	324.7	1.5	5.36	-63.5	0.1	-50.0
Nucleosides and nucleotides excluding reverse transcriptase inhibitors	0.7	0.0	0.01	-66.6	<0.05	-62.5
Inhibitors of HCV proteases	0.5	0.0	0.01	-91.5	<0.05	-90.3
Antacids and anti-ulcer	**912.4**	**4.1**	**15.06**	**-2.0**	**79.8**	**-1.5**
Proton pump inhibitors	808.6	3.6	13.35	-2.8	71.4	-1.5
Other drugs for peptic ulcer	51.4	0.2	0.85	-1.0	4.0	-1.0
H2 receptor antagonists	26.2	0.1	0.43	26.1	2.3	-1.9
Antacids	25.4	0.1	0.42	0.6	2.0	0.4
Prostaglandins	0.7	0.0	0.01	-12.2	<0.05	-12.0
Antidiabetic	**904.0**	**4.1**	**14.92**	**0.8**	**62.7**	**0.8**
Insulins and analogs	435.7	2.0	7.19	-2.7	15.4	1.1
Gliptins (DPP-4 inhibitors) plain or in combination	144.0	0.6	2.38	-7.7	5.1	6.8
Metformin	88.4	0.4	1.46	5.4	21.6	3.1
Glucagon-like peptide 1	80.3	0.4	1.32	24.5	1.3	33.0
Other oral hypoglycemic agents	56.5	0.3	0.93	-5.2	13.1	-8.1
Gliflozine plain or in combination	44.1	0.2	0.73	86.2	1.4	94.1
Pioglitazone plain or in combination	30.6	0.1	0.50	-11.2	1.7	-8.0
Repaglinide	24.4	0.1	0.40	-9.9	3.0	-9.8
Antibiotics	**827.7**	**3.7**	**13.66**	**-2.1**	**21.4**	**-1.6**
Penicillin combinations (including beta lactamase inhibitors)	205.3	0.9	3.39	-0.6	9.3	0.3
Quinolones	133.8	0.6	2.21	-2.5	3.1	-3.0
Cephalosporine im/ev III-IV gen	106.3	0.5	1.76	-4.3	0.6	-1.0
Macrolides and lincosamides	98.9	0.4	1.63	-6.0	3.7	-4.0
Oral cephalosporins	90.6	0.4	1.50	-0.3	1.6	-0.5
Antibiotics vs resistant germs	68.9	0.3	1.14	6.0	0.0	35.2
Glycopeptides	40.5	0.2	0.67	-12.4	0.1	-1.5
Broad-spectrum penicillins and penicillins sensitive to beta lactamases	19.6	0.1	0.32	-5.1	1.9	-6.7
Carbapenems	15.4	0.1	0.25	3.2	<0.05	6.8
Other	13.7	0.1	0.23	-4.5	<0.05	1.7
Aminoglycosides	12.3	0.1	0.20	18.7	0.1	-4.9
Cephalosporine im/ev I gen	7.0	0.0	0.12	-1.0	0.1	6.5
Tetracycline	4.5	0.0	0.07	-0.4	0.3	-0.4
Cephalosporine im/ev II gen	4.1	0.0	0.07	-11.1	0.1	-7.2
Sulfonamides and trimetropim	4.1	0.0	0.07	3.5	0.3	4.1
Monobactams	2.7	0.0	0.04	-21.1	<0.05	-20.9
Anti-HIV anti-virals	**683.8**	**3.1**	**11.29**	**-0.9**	**2.4**	**-0.7**
Anti-HIV anti-virals in coformulated regimens	253.5	1.1	4.18	30.9	0.5	28.2
Nucleosides and nucleotides inhibitors of reverse transcriptase	170.5	0.8	2.81	-20.1	0.9	-6.6
Protease inhibitors plain or in combination	128.0	0.6	2.11	-12.0	0.4	-8.9
Integrase inhibitors	96.4	0.4	1.59	1.3	0.3	1.4

Group Subgroup	Total Expenditure (in mil)	% on NHS expenditure	Per capita expenditure	Δ% 17/16	DDD/ 1000 inhab die	Δ% 17/16
Non-nucleoside inhibitors of reverse transcriptase	25.0	0.1	0.41	-17.0	0.2	-12.4
Other anti-viral antivirals	10.4	0.0	0.17	-17.1	<0.05	-15.4
Multiple sclerosis drugs	**583.7**	**2.6**	**9.63**	**47.6**	**1.0**	**28.9**
Interferons beta	152.1	0.7	2.51	49.3	0.5	10.3
Fingolimod	125.7	0.6	2.07	13.2	0.1	15.0
Monoclonal antibody	101.3	0.5	1.67	13.3	0.1	8.4
dimethylfumarate	100.8	0.5	1.66	-	0.1	-
Glatiramer	67.8	0.3	1.12	4.9	0.1	5.5
Teriflunomide	36.0	0.2	0.59	25.7	0.1	31.9
Osteoporosis drugs	**514.5**	**2.3**	**8.49**	**11.9**	**24.7**	**8.5**
Vitamin D and analogs	260.7	1.2	4.30	23.1	12.6	16.9
Teriparatide	85.4	0.4	1.41	26.0	0.2	17.5
Oral and injectable bisphosphonates	84.6	0.4	1.40	0.0	6.7	1.6
Denosumab	43.7	0.2	0.72	18.3	2.4	16.4
Alendronic acid + colecalciferol	38.9	0.2	0.64	-31.9	2.7	-11.7
SERM (selective estrogen-receptor modulators)	0.9	0.0	0.01	-6.9	0.1	-7.0
Strontium ranelate	0.2	0.0	0.00	-47.6	<0.05	-47.8
Coagulation factors	**488.2**	**2.2**	**8.06**	**6.3**	**0.1**	**5.6**
Hemophilia A (recombinant)	307.1	1.4	5.07	2.3	<0.05	5.3
Factor VII deficiency (recombinant)	61.2	0.3	1.01	18.8	<0.05	20.8
Hemophilia A (plasma derived)	57.1	0.3	0.94	-2.2	<0.05	-8.3
Hemophilia B (recombinant)	51.5	0.2	0.85	28.4	<0.05	1.8
Von Willebrand's disease	4.0	0.0	0.07	51.2	<0.05	53.8
Factor VII deficiency (plasma derived)	3.4	0.0	0.06	39.5	<0.05	18.6
Other deficiencies of coagulation factors (recombinant)	2.3	0.0	0.04	30.0	<0.05	33.0
Hemophilia B (plasma derivatives)	1.0	0.0	0.02	-22.7	<0.05	-20.4
Other deficiencies of coagulation factors (plasma-derived)	0.5	0.0	0.01	-17.9	<0.05	-4.2
Vaccines	**487.6**	**2.2**	**8.05**	**36.6**	**1.0**	**-15.6**
Meningococcal vaccines	164.3	0.7	2.71	>100	0.2	61.7
Pneumococcal vaccines	100.8	0.5	1.66	8.8	0.1	9.7
Bacterial and viral vaccines in combination	76.6	0.3	1.26	5.0	0.1	2.4
Flu vaccines	47.1	0.2	0.78	16.6	0.4	-37.6
Soft vaccines	35.7	0.2	0.59	66.2	0.1	25.1
Vaccines against papillomavirus	23.1	0.1	0.38	17.4	<0.05	-4.7
Varicellosis zoster vaccines	10.5	0.0	0.17	16.9	<0.05	-7.4
Pertussis vaccines	7.9	0.0	0.13	64.0	<0.05	53.1
Vaccines of rotavirus diarrhea	7.9	0.0	0.13	64.4	<0.05	56.0
Hepatitis vaccines	7.4	0.0	0.12	17.8	<0.05	3.8
Other vaccines	6.3	0.0	0.10	29.4	<0.05	-9.3
Pain therapy	**423.9**	**1.9**	**7.00**	**-3.6**	**7.0**	**1.0**
Major opioids	237.1	1.1	3.91	8.2	2.1	3.9
Neuropathic pain	127.6	0.6	2.11	-19.8	2.4	4.0
Minor opioids/opioids in combination	59.2	0.3	0.98	-3.9	2.4	-4.0
Drugs for eye disorders	**369.9**	**1.7**	**6.11**	**2.9**	**20.6**	**0.5**
Other antiglaucoma preparations	152.4	0.7	2.52	3.0	14.4	0.8
Antineovascular agents	118.0	0.5	1.95	7.9	0.3	18.5

Group Subgroup	Total Expenditure (in mil)	% on NHS expenditure	Per capita expenditure	Δ% 17/16	DDD/ 1000 inhab die	Δ% 17/16
Prostaglandin analogues plain or in combination with beta blocking agents	78.6	0.4	1.30	-5.7	5.7	-1.4
Corticosteroids (intravitreal plants)	20.6	0.1	0.34	11.5	0.2	13.1
Cortisteroids	0.2	0.0	0.00	8.1	<0.05	-2.0
Ocriplasmin	0.1	0.0	0.00	-41.9	<0.05	-48.2
Antidepressants	**369.0**	**1.7**	**6.09**	**2.9**	**40.4**	**1.7**
Antidepressant - SSRI	197.8	0.9	3.26	-1.6	29.1	-0.1
Antidepressant - SNRI	87.8	0.4	1.45	-0.8	6.2	1.2
Antidepressant - other	42.8	0.2	0.71	4.1	2.9	5.3
Antidepressant - SMS (serotonin modulators and stimulators)	19.7	0.1	0.33	238.7	0.8	>100
Antidepressant - tricyclic	10.5	0.0	0.17	-5.6	1.1	-5.3
Bupropion	9.9	0.0	0.16	-6.4	0.2	-4.8
Antidepressant - NaRI (norepinephrine reuptake inhibitors)	0.6	0.0	0.01	-15.9	<0.05	-14.6
Agomelatine	0.0	0.0	0.00	-22.6	<0.05	-26.3
Medicines for genitourinary disorders	**333.5**	**1.5**	**5.51**	**-7.6**	**34.5**	**2.3**
Alpha blocking agents	174.1	0.8	2.87	2.9	24.4	2.7
5-alpha reductase inhibitors	159.3	0.7	2.63	-17.0	10.1	1.3
Beta 3 selective agonist	0.1	0.0	0.00	6.6	<0.05	8.8
Alpha blocking agents in combination	0.0	0.0	0.00	>100	<0.05	>100
Antipsychotics	**259.7**	**1.2**	**4.29**	**-0.9**	**9.3**	**2.4**
Atypical and other antipsychotics	236.5	1.1	3.90	-0.7	6.7	4.7
Typical antipsychotics	23.2	0.1	0.38	-3.6	2.6	-3.0
Antiparkinson	**193.3**	**0.9**	**3.19**	**-8.5**	**5.1**	**2.2**
Dopamine-agonist	77.2	0.3	1.27	1.5	1.3	-1.5
Dopa-derivatives agonists	74.1	0.3	1.22	-6.4	2.3	1.2
MAO-B inhibitors	39.7	0.2	0.65	-25.6	1.4	7.9
COMT inhibitors	2.2	0.0	0.04	-10.1	<0.05	-8.5
Amantadine	0.1	0.0	0.00	-3.7	<0.05	-4.6
NSAIDs	**174.8**	**0.8**	**2.89**	**-10.4**	**19.2**	**-3.7**
NSAIDs (traditional)	101.0	0.5	1.67	-4.0	12.6	-2.6
Coxib	56.7	0.3	0.94	-21.4	3.8	-7.0
Nimesulide	10.6	0.0	0.17	-5.3	2.2	-5.1
Ketorolac	6.6	0.0	0.11	0.1	0.6	2.2
Thyroid medications	**59.6**	**0.3**	**0.98**	**6.6**	**21.6**	**1.3**
Thyroid hormones	56.4	0.3	0.93	7.1	20.3	1.5
Antithyroid preparations	3.1	0.0	0.05	-1.7	1.4	-1.2
Drugs for cystic fibrosis	**47.8**	**0.2**	**0.79**	**43.5**	**<0.05**	**82.8**
Antidementia drugs	**33.2**	**0.1**	**0.55**	**-20.1**	**2.4**	**0.6**
Anticholinesterase	23.4	0.1	0.39	-14.8	1.5	-0.6
Other antidementia drugs	9.8	0.0	0.16	-30.4	0.9	2.6

Antineoplastic agents

Figure 3.2.2. Antineoplastic agents, trend of consumption (2013-2017)

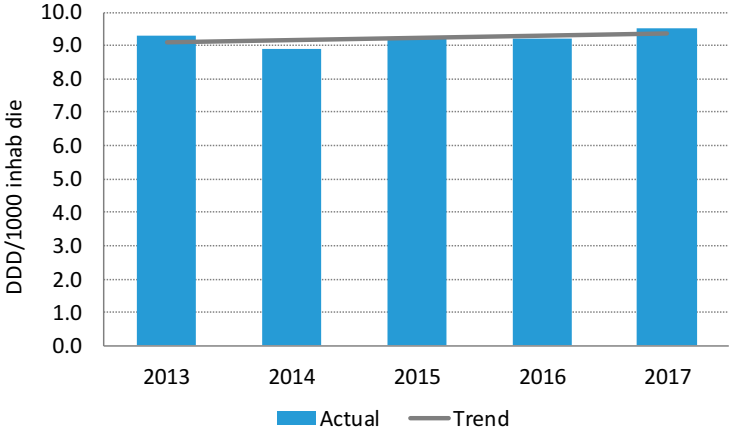


Table 3.2.2a. Antineoplastic agents, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Monoclonal antibodies	0.6	0.7	0.8	0.9	1.0	13.5
Protein kinase inhibitors	-	-	-	0.3	0.4	17.1
Cytostatic antineoplastic - cytostatic – others	0.4	0.4	0.4	0.4	0.4	1.9
Cytostatic antineoplastics – antimetabolites	0.9	0.9	0.9	0.7	0.7	-4.8
Endocrine therapy - hormones and GnRH analogs	1.6	1.0	1.0	1.0	1.0	0.2
Endocrine therapy - aromatase inhibitors	2.3	2.4	2.5	2.7	2.8	6.3
Endocrine therapy - other hormonal antagonists	0.1	0.1	0.1	0.1	0.1	4.7
Endocrine therapy – antiandrogens	1.1	1.2	1.1	1.1	1.1	-4.5
Cytotoxic antineoplastics - products derived from natural-taxanes	0.1	0.1	0.2	0.2	0.2	11.4
Endocrine therapy - anti-estrogens	1.2	1.2	1.1	1.1	1.1	0.6
Cytotoxic antineoplastics - products of natural derivation – other	0.1	0.1	0.1	0.1	0.1	2.5
Cytostatic antineoplastics - alkylating agents	0.2	0.2	0.2	0.2	0.2	-19.8
Antineoplastic – other				0.0	0.0	>100
Cytotoxic antineoplastics - cytotoxic-anthracycline antibiotics and related active ingredients	0.1	0.1	0.1	0.1	0.1	-7.2
Cytotoxic antineoplastics - cytotoxic antibiotics – other	0.1	0.1	0.1	0.1	0.1	-9.9
Cytostatic antineoplastics - platinum compounds	0.2	0.2	0.2	0.2	0.2	3.1
Antineoplastic agents	**9.3**	**8.9**	**9.2**	**9.2**	**9.5**	**2.8**
trastuzumab	0.1	0.1	0.2	0.2	0.2	7.3
bevacizumab	0.1	0.1	0.1	0.1	0.1	5.4
rituximab	0.4	0.4	0.4	0.5	0.6	7.0
nivolumab	0.0	0.0	0.0	0.0	0.0	253.8
imatinib	0.1	0.1	0.1	0.1	0.1	-3.4
pertuzumab	0.0	0.0	0.0	0.0	0.0	28.9
abiraterone	0.0	0.0	0.0	0.0	0.0	0.8
ibrutinib	-	-	-	0.0	0.0	113.5
bortezomib	0.1	0.1	0.1	0.1	0.1	-4.4

Table 3.2.2c. Antineoplastic agents, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Monoclonal antibodies	20.36	21.7	1.0	13.5
Protein kinase inhibitors	12.85	5.2	0.4	17.1
Cytostatic antineoplastic - cytostatic – other	2.90	10.2	0.4	1.9
Cytostatic antineoplastics – antimetabolites	2.45	-6.1	0.7	-4.8
Endocrine therapy - hormones and analogous gnrh	1.80	-3.6	1.0	0.2
Endocrine therapy - aromatase inhibitors	1.77	6.9	2.8	6.3
Endocrine therapy - other hormonal antagonists	1.74	-4.6	0.1	4.7
Endocrine therapy – antiandrogens	1.04	39.5	1.1	-4.5
Cytotoxic antineoplastics - natural products - taxanes	0.68	1.8	0.2	11.4
Endocrine therapy - anti-estrogens	0.66	10.9	1.1	0.6
Cytotoxic antineoplastics - products of natural derivation - other	0.56	-0.1	0.1	2.5
Cytostatic antineoplastics - alkylating agents	0.50	-28.4	0.2	-19.8
Antineoplastic –other	0.49	-	0.0	>100
Cytotoxic antineoplastics - cytotoxic - anthracycline antibiotics and related active ingredients	0.47	-5.3	0.1	-7.2
Cytotoxic antineoplastics - cytotoxic antibiotics - other	0.09	-3.0	0.1	-9.9
Cytostatic antineoplastics - platinum compounds	0.09	-8.9	0.2	3.1
Antineoplastic agents	**48.44**	**11.4**	**9.5**	**2.8**
trastuzumab	4.62	1.9	0.2	7.3
bevacizumab	3.68	1.7	0.1	5.4
rituximab	3.07	-1.8	0.6	7.0
nivolumab	3.00	>100	0.0	>100
imatinib	1.73	-36.9	0.1	-3.4
pertuzumab	1.67	29.6	0.0	28.9
abiraterone	1.63	-5.4	0.0	0.8
ibrutinib	1.34	>100	0.0	>100
bortezomib	1.25	-4.7	0.1	-4.4
dasatinib	1.19	5.1	0.0	5.3

Table 3.2.2d. Prescription of antineoplastic agents patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Expired patent	3.49	7.2	57.8	5.0	53.1	3.5	1.90
Equivalent	1.09	31.2	20.4	2.9	57.3	30.9	1.03
Ex originator	2.40	68.8	83.6	2.2	42.7	-2.5	3.06
Patent covered	44.95	92.8	8.9	4.5	46.9	2.2	27.63
Antineoplastic agents	**48.44**	**100.0**	**11.4**	**9.5**	**100.0**	**2.8**	**13.98**

** the monthly transparency lists published by the Italian Medicines Agency in 2017 were used*

Medicines for hypertension and heart failure

Figure 3.2.3a. Medicines for hypertension and heart failure, consumption trend (2013-2017)

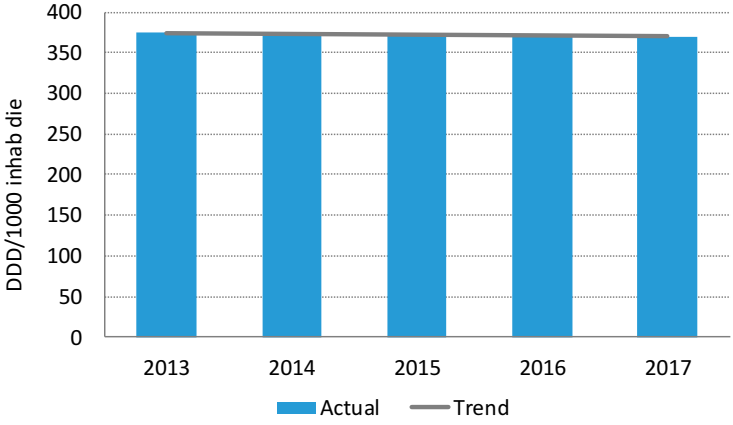


Table 3.2.3a. Medicines for hypertension and heart failure, consumption (DDD/1000 inhab die) by therapeutic category and active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Beta-blocking agents	41.6	41.8	42.2	42.5	43.1	1.3
Calcium channel blockers (dihydro)	55.1	54.0	52.8	52.2	51.2	-2.1
ACE inhibitors	91.3	90.6	89.3	88.6	87.4	-1.4
Angiotensin II antag. and diur (ass)	34.0	32.9	31.7	30.8	29.5	-3.9
Angiotensin II antag. Plain	49.4	49.1	48.5	48.3	47.8	-1.0
ACE inhibitors and diur. (ass)	25.9	25.0	23.9	23.0	22.1	-4.1
ACE inhibitors and calcium channel blockers (ass)	5.0	6.6	8.0	9.6	10.5	9.7
Olmesartan+amlodipin	2.3	2.8	3.6	4.2	4.8	13.4
Olmesartan	7.0	7.3	7.7	8.0	8.6	7.1
Alpha-blocking agents peripheral	7.8	7.8	7.7	7.7	7.6	-1.4
Olmesartan+idroclorotiazide	6.2	6.6	6.9	7.1	7.2	2.1
High-ceiling diuretics plain or in comb. with potassium-sparing agents	29.3	29.7	30.7	30.7	30.5	-0.6
Beta blocking agents in combination with diuretics	5.8	6.4	6.7	7.1	7.3	2.9
Potassium-sparing agents	3.4	3.5	3.5	3.0	3.5	16.5
Calcium channel blockers (not dihydro)	3.9	3.6	3.3	3.0	2.8	-8.1
ACE inhibitors, other associations	0.0	0.0	0.0	0.5	1.6	>100
Thiazide diuretics and similar, plain or in comb.	5.8	5.5	5.2	4.9	4.7	-4.1
Medicines for hypertension and heart failure	**374.6**	**373.8**	**372.3**	**371.6**	**370.5**	**-0.3**
bisoprolol	7.6	8.2	8.9	9.5	10.2	7.0
ramipril	60.9	62.1	62.7	63.6	63.6	0.1
amlodipin	28.5	28.2	27.8	27.7	27.4	-1.2
olmesartan/amlodipin	2.3	2.8	3.6	4.2	4.8	13.4
nebivolol	13.2	13.5	13.9	14.3	14.7	2.9
olmesartan	7.0	7.3	7.7	8.0	8.6	7.1
doxazosin	8.1	8.0	7.9	7.7	7.6	-1.3
olmesartan/idroclorotiazide	6.2	6.6	6.9	7.1	7.2	2.1
valsartan/idroclorotiazide	11.6	11.3	10.9	10.6	10.2	-3.8
valsartan	14.6	14.8	14.8	14.9	14.9	0.1

Table 3.2.3c. Medicines for hypertension and heart failure, prescription by therapeutic category and active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Beta-blocking agents	4.97	1.8	43.1	1.3
Calcium channel blockers (dihydro)	4.34	-2.6	51.2	-2.1
ACE inhibitors	3.94	-2.3	87.4	-1.4
Angiotensin II antag. and diur. (ass)	3.51	-4.7	29.5	-3.9
Angiotensin II antag.	3.39	-2.0	47.8	-1.0
ACE inhibitors and diur. (ass)	2.83	-6.2	22.1	-4.1
ACE inhibitors e calcium channel blockers (ass)	1.73	-0.9	10.5	9.7
Olmesartan+amlodipin	1.53	8.5	4.8	13.4
Olmesartan	1.36	-43.3	8.6	7.1
Alpha blocking agents peripheral	1.23	-1.6	7.6	-1.4
Olmesartan+idroclorotiazide	1.18	-45.5	7.2	2.1
High-ceiling diuretics plain or in comb. with potassium-sparing agents	1.05	-0.9	30.5	-0.6
Beta-blocking agents and diur. (ass)	0.76	-2.0	7.3	2.9
Potassium-sparing agents	0.53	14.1	3.5	16.5
Calcium channel blockers (not dihydro)	0.39	-8.6	2.8	-8.1
ACE inhibitors, other associations	0.32	>100	1.6	>100
Thiazide diuretics and similar, plain or in comb.	0.25	-3.7	4.7	-4.1
Medicines for hypertension and heart failure	**33.53**	**-6.1**	**370.5**	**-0.3**
bisoprolol	2.16	7.4	10.2	7.0
ramipril	2.02	0.2	63.6	0.1
amlodipin	1.55	-1.3	27.4	-1.2
olmesartan/amlodipin	1.53	8.5	4.8	13.4
nebivolol	1.37	1.9	14.7	2.9
olmesartan	1.36	-43.3	8.6	7.1
doxazosin	1.21	-1.4	7.6	-1.3
olmesartan/idroclorotiazide	1.18	-45.5	7.2	2.1
valsartan/idroclorotiazide	1.08	-4.2	10.2	-3.8
valsartan	0.91	-0.2	14.9	0.1

Table 3.2.3d. Prescription of medicine for hypertension and heart failure patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	27.30	81.4	10.2	338.4	91.3	5.1	0.22
Equivalent	6.83	25.0	6.3	117.3	34.7	-43.9	0.16
Ex originator	20.47	75.0	11.6	221.1	65.3	5.7	0.25
Patent covered	6.23	18.6	-43.0	32.1	8.7	-35.5	0.53
Medicines for hypertension and heart failure	**33.53**	**100.0**	**-6.1**	**370.5**	**100.0**	**-0.3**	**0.25**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Immunosuppressants and immunomodulators

Figure 3.2.4a. Immunosuppressant and immunomodulating agents, consumption trend (2013-2017)

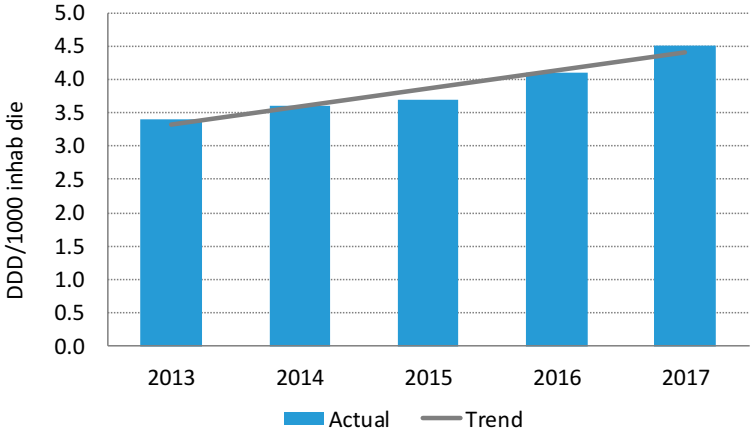


Table 3.2.4a. Immunosuppressant and immunomodulating agents, consumption (DDD/1000 inhab die) by therapeutic category and by substance active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Tumor necrosis factor alpha (TNF-alpha) inhibitors	0.9	0.9	1.0	1.0	1.1	7.1
Other immunosuppressant and immunomodulating agents	0.2	0.2	0.2	0.1	0.1	21.7
Selective Immunosuppressant	0.6	0.6	0.6	0.6	0.6	14.4
Interleukin inhibitors	0.1	0.1	0.1	0.2	0.3	59.1
Calcineurin inhibitors	0.6	0.6	0.6	0.6	0.6	5.0
Growth factor (G-CSF)	0.1	0.1	0.1	0.1	0.1	7.1
Immunosuppressant	0.2	0.2	0.1	0.0	0.0	-28.5
Interferons	0.9	0.9	1.0	1.0	1.1	7.1
Immunosuppressant and immunomodulating agents	**2.5**	**2.6**	**2.6**	**4.1**	**4.5**	**8.7**
adalimumab	0.3	0.3	0.3	0.4	0.4	7.8
lenalidomide	0.0	0.0	0.0	0.1	0.1	29.2
etanercept	0.3	0.3	0.3	0.3	0.3	2.2
eculizumab	0.0	0.0	0.0	0.0	0.0	15.2
infliximab	0.2	0.3	0.3	0.3	0.3	9.4
ustekinumab	0.1	0.1	0.1	0.1	0.1	20.8
golimumab	0.0	0.1	0.1	0.1	0.1	7.7
abatacept	0.0	0.0	0.0	0.0	0.1	16.9
tocilizumab	0.0	0.0	0.0	0.1	0.1	22.9
secukinumab				0.0	0.1	>100

Table 3.2.4c. Immunosuppressant and immunomodulating agents, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Tumor necrosis factor alpha (TNF-alpha) inhibitors	10.94	2.4	1.1	7.1
Other immunosuppressant and immunomodulating agents	4.97	9.7	0.1	21.7
Selective Immunosuppressant	4.42	23.6	0.6	14.4
Interleukin inhibitors	3.51	56.9	0.3	59.1
Calcineurin inhibitors	1.53	1.2	0.6	5.0
Growth factor (G-CSF)	0.95	-6.9	0.1	7.1
Immunosuppressant	0.69	-5.7	1.6	2.7
Interferons	0.14	-31.4	0.0	-28.5
Immunosuppressants and immunomodulating agents	**27.14**	**10.8**	**4.5**	**8.7**
adalimumab	4.70	7.9	0.4	7.8
lenalidomide	3.35	10.0	0.1	29.2
etanercept	3.02	-5.0	0.3	2.2
eculizumab	1.73	12.3	0.0	15.2
infliximab	1.50	-3.0	0.3	9.4
ustekinumab	1.33	19.5	0.1	20.8
golimumab	1.22	4.5	0.1	7.7
abatacept	0.95	17.7	0.1	16.9
tocilizumab	0.83	15.8	0.1	22.9
secukinumab	0.83	975.1	0.1	969.0

Table 3.2.4d. Prescription of immunosuppressants and immunomodulators agents patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	1.91	7.0	25.9	2.0	45.5	52.1	2.57
Equivalent	0.15	7.8	2.9	0.5	25.5	-39.8	0.78
Ex originator	1.76	92.2	28.4	1.5	74.5	75.7	3.19
Patent covered	25.23	93.0	9.8	2.4	54.5	-12.3	28.37
Immunosuppressant and immunomodulating agents	**27.14**	**100.0**	**10.8**	**4.5**	**100.0**	**8.7**	**16.64**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Lipid lowering agents

Figure 3.2.5a. Lipid lowering agents, trend of consumption (2013-2017)

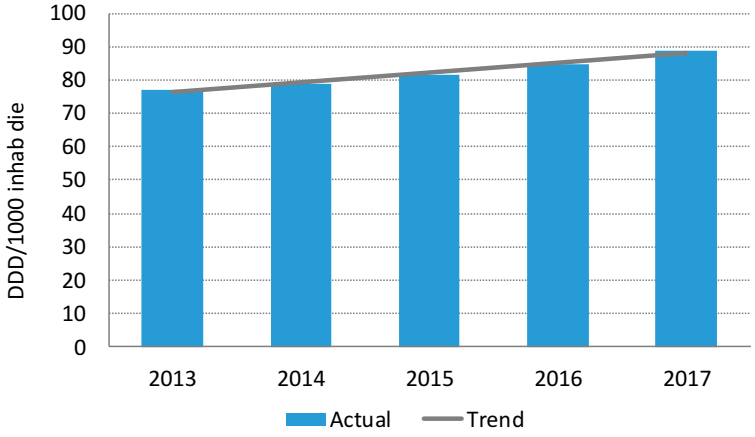


Table 3.2.5a. Lipid lowering agents, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Statins	65.6	67.9	69.8	72.0	74.9	3.9
Ezetimibe plain or in combination	4.4	4.9	5.5	6.3	7.2	14.3
Omega 3	4.5	3.6	3.7	3.8	4.1	7.1
Fibrates	2.4	2.5	2.6	2.6	2.6	2.0
PCSK9 inhibitors	-	-	-	0.0	0.0	>100
MTP inhibitors	-	-	-	0.0	0.0	5.0
Lipid lowering agents	**76.9**	**79.0**	**81.6**	**84.7**	**88.8**	**4.8**
rosuvastatin	15.2	14.0	13.1	12.5	12.1	-2.6
atorvastatin	29.0	33.0	36.2	39.5	43.1	8.9
ezetimibe/simvastatin	3.4	3.5	3.7	3.9	4.2	7.1
ezetimibe	1.0	1.4	1.9	2.4	3.0	26.2
omega 3	4.5	3.6	3.7	3.8	4.1	7.1
simvastatin	16.1	15.7	15.3	15.0	14.6	-2.4
lovastatin	0.9	0.9	1.0	1.1	1.2	6.1
pravastatin	3.1	3.1	3.0	3.0	3.0	-0.4
fenofibrate	2.1	2.3	2.3	2.3	2.4	3.2
lomitapide	15.2	14.0	13.1	12.5	12.1	-2.6

Table 3.2.5c. Lipid lowering agents, prescription by therapeutic category and by active ingredient in 2017

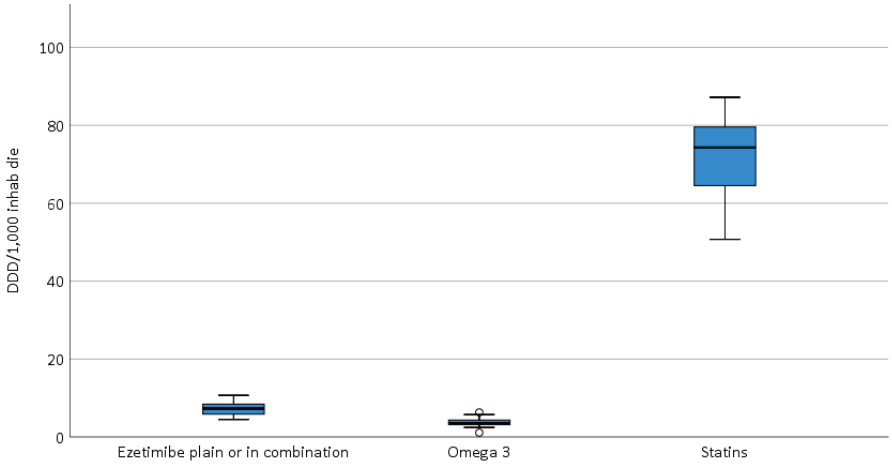
Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Statins	10.53	0.9	74.9	3.9
Ezetimibe plain or in combination	5.04	13.2	7.2	14.3
Omega 3	1.86	5.7	4.1	7.1
Fibrates	0.37	0.9	2.6	2.0
PCSK9 inhibitors	0.11	>100	0.0	>100
MTP inhibitors	0.10	-5.2	0.0	5.0
Lipid lowering agents	**18.01**	**5.2**	**88.8**	**4.8**
rosuvastatin	4.07	-3.2	12.1	-2.6
atorvastatin	3.87	7.8	43.1	8.9
ezetimibe/simvastatin	3.14	6.7	4.2	7.1
ezetimibe	1.90	25.7	3.0	26.2
omega 3	1.86	5.7	4.1	7.1
simvastatin	1.72	-2.8	14.6	-2.4
lovastatin	0.41	5.9	1.2	6.1
pravastatin	0.38	-1.4	3.0	-0.4
fenofibrate	0.34	2.1	2.4	3.2
lomitapide	0.10	-5.2	0.0	5.0

Table 3.2.5d. Prescription of lipid lowering agents patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	8.26	45.9	4.1	68.2	76.8	5.3	0.33
Equivalent	2.41	29.2	7.5	27.1	39.8	-31.9	0.24
Ex originator	5.85	70.8	2.7	41.1	60.2	3.1	0.39
Patent covered	9.75	54.1	6.2	20.6	23.2	3.2	1.30
Lipid lowering agents	**18.01**	**100.0**	**5.2**	**88.8**	**100.0**	**4.8**	**0.56**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Figure 3.2.5d. Lipid lowering agents, regional consumption variability (DDD/1000 inhab die weighed) by subgroup



(The line inside the box represents the median of the regional distribution; the extremes of the box represent the first and third quartiles; the mustache represents the minimum and the maximum).

Platelet aggregation inhibitors and anticoagulants

Figure 3.2.6a. Platelet aggregation inhibitors and anticoagulants, consumption trend (2013-2017)

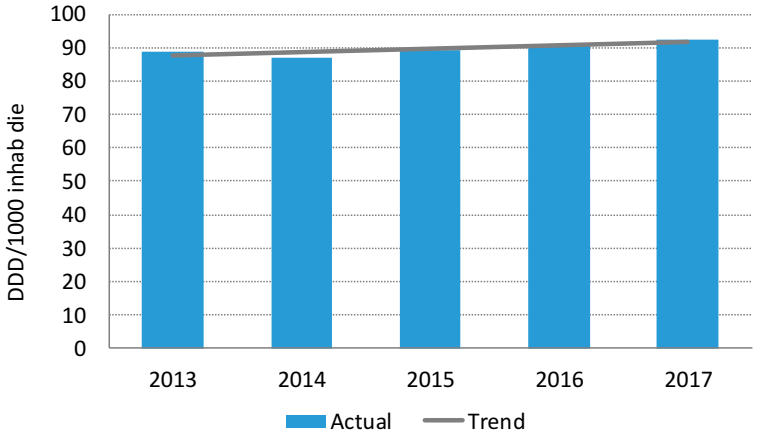


Table 3.2.6a. Platelet aggregation inhibitors and anticoagulants, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
New oral anticoagulants	0.2	1.6	3.4	5.3	7.3	37.2
Low molecular weight heparins	9.7	9.7	9.7	9.5	9.2	-2.9
Platelet aggregation inhibitors excl. clopidogrel, prasugrel and ticagrelor	64.9	60.3	60.2	57.8	57.6	-0.5
Clopidogrel plain or in combination	5.9	7.1	8.1	10.5	11.1	5.7
Platelet aggregation inhibitors with vasodilator effect	0.0	0.0	0.0	0.0	0.0	0.8
Ticagrelor	0.3	0.5	0.6	0.7	0.8	12.7
Fondaparinux	0.3	0.3	0.4	0.4	0.5	6.7
Vitamin K antagonists	6.9	6.5	6.1	5.6	5.1	-8.9
Heparin group	0.5	0.6	0.4	0.5	0.4	-6.7
Prasugrel	0.3	0.3	0.3	0.3	0.2	-19.9
Glycoprotein IIb/IIIa inhibitors	0.0	0.0	0.0	0.0	0.0	-7.3
Direct thrombin III inhibitors	0.0	0.0	0.0	0.0	0.0	-5.4
Platelet aggregation inhibitors and anticoagulants	**89.0**	**86.9**	**89.2**	**90.7**	**92.3**	**1.7**
enoxaparin sodium	7.1	7.5	7.6	7.7	7.3	-4.6
apixaban	0.0	0.2	0.8	1.6	2.3	43.7
rivaroxaban	0.1	0.6	1.5	2.3	2.8	21.7
dabigatran	0.2	0.8	1.1	1.4	1.8	26.5
acetylsalicylic acid	47.0	43.6	44.4	44.5	45.0	1.3
clopidogrel	5.9	7.1	8.1	8.8	9.3	5.2
calcium nadroparin	1.6	1.4	1.4	1.2	1.2	3.6
ticagrelor	0.3	0.5	0.6	0.7	0.8	12.7
treprostinil	0.0	0.0	0.0	0.0	0.0	6.2
edoxaban	-	-	-	0.0	0.4	>100

Table 3.2.6c. Platelet aggregation inhibitors and anticoagulants, prescription by therapeutic category and by active ingredient in 2017

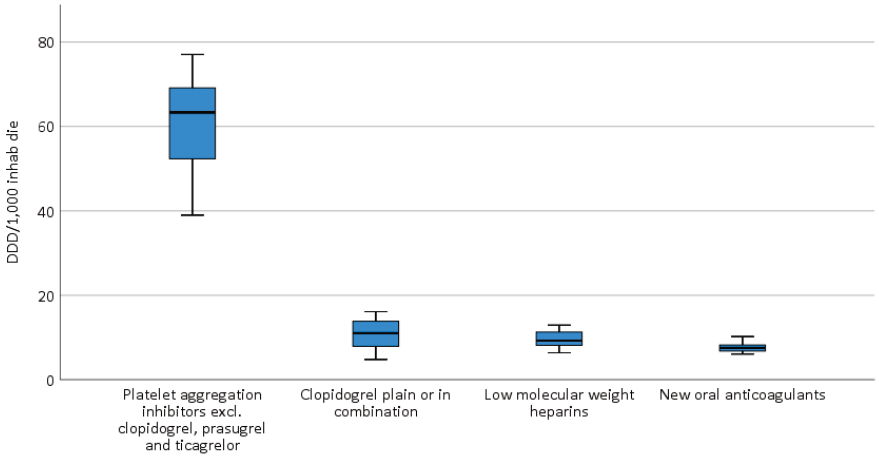
Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
New oral anticoagulants	6.25	36.0	7.3	37.2
Low molecular weight heparins	4.88	-6.8	9.2	-2.9
Platelet aggregation inhibitors excl. clopidogrel, prasugrel and ticagrelor	1.78	-3.8	57.6	-0.5
Clopidogrel plain or in combination	1.48	1.4	11.1	5.7
Platelet aggregation inhibitors with vasodilator effect	0.89	2.4	0.0	0.8
Ticagrelor	0.75	8.0	0.8	12.7
Fondaparinux	0.28	4.6	0.5	6.7
Vitamin K antagonists	0.21	-9.3	5.1	-8.9
Heparin group	0.17	-5.6	0.4	-6.7
Prasugrel	0.11	-20.5	0.2	-19.9
Glycoprotein IIb/IIIa inhibitors	0.11	-16.6	0.0	-7.3
Direct thrombin III inhibitors	0.05	-15.5	0.0	-5.4
Platelet aggregation inhibitors and anticoagulants	**16.96**	**7.9**	**92.3**	**1.7**
enoxaparin sodium	3.55	-9.0	7.3	-4.6
apixaban	2.35	44.3	2.3	43.7
rivaroxaban	1.92	17.0	2.8	21.7
dabigatran	1.59	22.0	1.8	26.5
acetylsalicylic acid	1.16	-0.3	45.0	1.3
clopidogrel	1.10	0.2	9.3	5.2
calcium nadroparin	0.91	0.8	1.2	3.6
ticagrelor	0.75	8.0	0.8	12.7
treprostinil	0.61	5.9	0.0	6.2

Table 3.2.6d. Prescription of platelet aggregation inhibitors and anticoagulants patented expired in 2017*

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	2.55	15.0	-1.8	57.4	62.2	1.0	0.12
Equivalent	0.68	26.6	3.1	16.3	28.4	-61.1	0.11
Ex originator	1.87	73.4	-3.4	41.1	71.6	-1.9	0.12
Patent covered	14.42	85.0	9.8	34.9	37.8	3.0	1.13
Platelet aggregation inhibitors and anticoagulants	**16.96**	**100.0**	**7.9**	**92.3**	**100.0**	**1.7**	**0.50**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Figure 3.2.6d. Platelet aggregation inhibitors and anticoagulants, regional consumption variability (DDD/1000 inhab die weighed) by subgroup



(The line inside the box represents the median of the regional distribution; the extremes of the box represent the first and third quartiles; the mustache represents the minimum and the maximum)

Antiasthmatics

Figure 3.2.7a. Antiasthmatics, consumption trend (2013-2017)

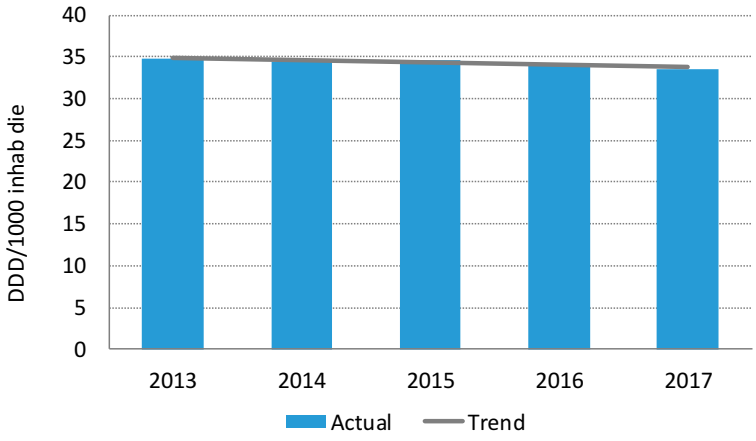


Table 3.2.7a. Antiasthmatics, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Beta-2-adrenoreceptor agonists ass.	11.4	11.6	12.2	13.0	13.5	3.9
Bronchodilators – anticholinergics	6.0	6.4	6.7	6.5	6.4	-1.7
Anti-inflammatory - corticosteroids inha.	7.6	7.2	7.0	6.6	6.2	-5.6
Bronchodilators - beta2 agonists	6.3	6.0	5.7	5.2	4.7	-9.6
Other antiasthmatics	0.0	0.1	0.1	0.1	0.1	17.6
Leukotriene receptor antagonists	2.2	2.1	2.1	2.0	2.0	-2.0
Bronchodilators – theophylline	1.2	1.0	0.8	0.7	0.6	-12.0
Anti-inflammatories – chromones	0.1	0.1	0.1	0.1	0.1	-13.8
Antiasthmatics	**34.8**	**34.5**	**34.6**	**34.2**	**33.6**	**-1.8**
salmeterole/fluticasone	6.0	5.9	5.3	4.4	3.8	-14.2
beclometasone/formoterole	2.5	2.7	2.8	3.0	3.2	7.4
tiotropium	4.7	4.1	3.8	3.4	3.0	-12.9
fluticasone/vilanterol	0.0	0.0	1.0	2.0	2.6	25.8
beclomethasone	4.0	3.8	3.9	3.6	3.4	-8.0
budesonide/formoterole	1.4	1.4	1.3	1.3	1.3	4.3
aclidinium	0.2	0.6	0.9	1.1	1.2	5.1
omalizumab	0.0	0.0	0.0	0.1	0.1	25.8
glycopyrronium	0.2	0.8	1.1	1.1	1.1	-1.9
montelukast	2.1	2.1	2.1	2.0	2.0	-1.4

Table 3.2.7c. Antiasthmatic, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Beta-2-adrenoreceptor agonists ass.	8.72	4.4	13.5	3.9
Bronchodilators – anticholinergics	3.18	-7.8	6.4	-1.7
Anti-inflammatory - corticosteroids inha.	2.29	-5.1	6.2	-5.6
Bronchodilators - beta2 agonists	0.87	-13.2	4.7	-9.6
Other antiasthmatics	0.61	18.3	0.1	17.6
Leukotriene receptor antagonists	0.48	-4.0	2.0	-2.0
Bronchodilators – theophylline	0.07	-9.1	0.6	-11.9
Anti-inflammatories – chromones	0.02	-13.8	0.1	-13.8
Antiasthmatic	**16.25**	**-0.6**	**33.6**	**-1.8**
salmeterol/fluticasone	2.71	-14.4	3.8	-14.2
beclomethasone/formoterol	2.08	8.2	3.2	7.4
tiotropium	1.67	-18.0	3.0	-12.9
fluticasone/vilanterol	1.61	31.2	2.6	25.8
beclomethasone	1.22	-8.0	3.4	-8.0
budesonide/formoterol	1.03	1.4	1.3	4.3
aclidinium	0.68	4.6	1.2	5.1
omalizumab	0.60	18.9	0.1	25.8
glycopyrronium	0.58	-3.5	1.1	-1.9
montelukast	0.48	-2.6	2.0	-1.4

Table 3.2.7d. Prescription of antiasthmatic medications patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	1.60	9.8	22.1	7.9	23.4	7.1	0.56
Equivalent	0.18	11.5	0.0	1.1	13.4	-83.2	0.48
Ex originator	1.42	88.5	25.7	6.8	86.6	8.2	0.57
Patent covered	14.65	90.2	-2.6	25.7	76.6	-4.2	1.56
Antiasthmatic	**16.25**	**100.0**	**-0.6**	**33.6**	**100.0**	**-1.8**	**1.32**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Anti-HCV agents

Figure 3.2.8a. Anti-HCV agents, time trend of expenditure (2013-2017)

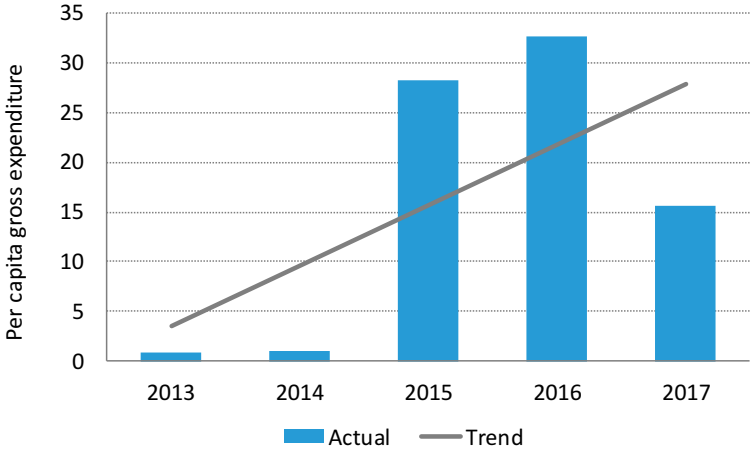


Table 3.2.8a. Anti-HCV agents, per capita expenditure by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Anti-HCV agents in combination	0.00	0.00	9.46	17.90	10.23	-42.8
Anti-HCV agents others	0.00	0.03	16.65	14.67	5.36	-63.5
Nucleosides and nucleotides excl.reverse transcriptase inhibitors	0.08	0.10	0.08	0.04	0.01	-66.6
Inhibitors of HCV proteases	0.82	0.86	2.12	0.10	0.01	-91.5
Anti-HCV agents	**0.91**	**0.99**	**28.32**	**32.71**	**15.61**	**-52.3**
ledipasvir/sofosbuvir	0.00	0.00	7.13	15.50	4.81	-68.9
sofosbuvir	0.00	0.03	14.69	11.37	4.35	-61.7
sofosbuvir/velpatasvir	-	-	-	-	2.59	-
elbasvir/grazoprevir	-	-	-	-	1.45	-
ombitasvir/paritaprevir/ritonavir	0.00	0.00	2.17	2.41	0.95	-20.6
daclatasvir	0.00	0.00	1.96	3.12	0.94	-52.9
glecaprevir/pibrentasvir	-	-	-	-	0.44	-
dasabuvir	0.00	0.00	0.16	0.18	0.07	-16.8
ribavirine	0.08	0.10	0.08	0.04	0.01	-62.5
simeprevir	0.00	0.00	2.15	0.10	0.01	-90.2

Table 3.2.8c. Anti-HCV agents, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Anti-HCV agents in combination	10.23	-42.8	0.2	41.6
Anti-HCV agents others	5.36	-63.5	0.1	-50.1
Nucleosides and nucleotides excl.reverse transcriptase inhibitors	0.01	-66.6	0.0	-62.5
Inhibitors of HCV proteases	0.01	-91.5	0.0	-90.3
Anti-HCV agents	**15.61**	**-52.3**	**0.3**	**-21.7**
ledipasvir/sofosbuvir	4.81	-68.9	0.0	-68.9
sofosbuvir	4.35	-61.8	0.0	-61.7
sofosbuvir/velpatasvir	2.59	-	0.1	-
elbasvir/grazoprevir	1.45	-	0.0	-
ombitasvir/paritaprevir/ritonavir	0.95	-60.6	0.0	-20.6
daclatasvir	0.94	-69.9	0.0	-52.9
glecaprevir/pibrentasvir	0.44	-	0.0	-
dasabuvir	0.07	-58.5	0.0	-16.8
ribavirine	0.01	-66.6	0.0	-62.5
simeprevir	0.01	-91.5	0.0	-90.2

Antacid and antiulcer medications

Figure 3.2.9a. Antacid and antiulcer medications, consumption trend (2013-2017)

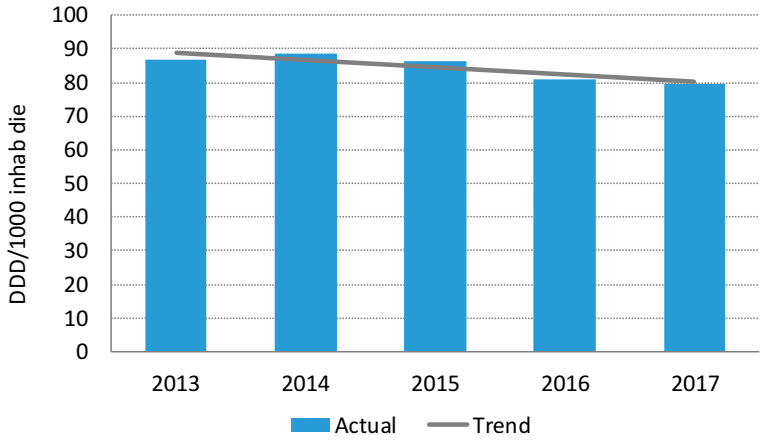


Table 3.2.9a. Antacid and antiulcer medications, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Proton pump inhibitors	78.2	80.1	77.9	72.6	71.4	-1.5
Other drugs for peptic ulcer	3.9	4.0	4.0	4.1	4.0	-1.0
H2-receptor antagonists	2.6	2.5	2.4	2.4	2.3	-1.9
Antacids	1.8	1.9	2.0	2.0	2.0	0.4
Prostaglandins	0.0	0.0	0.0	0.0	0.0	-12.0
Antacid and antiulcer medications	**86.6**	**88.6**	**86.4**	**81.0**	**79.8**	**-1.5**
pantoprazole	19.8	21.7	22.1	21.5	21.8	1.6
lansoprazole	22.9	21.8	20.0	17.8	16.7	-5.9
omeprazole	20.4	20.5	19.8	18.5	17.9	-3.4
esomeprazole	12.6	13.4	13.2	12.4	12.7	2.9
sodium alginate/potassium bicarbonate	3.5	3.7	3.8	3.8	3.8	-0.6
ranitidine	2.6	2.5	2.4	2.4	2.3	-1.9
rabeprazole	2.4	2.7	2.7	2.5	2.3	-5.3
magaldrate	1.7	1.8	1.8	1.9	1.9	0.4
sucralphate	0.4	0.3	0.3	0.3	0.2	-6.8

Table 3.2.9c. Antacid and antiulcer medications, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Proton pump inhibitors	13.35	-2.8	71.4	-1.5
Other drugs for peptic ulcer	0.85	-1.0	4.0	-1.0
H2-receptor antagonists	0.43	26.1	2.3	-1.9
Antacids	0.42	0.6	2.0	0.4
Prostaglandins	0.01	-12.2	0.0	-12.0
Antacid and antiulcer medications	**15.06**	**-2.0**	**79.8**	**-1.5**
pantoprazole	4.68	0.6	21.8	1.6
lansoprazole	2.98	-7.3	16.7	-5.9
omeprazole	2.77	-5.1	17.9	-3.4
esomeprazole	2.50	0.0	12.7	2.9
sodium alginate/potassium bicarbonate	0.81	-0.7	3.8	-0.6
ranitidine	0.43	26.4	2.3	-1.9
rabeprazole	0.42	-6.1	2.3	-5.3
magaldrate	0.41	0.6	1.9	0.4
sucralphate	0.04	-5.4	0.2	-6.8
misoprostol	0.01	-12.2	0.0	-12.0

Table 3.2.9d. Prescription of antacid and antiulcer medications patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	13.51	89.7	-2.7	73.3	91.8	-1.5	0.51
Equivalent	6.06	44.8	0.9	35.9	48.9	-8.7	0.46
Ex originator	7.46	55.2	-5.4	37.4	51.1	-4.6	0.55
Patent covered	1.54	10.3	5.0	6.5	8.2	-1.2	0.65
Antacid and antiulcer medications	**15.06**	**100.0**	**-2.0**	**79.8**	**100.0**	**-1.5**	**0.52**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Antidiabetic agents

Figure 3.2.10a. Antidiabetic agents, consumption trend (2013-2017)

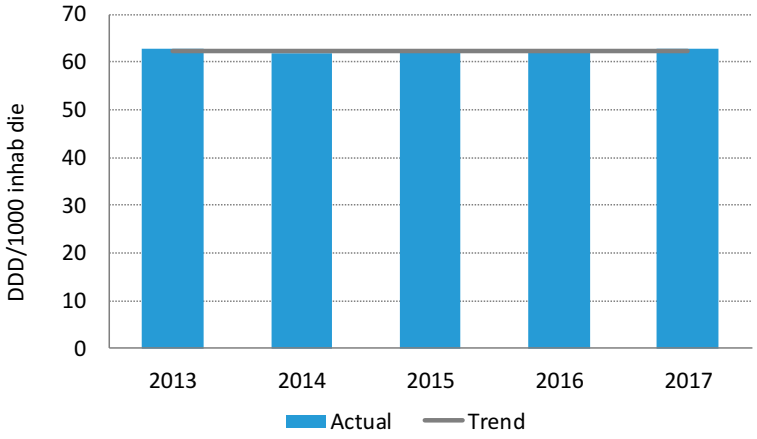


Table 3.2.10a. Antidiabetic agents, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredeint: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Insulins and analogues	14.7	14.8	15.1	15.2	15.4	1.1
Gliptins (DPP-4 inhibitors) plain or in comb.	3.5	3.4	4.1	4.8	5.1	6.8
Metformin	19.8	20.3	20.6	21.0	21.6	3.1
GLP-1 (glucagon-like peptide 1) analogues	0.8	0.7	0.8	1.0	1.3	33.0
Other oral hypoglycemic agents	17.9	16.6	15.5	14.3	13.1	-8.1
Gliflozine plain or in comb.	0.0	0.0	0.1	0.7	1.4	94.1
Pioglitazone plain or in comb.	2.1	2.2	2.1	1.9	1.7	-8.0
Repaglinide	4.0	3.9	3.6	3.3	3.0	-9.8
Antidiabetic agents	**62.8**	**62.0**	**62.1**	**62.2**	**62.7**	**0.8**
insulin lispro	4.0	4.0	4.0	4.0	4.0	0.1
insulin glargine	3.9	4.0	4.0	4.2	4.4	6.4
insulin aspart	3.1	3.2	3.2	3.2	3.1	-0.9
metformin	19.8	20.3	20.6	21.0	21.6	3.1
insulin degludec	0.0	0.0	0.7	1.0	1.2	16.9
insulin glulisine	1.3	1.3	1.4	1.4	1.4	0.4
liraglutide	0.7	0.6	0.6	0.6	0.7	5.9
sitagliptin/metformin	1.3	1.1	1.1	1.3	1.3	3.4
dulaglutide	1.1	0.9	0.8	0.9	0.9	1.5
sitagliptin	4.0	4.0	4.0	4.0	4.0	0.1

Table 3.2.10c. Antidiabetic agents, prescription by therapeutic category and by active ingredient in 2017

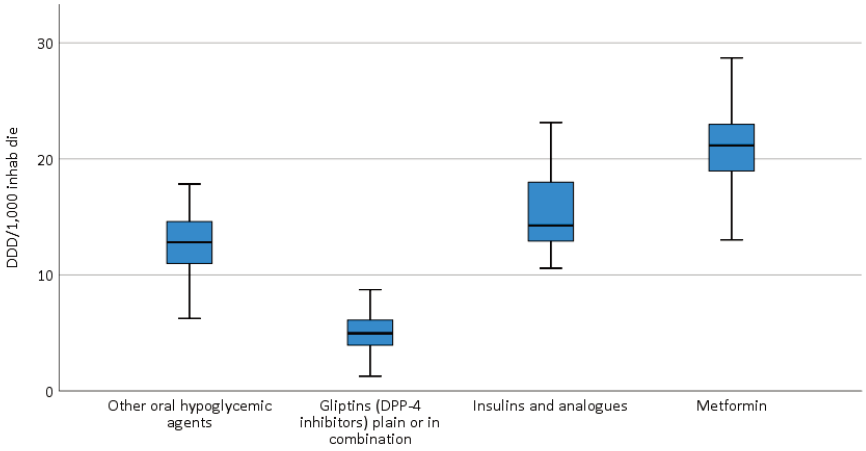
Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Insulins and analogues	7.19	-2.7	15.4	1.1
Gliptins (DPP-4 inhibitors) plain or in comb.	2.38	-7.7	5.1	6.8
Metformin	1.46	5.4	21.6	3.1
GLP-1 (glucagon-like peptide 1) analogues	1.32	24.5	1.3	33.0
Other oral hypoglycemic agents	0.93	-5.2	13.1	-8.1
Gliflozine plain or in comb.	0.73	86.2	1.4	94.1
Pioglitazone plain or in comb.	0.50	-11.2	1.7	-8.0
Repaglinide	0.40	-9.9	3.0	-9.8
Antidiabetic agents	**14.92**	**0.8**	**62.7**	**0.8**
insulin lispro	1.94	-0.5	4.0	0.1
insulin glargine	1.77	-3.7	4.4	6.4
insulin aspart	1.56	-1.5	3.1	-0.9
metformin	1.46	5.4	21.6	3.1
insulin degludec	0.81	0.3	1.2	16.9
insulin glulisine	0.64	0.1	1.4	0.4
liraglutide	0.61	2.5	0.7	5.9
sitagliptin/metformin	0.57	-14.4	1.3	3.4
dulaglutide	0.50	>100	0.5	>100
sitagliptin	0.47	-14.0	0.9	1.5

Table 3.2.10d. Prescription of antidiabetic agents patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	2.73	18.3	-0.1	36.1	57.5	-1.2	0.21
Equivalent	0.97	35.6	-3.3	16.3	45.2	-16.7	0.16
Ex originator	1.76	64.4	1.7	19.8	54.8	1.1	0.24
Patent covered	12.19	81.7	1.0	26.6	42.5	3.7	1.25
Antidiabetic agents	**14.92**	**100.0**	**0.8**	**62.7**	**100.0**	**0.8**	**0.65**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Figure 3.2.10d. Antidiabetic agents, regional consumption variability (DDD/1000 inhab die weighed) by subgroup



(The line inside the box represents the median of the regional distribution; the extremes of the box represent the first and third quartiles; the mustache represents the minimum and the maximum)

Antibiotics

Figure 3.2.11a. Antibiotics consumption trend (2013-2017)

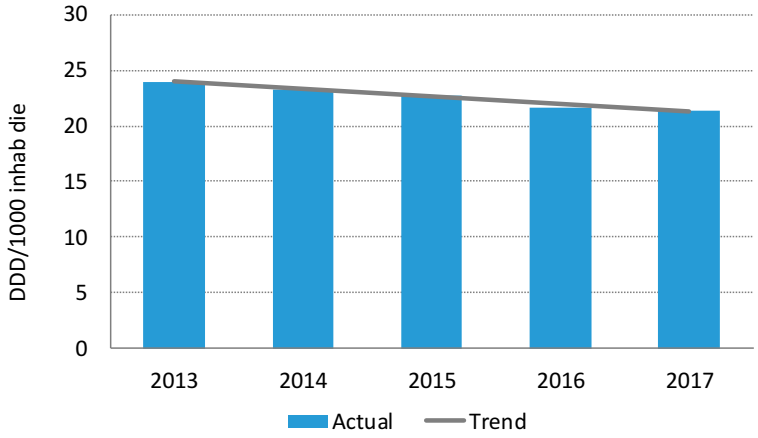


Table 3.2.11a. Antibiotics consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Combinations of penicillins, incl. betalactamase inhibitors	9.8	9.7	9.5	9.3	9.3	0.3
Quinolones	3.7	3.5	3.5	3.2	3.1	-3.0
Cephalosporins im/ev III-IV gen	0.7	0.6	0.6	0.6	0.6	-1.0
Macrolides and licosamides	4.4	4.3	4.1	3.9	3.7	-4.0
Oral cephalosporins	1.7	1.6	1.6	1.6	1.6	-0.5
Antibiotici vs germi resistenti	0.0	0.0	0.0	0.0	0.0	35.2
Glycopeptides	0.1	0.1	0.1	0.1	0.1	-1.5
Penicillins with extended spectrum incl. beta-lactamase inhibitors	2.6	2.3	2.2	2.1	1.9	-6.7
Carbapenems	0.1	0.1	0.1	0.0	0.0	6.8
Others	0.0	0.0	0.0	0.0	0.0	1.7
Aminoglycosides	0.1	0.1	0.1	0.1	0.1	-4.9
Cephalosporins im/ev I gen	0.1	0.1	0.1	0.1	0.1	6.5
Tetracyclines	0.3	0.3	0.3	0.3	0.3	-0.4
Cephalosporins im/ev II gen	0.2	0.2	0.1	0.1	0.1	-7.2
Sulfonamides and trimetropim	0.3	0.3	0.3	0.3	0.3	4.1
Monobactams	0.0	0.0	0.0	0.0	0.0	-20.9
Antibiotics	**24.0**	**23.3**	**22.7**	**21.7**	**21.4**	**-1.6**
amoxicillin/clavulanic acid	9.6	9.5	9.4	9.2	9.2	0.4
ceftriaxone	0.5	0.5	0.5	0.5	0.5	-3.1
ciprofloxacin	1.2	1.2	1.2	1.2	1.1	-3.9
levofloxacin	1.9	1.9	1.9	1.8	1.7	-1.7
cefixime	1.0	1.0	1.0	1.0	1.0	-0.6
clarithromycin	2.8	2.7	2.6	2.4	2.3	-5.6
azithromycin	1.4	1.4	1.4	1.3	1.3	-0.2
teicoplanin	0.1	0.0	0.0	0.0	0.0	-1.1
tigecycline	0.0	0.0	0.0	0.0	0.0	14.8
piperacillin/tazobactam	0.1	0.1	0.1	0.1	0.1	4.9

Table 3.2.11c. Antibiotics prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Combinations of penicillins, incl. betalactamase inhibitors	3.39	-0.6	9.3	0.3
Quinolones	2.21	-2.5	3.1	-3.0
Cephalosporins im/ev III-IV gen	1.76	-4.3	0.6	-1.0
Macrolides and licosamides	1.63	-6.0	3.7	-4.0
Oral cephalosporins	1.50	-0.3	1.6	-0.5
Antibiotics vs resistant germs	1.14	6.0	0.0	35.2
Glycopeptides	0.67	-12.4	0.1	-1.5
Penicillins with extended spectrum incl. beta-lactamase inhibitors	0.32	-5.1	1.9	-6.7
Carbapenems	0.25	3.2	0.0	6.8
Others	0.23	-4.5	0.0	1.7
Aminoglycosides	0.20	18.7	0.1	-4.9
Cephalosporins im/ev I gen	0.12	-1.0	0.1	6.5
Tetracyclines	0.07	-0.4	0.3	-0.4
Cephalosporins im/ev II gen	0.07	-11.1	0.1	-7.2
Sulfonamides and trimetropim	0.07	3.5	0.3	4.1
Monobactams	0.04	-21.1	0.0	-20.9
Antibiotics	**13.66**	**-2.1**	**21.4**	**-1.6**
amoxicillin/clavulanic acid	2.97	-0.5	9.2	0.4
ceftriaxone	1.34	-9.2	0.5	-3.1
ciprofloxacin	1.00	-4.5	1.1	-3.9
levofloxacin	0.88	1.6	1.7	-1.7
cefixime	0.86	-0.7	1.0	-0.6
clarithromycin	0.79	-8.5	2.3	-5.6
azithromycin	0.68	-1.5	1.3	-0.2
teicoplanin	0.61	-17.0	0.0	-1.1
tigecycline	0.44	11.5	0.0	14.8
piperacillin/tazobactam	0.39	12.3	0.1	4.9

Table 3.2.11d. Prescription of antibiotics patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	9.45	69.2	-1.1	19.3	90.2	-1.7	1.34
Equivalent	2.05	21.7	-2.4	4.8	25.1	-66.8	1.16
Ex originator	7.40	78.3	-0.7	14.5	74.9	-1.2	1.40
Patent covered	4.21	30.8	-4.5	2.1	9.8	-0.7	5.53
Antibiotics	**13.66**	**100.0**	**-2.1**	**21.4**	**100.0**	**-1.6**	**1.75**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Anti-HIV agents

Figure 3.2.12a. Anti-HIV agents consumption trend (2013-2017)

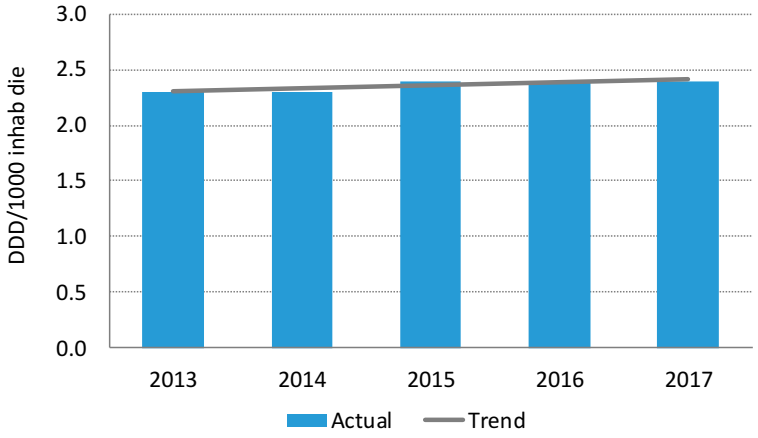


Table 3.2.12a. Anti-HIV agents, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Antivirals for treatment of HIV infections, combinations	0.2	0.3	0.3	0.4	0.5	28.2
Nucleoside and nucleotide reverse transcriptase inhibitors	1.0	1.0	1.0	1.0	0.9	-6.6
Protease inhibitors plain or in comb.	0.6	0.6	0.5	0.5	0.4	-8.9
Integrase inhibitors	0.1	0.2	0.2	0.3	0.3	1.4
Non-nucleoside reverse transcriptase inhibitors	0.2	0.2	0.2	0.2	0.2	-12.4
Other antivirals for treatment of HIV infections	0.0	0.0	0.0	0.0	0.0	-15.4
Anti-HIV agents	**2.3**	**2.3**	**2.4**	**2.4**	**2.4**	**-0.7**
emtricitabine/tenofovir disoproxil	0.4	0.4	0.3	0.3	0.3	-3.9
emtricitabine/rilpivirine/tenofovir disoproxil	0.0	0.1	0.1	0.2	0.2	12.4
dolutegravir/abacavir/lamivudine	0.0	0.0	0.0	0.0	0.1	>100
dolutegravir	0.0	0.0	0.1	0.1	0.1	17.5
raltegravir	0.1	0.2	0.2	0.2	0.2	-9.7
efavirenz/emtricitabine/tenofovir disoproxil	0.2	0.2	0.2	0.1	0.1	-26.0
tenofovir disoproxil	0.2	0.2	0.2	0.2	0.2	-0.4
darunavir	0.2	0.2	0.2	0.2	0.1	-40.7
darunavir/cobicistat	0.0	0.0	0.0	0.0	0.1	>100
elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide	0.0	0.0	0.0	-	0.1	-

Table 3.2.12c. Anti-HIV agents, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Antivirals for treatment of HIV infections, combinations	4.18	30.9	0.5	28.2
Nucleoside and nucleotide reverse transcriptase inhibitors	2.81	-20.1	0.9	-6.6
Protease inhibitors plain or in comb.	2.11	-12.0	0.4	-8.9
Integrase inhibitors	1.59	1.3	0.3	1.4
Non-nucleoside reverse transcriptase inhibitors	0.41	-17.0	0.2	-12.4
Other antivirals for treatment of HIV infections	0.17	-17.1	0.0	-15.4
Anti-HIV agents	**11.29**	**-0.9**	**2.4**	**-0.7**
emtricitabine/tenofovir disoproxil	1.55	-6.0	0.3	-3.9
emtricitabine/rilpivirine/tenofovir disoproxil	1.44	12.1	0.2	12.4
dolutegravir/abacavir/lamivudine	1.03	>100	0.1	>100
dolutegravir	0.80	19.7	0.1	17.5
raltegravir	0.79	-12.3	0.2	-9.7
efavirenz/emtricitabine/tenofovir disoproxil	0.67	-26.2	0.1	-26.0
tenofovir disoproxil	0.67	-11.2	0.2	-0.4
darunavir	0.64	-40.8	0.1	-40.7
darunavir/cobicistat	0.58	>100	0.1	>100
elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide	0.54	-	0.1	-

Table 3.2.12d. Prescription of anti-HIV agents patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	0.04	0.4	-14.8	0.1	2.8	2.7	1.66
Equivalent	0.03	63.0	22.9	0.0	56.2	-16.2	1.86
Ex originator	0.02	37.0	-44.1	0.0	43.8	-34.7	1.40
Patent covered	11.24	99.6	-0.9	2.3	97.2	-0.8	13.24
Anti-HIV agents	**11.29**	**100.0**	**-0.9**	**2.4**	**100.0**	**-0.7**	**12.91**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Medications for multiple sclerosis

Figure 3.2.13a. Medications for multiple sclerosis, consumption trend (2013-2017)

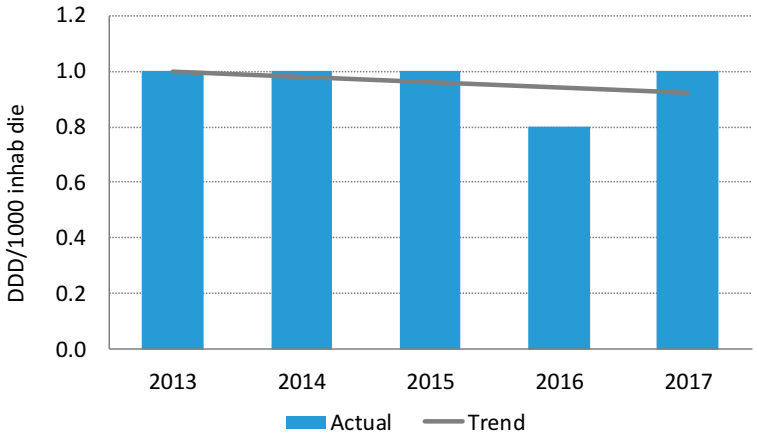


Table 3.2.13a. Medications for multiple sclerosis, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Interferon beta	0.8	0.8	0.7	0.5	0.5	10.3
Fingolimod	0.0	0.1	0.1	0.1	0.1	15.0
Monoclonal antibodies	0.1	0.1	0.1	0.1	0.1	8.4
Dimethyl fumarate	-	-	0.0	0.0	0.1	-
Glatiramer	0.1	0.1	0.1	0.1	0.1	5.5
Teriflunomide	-	0.0	0.0	0.0	0.1	31.9
Medications for multiple sclerosis	**1.0**	**1.0**	**1.0**	**0.8**	**1.0**	**28.9**
interferon beta 1a	0.7	0.7	0.6	0.4	0.5	3.6
fingolimod	0.0	0.1	0.1	0.1	0.1	15.0
dimethyl fumarate	-	-	0.0	-	0.1	-
natalizumab	-	-	-	0.1	0.1	8.2
glatiramer	0.1	0.1	0.1	0.1	0.1	5.5
teriflunomide	-	0.0	0.0	0.0	0.1	31.9
peginterferon beta-1	-	-	-	-	0.0	-
alemtuzumab	-	-	-	0.0	0.0	43.5
interferon beta 1b	0.1	0.1	0.1	0.0	0.0	-12.9
daclizumab	-	-	-	-	0.0	-

Table 3.2.13c. Medications for multiple sclerosis, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Interferon beta	2.51	49.3	0.5	10.3
Fingolimod	2.07	13.2	0.1	15.0
Monoclonal antibodies	1.67	13.3	0.1	8.4
Dimethyl fumarate	1.66	-	0.1	-
Glatiramer	1.12	4.9	0.1	5.5
Teriflunomide	0.59	25.7	0.1	31.9
Medications for multiple sclerosis	**9.63**	**47.6**	**1.0**	**28.9**
fingolimod	2.07	13.2	0.1	15.0
interferon beta 1a	1.93	30.5	0.5	3.6
dimethyl fumarate	1.66	-	0.1	-
natalizumab	1.35	7.9	0.1	8.2
glatiramer	1.12	4.9	0.1	5.5
teriflunomide	0.59	25.7	0.1	31.9
peginterferon beta-1	0.42	-	0.0	-
alemtuzumab	0.32	43.0	0.0	43.5
interferon beta 1b	0.16	-20.5	0.0	-12.9
daclizumab	0.00	-	0.0	-

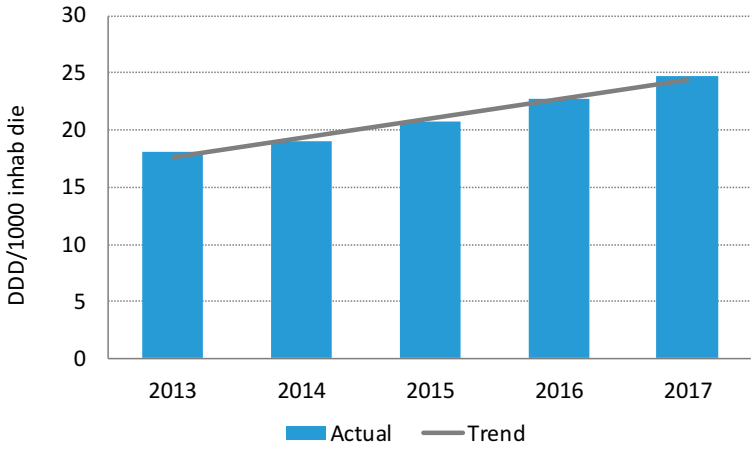
Table 3.2.13d. Prescription of medications for multiple sclerosis patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	0.06	0.6	-	0.0	0.7	-	23.68
Equivalent							
Ex originator	0.06	100.0	-	0.0	100.0	-	23.68
Patent covered	9.57	99.4	46.6	1.0	99.3	28.0	26.51
Medications for multiple sclerosis	**9.63**	**100.0**	**47.6**	**1.0**	**100.0**	**28.9**	**26.49**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Medications for osteoporosis

Figure 3.2.14a. Medications for osteoporosis*, consumption trend (2013-2017)



** raloxifene excluded*

Table 3.2.14a. Medications for osteoporosis, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Vitamin D and analogues	6.2	7.2	8.8	10.8	12.6	16.9
Teriparatide	0.2	0.2	0.2	0.2	0.2	17.5
Oral and injectable bisphosphonates	6.8	6.9	6.7	6.6	6.7	1.6
Denosumab	0.3	1.0	1.6	2.1	2.4	16.4
Alendronic acid + colecalciferol	3.3	3.5	3.3	3.0	2.7	-11.7
SERM (selective modulators of the estrogen-receptor)	0.1	0.1	0.1	0.1	0.1	-7.0
Medications for osteoporosis	**18.1**	**19.0**	**20.7**	**22.7**	**24.7**	**8.5**
colecalciferol	4.5	5.6	7.2	9.1	10.9	19.5
teriparatide	0.2	0.2	0.2	0.2	0.2	17.5
denosumab	0.3	1.0	1.6	2.1	2.4	16.4
alendronic acid	2.7	2.9	3.1	3.2	3.5	7.7
alendronic acid/colecalciferol	3.3	3.5	3.3	3.0	2.7	-11.7
risedronate	2.8	2.8	2.6	2.4	2.3	-2.8
calcitriol	1.0	1.0	1.0	1.0	1.0	0.0
ibandronic acid	1.3	1.2	1.1	1.0	0.9	-7.8
alphacalcidol	0.6	0.5	0.6	0.6	0.7	7.7
calcifediol	0.1	0.1	0.1	0.1	0.1	9.4

Table 3.2.14c. Medications for osteoporosis, prescription by therapeutic category and by active ingredient in 2017

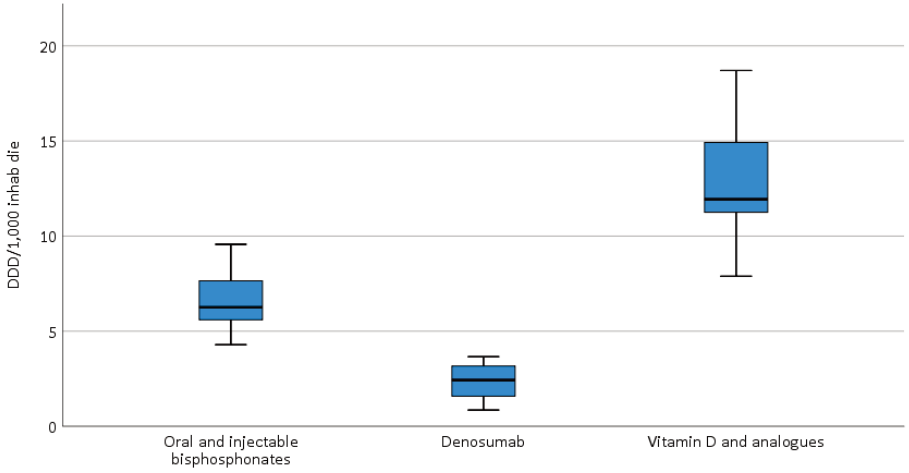
Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Vitamin D and analogues	4.30	23.1	12.6	16.9
Teriparatide	1.41	26.0	0.2	17.5
Oral and injectable bisphosphonates	1.40	0.0	6.7	1.6
Denosumab	0.72	18.3	2.4	16.4
Alendronic acid + colecalciferol	0.64	-31.9	2.7	-11.7
SERM (selective modulators of the estrogen-receptor)	0.01	-6.9	0.1	-7.0
Medications for osteoporosis	**8.49**	**11.9**	**24.7**	**8.5**
colecalciferol	3.87	25.7	10.9	19.5
teriparatide	1.41	26.0	0.2	17.5
denosumab	0.72	18.3	2.4	16.4
alendronic acid	0.68	6.9	3.5	7.7
alendronic acid/colecalciferol	0.64	-31.9	2.7	-11.7
risedronate	0.42	-5.7	2.3	-2.8
calcitriol	0.22	0.7	1.0	0.0
ibandronic acid	0.19	-9.0	0.9	-7.8
alphacalcidol	0.11	6.7	0.7	7.7
calcifediol	0.10	9.7	0.1	9.4

Table 3.2.14d. Prescription of medications for osteoporosis patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	5.60	65.9	28.3	16.6	67.1	29.3	0.93
Equivalent	0.75	13.4	20.1	3.7	22.3	-61.6	0.56
Ex originator	4.85	86.6	29.7	12.9	77.7	33.4	1.03
Patent covered	2.90	34.1	-10.2	8.1	32.9	-18.3	0.98
Medications for osteoporosis	**8.49**	**100.0**	**11.9**	**24.7**	**100.0**	**8.5**	**0.94**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Figure 3.2.14d. Medications for osteoporosis, regional consumption variability (DDD/1000 inhab weighed) by subgroup



(The line inside the box represents the median of the regional distribution; the extremes of the box represent the first and third quartiles; the mustache represents the minimum and the maximum).

Coagulation factors

Figure 3.2.15a. Coagulation factors expenditure trend (2013-2017)

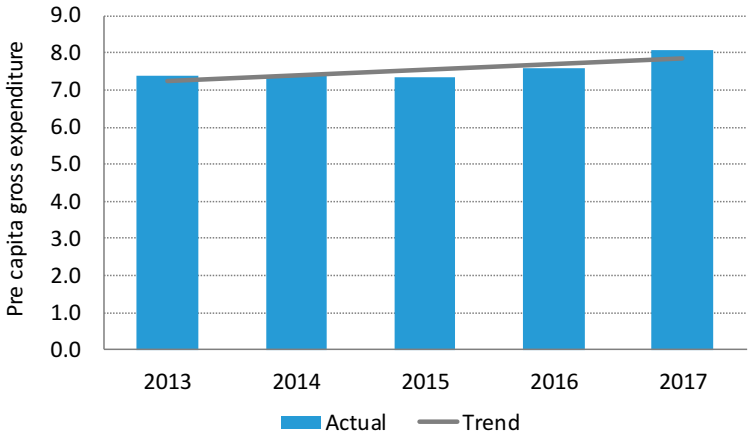


Table 3.2.15a. Coagulation factors, per capita expenditure by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Hemophilia A (recombinant)	4.70	4.67	4.67	4.96	5.07	2.3
Factor VII deficiency (recombinant)	1.15	0.99	0.97	0.85	1.01	18.8
Hemophilia A (plasmaderivated)	0.91	1.01	0.96	0.96	0.94	-2.2
Hemophilia B (recombinant)	0.51	0.60	0.62	0.66	0.85	28.4
Von Willebrand's disease	0.04	0.05	0.04	0.04	0.07	51.2
Factor VII deficiency (plasmaderivated)	0.04	0.04	0.04	0.04	0.06	39.5
Other deficiencies of coagulation factors (recombinant)	-	0.00	0.02	0.03	0.04	30.0
Hemophilia B (plasmaderivatived)	0.03	0.02	0.02	0.02	0.02	-22.7
Other deficiencies of coagulation factors (plasmaderivated)	-	-	0.01	0.01	0.01	-17.9
Coagulation factors	**7.38**	**7.39**	**7.35**	**7.58**	**8.06**	**6.3**
factor VIII	4.78	4.71	4.68	4.96	5.07	2.1
eptacog alpha activated (recombinant DNA coagulation factor VII)	1.15	0.99	0.97	0.85	1.01	18.8
nonacog alpha (coagulation factor IX, recombinant)	0.51	0.60	0.62	0.66	0.57	-13.9
human coagulation factor VIII/Von Willebrand factor	0.36	0.55	0.51	0.50	0.49	-3.3
human anti-hemophilic prothrombin complex activated	0.47	0.42	0.44	0.46	0.45	-1.0
albutrepenonacog alpha	-	-	-	-	0.24	-
factor of Von Willebrand	0.04	0.05	0.04	0.04	0.07	51.2
factor VII of coagulation of the lyophilized human blood	0.04	0.04	0.04	0.04	0.06	39.5
eftrenonacog alpha	-	-	-	-	0.04	-
catridecacog (coagulation factor XIII, recombinant)	0.00	0.00	0.00	0.00	0.04	30.0

Table 3.2.15c. Coagulation factors, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Hemophilia A (recombinant)	5.07	2.3	0.0	5.3
Factor VII deficiency (recombinant)	1.01	18.8	0.0	20.8
Hemophilia A (plasmaderivated)	0.94	-2.2	0.0	-8.3
Hemophilia B (recombinant)	0.85	28.4	0.0	1.8
Von Willebrand's disease	0.07	51.2	0.0	53.8
Factor VII deficiency (plasmaderivated)	0.06	39.5	0.0	18.6
Other deficiencies of coagulation factors (recombinant)	0.04	30.0	0.0	33.0
Hemophilia B (plasmaderivatived)	0.02	-22.7	0.0	-20.4
Other deficiencies of coagulation factors (plasmaderivated)	0.01	-17.9	0.0	-4.2
Coagulation factors	**8.06**	**6.3**	**0.1**	**5.6**
factor VIII	5.07	2.1	0.0	5.1
eptacog alpha activated (recombinant DNA coagulation factor VII)	1.01	18.8	0.0	20.8
nonacog alpha (coagulation factor IX, recombinant)	0.57	-13.9	0.0	-12.8
human coagulation factor VIII/Von Willebrand factor	0.49	-3.3	0.0	-8.4
human anti-hemophilic prothrombin complex activated	0.45	-1.0	0.0	-2.0
albutrepenonacog alpha	0.24	-	0.0	-
factor of Von Willebrand	0.07	51.2	0.0	53.8
factor VII of coagulation of the lyophilized human blood	0.06	39.5	0.0	18.6
eftrenonacog alpha	0.04	-	0.0	-
catridecacog (coagulation factor XIII, recombinant)	0.04	30.0	0.0	33.0

Vaccines

Figure 3.2.16a. Vaccines expenditure trend (2013-2017)

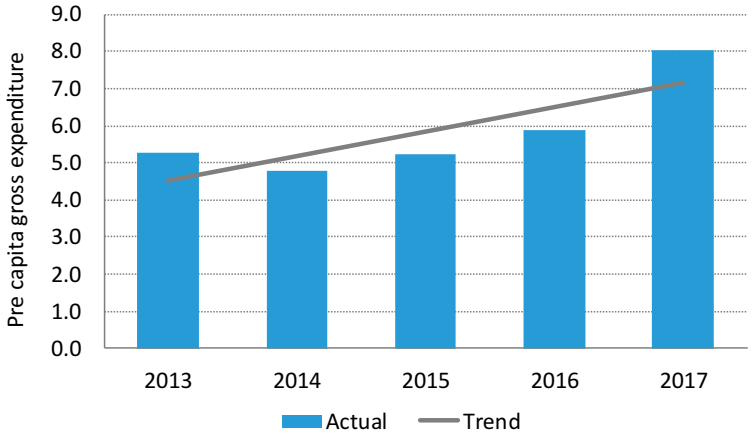


Table 3.2.16a. Vaccines per capita expenditure by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredient	2013	2014	2015	2016	2017	Δ % 17-16
Meningococcal vaccines	0.18	0.23	0.64	1.32	2.71	>100
Pneumococcal vaccines	1.44	1.38	1.47	1.53	1.66	8.8
Bacterial and viral vaccines, combined	1.46	1.39	1.29	1.20	1.26	5.0
Influenza vaccines	0.82	0.64	0.69	0.67	0.78	16.6
Measles vaccines	0.36	0.32	0.35	0.35	0.59	66.2
Papillomavirus vaccines	0.57	0.38	0.33	0.32	0.38	17.4
Varicella zoster vaccines	0.14	0.12	0.15	0.15	0.17	16.9
Pertussis vaccines	0.09	0.10	0.08	0.08	0.13	64.0
Rota virus diarrhea vaccines	0.05	0.05	0.07	0.08	0.13	64.4
Hepatitis vaccines	0.10	0.11	0.10	0.10	0.12	17.8
Other vaccines	0.08	0.07	0.06	0.08	0.10	29.4
Vaccines	**5.28**	**4.79**	**5.23**	**5.89**	**8.05**	**36.6**
meningococcal vaccine B group	0.00	0.07	0.34	0.97	1.96	>100
pneumococcal vaccine	1.44	1.38	1.47	1.53	1.66	8.8
hexavalent vaccine	1.28	1.24	1.16	1.04	1.06	1.7
measles/mumps/rubella and varicella vaccine	0.20	0.18	0.23	0.24	0.45	89.5
mengocococcal acwy vaccine	0.07	0.05	0.22	0.23	0.69	>100
influenza vaccine adjuvant with mf59c.1	0.28	0.29	0.21	0.21	0.26	25.4
inactivated split virion influenza vaccine	0.12	0.12	0.23	0.12	0.24	>100
diphtheria/pertussis/polyomelitic/tetanus vaccine	0.18	0.15	0.13	0.16	0.20	26.4
human papillomavirus vaccine	0.32	0.22	0.20	0.24	0.19	-21.2

Table 3.2.16c. Vaccines prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Meningococcal vaccines	2.71	>100	0.2	61.7
Pneumococcal vaccines	1.66	8.8	0.1	9.7
Bacterial and viral vaccines, combined	1.26	5.0	0.1	2.4
Influenza vaccines	0.78	16.6	0.4	-37.6
Measles vaccines	0.59	66.2	0.1	25.1
Papillomavirus vaccines	0.38	17.4	0.0	-4.7
Varicella zoster vaccines	0.17	16.9	0.0	-7.4
Pertussis vaccines	0.13	64.0	0.0	53.1
Rota virus diarrhea vaccines	0.13	64.4	0.0	56.0
Hepatitis vaccines	0.12	17.8	0.0	3.8
Other vaccines	0.10	29.4	0.0	-9.3
Vaccines	**8.05**	**36.6**	**1.0**	**-15.6**
meningococcal vaccine b group	1.96	>100	0.1	96.1
pneumococcal vaccine	1.66	8.8	0.1	9.7
hexavalent vaccine	1.06	1.7	0.1	-2.3
measles/mumps/rubella and varicella vaccine	0.45	89.5	0.0	77.7
mengocococcal acwy vaccine	0.69	>100	0.1	>100
influenza vaccine adjuvant with mf59c.1	0.26	25.4	0.1	38.4
inactivated split virion influenza vaccine	0.24	>100	0.1	-66.0
diphtheria/pertussis/polyomelitic/tetanus vaccine	0.20	26.4	0.0	15.7
human papillomavirus vaccine	0.19	-21.2	0.0	-26.8

Pain relief medications

(This paragraph includes data on the prescription of pregabalin and gabapentin for all authorized indications)

Figure 3.2.17a. Pain relief medications consumption trend (2013-2017)

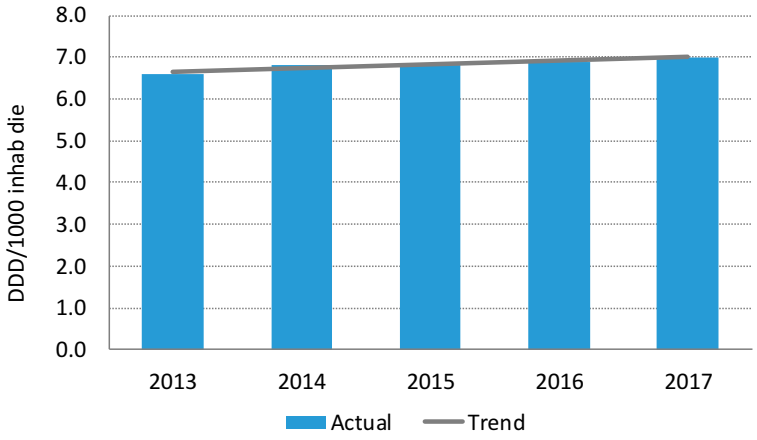


Table 3.2.17a. Pain relief medications, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Major opioids	1.7	1.8	1.9	2.1	2.1	3.9
Neuropathic pain	2.0	2.2	2.3	2.3	2.4	4.0
Minor opioids/opioids in combination	2.9	2.8	2.6	2.5	2.4	-4.0
Pain relief medications	**6.6**	**6.8**	**6.8**	**6.9**	**7.0**	**1.0**
pregabalin	1.6	1.7	1.8	1.8	1.9	4.8
fentanyl	0.6	0.6	0.6	0.6	0.6	2.8
naloxone/oxycodone	0.2	0.3	0.3	0.4	0.4	10.9
tapentadol	0.2	0.3	0.3	0.4	0.5	17.5
paracetamol/codeine	1.7	1.6	1.5	1.4	1.3	-4.6
gabapentin	0.5	0.5	0.5	0.5	0.5	1.2
tramadol	0.8	0.8	0.7	0.7	0.7	-4.6
oxycodone/acetaminophen	0.3	0.3	0.3	0.3	0.3	-0.7
oxycodone	0.2	0.1	0.1	0.1	0.1	-1.5
buprenorphine	0.1	0.1	0.1	0.1	0.1	-2.0

Table 3.2.17c. Pain relief medications prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Major opioids	3.91	8.2	2.1	3.9
Neuropathic pain	2.11	-19.8	2.4	4.0
Minor opioids/opioids in combination	0.98	-3.9	2.4	-4.0
Pain relief medications	**7.00**	**-3.6**	**7.0**	**1.0**
pregabalin	1.78	-22.7	1.9	4.8
fentanyl	1.29	5.0	0.6	2.8
naloxone/oxycodone	1.12	9.9	0.4	10.9
tapentadol	1.07	17.0	0.5	17.5
paracetamol/codeine	0.36	-6.0	1.3	-4.6
gabapentin	0.32	1.3	0.5	1.2
tramadol	0.30	-4.8	0.7	-4.6
oxycodone/acetaminophen	0.25	-1.0	0.3	-0.7
oxycodone	0.15	-7.4	0.1	-1.5
buprenorphine	0.11	-2.6	0.1	-2.0

° includes the prescription of pregabalin and gabapentin for all authorized indications

Table 3.2.17d. Prescription of pain relief medications patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	2.41	34.4	-18.1	3.6	52.0	1.5	1.81
Equivalent	0.43	17.7	20.6	0.8	21.4	-73.7	1.50
Ex originator	1.98	82.3	-23.4	2.9	78.6	-3.5	1.90
Patent covered	4.59	65.6	6.3	3.4	48.0	0.5	3.74
Pain relief medications	**7.00**	**100.0**	**-3.6**	**7.0**	**100.0**	**1.0**	**2.74**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Medications for eye disorders

Figure 3.2.18a. Medications for eye disorders, consumption trend (2013-2017)

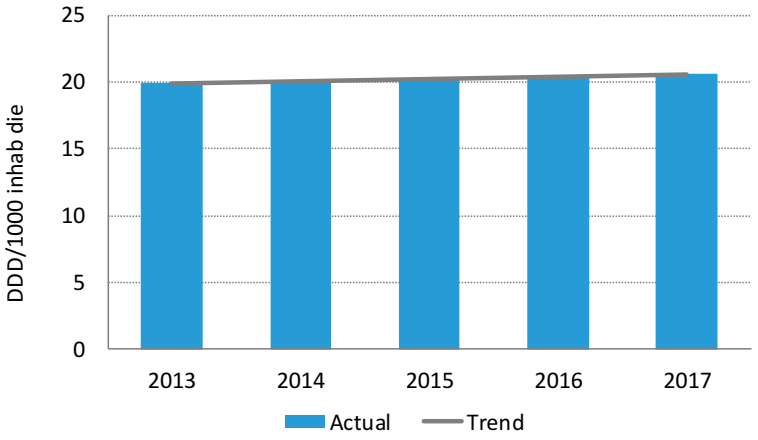


Table 3.2.18a. Medications for eye disorders, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Other antiglaucoma preparations	14.2	14.0	14.2	14.3	14.4	0.8
Antineovascularisation agents	0.2	0.2	0.2	0.3	0.3	18.5
Prostaglandin analogues plain or in comb. with beta blocking agents	5.6	5.6	5.6	5.7	5.7	-1.4
Corticosteroids (intravitreal plants)	0.1	0.1	0.2	0.0	0.0	-2.0
Medications for eye disorders	**20.0**	**19.9**	**20.2**	**20.5**	**20.6**	**0.5**
ranibizumab	0.0	0.0	0.1	0.2	0.2	26.4
aflibercept	1.7	1.8	1.9	1.9	1.9	2.2
bimatoprost	1.1	1.2	1.3	1.3	1.4	3.2
timolol/bimatoprost	1.1	1.2	1.3	1.5	1.6	6.3
brinzolamide/timolol	0.7	0.8	0.9	1.2	1.2	1.0
tafluprost	0.1	0.1	0.2	0.2	0.2	12.2
dexamethasone	3.3	3.2	3.1	3.3	3.0	-6.8
timolol	0.9	0.9	0.9	0.9	0.9	-4.3
timolol/travoprost	2.0	2.0	2.0	1.8	1.9	9.7
dorzolamide/timolol	0.1	0.2	0.1	0.1	0.1	7.0

Table 3.2.18c. Medications for eye disorders, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Other antiglaucoma preparations	2.52	3.0	14.4	0.8
Antineovascularisation agents	1.95	7.9	0.3	18.5
Prostaglandin analogues plain or in comb. with beta blocking agents	1.30	-5.7	5.7	-1.4
Corticosteroids (intravitreal plants)	0.34	11.5	0.2	13.1
Medications for eye disorders	**6.11**	**2.9**	**20.6**	**0.5**
ranibizumab	1.10	2.9	0.1	7.0
aflibercept	0.83	15.8	0.2	26.4
bimatoprost	0.47	1.7	1.9	2.2
timolol/bimatoprost	0.42	3.6	1.4	3.2
brinzolamide/timolol	0.40	5.0	1.6	6.3
tafluprost	0.38	0.8	1.2	1.0
dexamethasone	0.34	11.0	0.2	12.2
timolol	0.31	0.0	3.0	-6.8
timolol/travoprost	0.30	-9.8	0.9	-4.3
dorzolamide/timolol	0.27	11.2	1.9	9.7

Table 3.2.18d. Prescription medications for eye disorders patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	1.01	16.5	8.9	8.3	40.4	2.2	0.33
Equivalent	0.13	13.1	-10.2	1.7	20.8	-71.8	0.21
Ex originator	0.88	86.9	12.5	6.6	79.2	7.6	0.36
Patent covered	5.10	83.5	1.8	12.3	59.6	-0.6	1.14
Medications for eye disorders	**6.11**	**100.0**	**2.9**	**20.6**	**100.0**	**0.5**	**0.81**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Antidepressants

Figure 3.2.19a. Antidepressants, consumption trend (2013-2017)

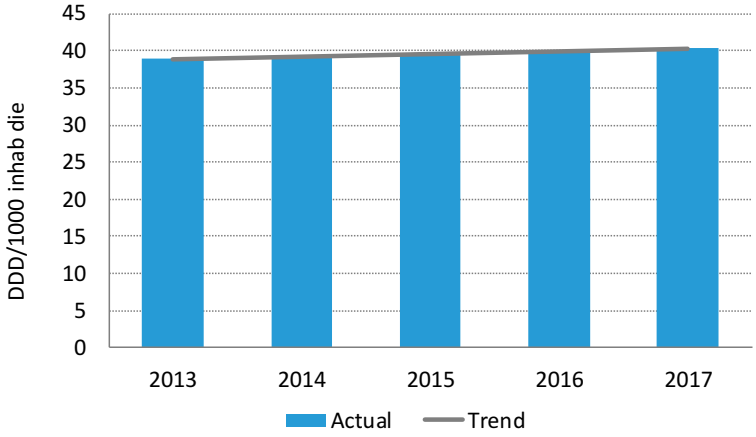


Table 3.2.19a. Antidepressants, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
SSRI-antidepressants	29.2	29.2	29.3	29.2	29.1	-0.1
SNRI-antidepressants	6.0	6.1	6.2	6.2	6.2	1.2
Other antidepressants	2.3	2.4	2.6	2.7	2.9	5.3
SMS-antidepressants (serotonin modulators and stimulators)				0.2	0.8	>100
Tricyclic-antidepressants	1.1	1.2	1.1	1.1	1.1	-5.3
Bupropion	0.3	0.3	0.2	0.2	0.2	-4.8
NaRI-antidepressants (noradrenaline reuptake inhibitors)	0.0	0.0	0.0	0.0	0.0	-14.6
Antidepressants	**39.0**	**39.2**	**39.5**	**39.7**	**40.4**	**1.7**
paroxetine	8.0	8.0	7.9	7.8	7.8	0.5
escitalopram	7.4	7.3	7.3	7.3	7.2	-1.3
venlafaxine	3.4	3.4	3.5	3.5	3.5	-0.2
duloxetine	2.6	2.7	2.7	2.7	2.8	2.9
sertraline	7.0	7.2	7.6	7.7	7.9	2.2
citalopram	5.0	4.8	4.6	4.4	4.3	-2.0
trazodone	0.7	0.8	1.0	1.1	1.1	6.9
vortioxetine	-	-	-	0.2	0.8	>100
mirtazapine	1.5	1.6	1.6	1.6	1.7	4.6
bupropion	0.3	0.3	0.2	0.2	0.2	-4.8

Table 3.2.19c. Antidepressants, prescription by therapeutic category and by active ingredients in 2017

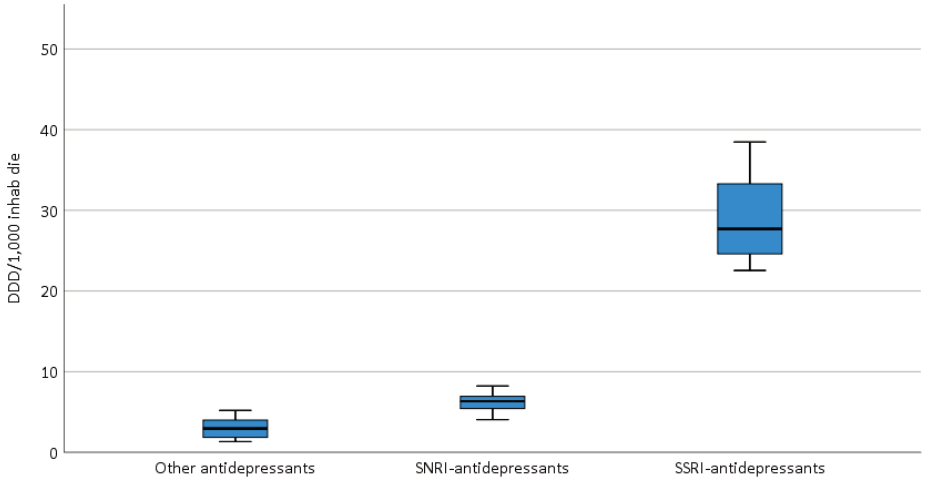
Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
SSRI-antidepressants	3.26	-1.6	29.1	-0.1
SNRI-antidepressants	1.45	-0.8	6.2	1.2
Other antidepressants	0.71	4.1	2.9	5.3
SMS-antidepressants (serotonin modulators and stimulators)	0.33	>100	0.8	>100
Tricyclic-antidepressants	0.17	-5.6	1.1	-5.3
Bupropion	0.16	-6.4	0.2	-4.8
NaRI-antidepressants (noradrenaline reuptake inhibitors)	0.01	-15.9	0.0	-14.6
Antidepressants	**6.09**	**2.9**	**40.4**	**1.7**
paroxetine	1.03	-2.1	7.8	0.5
escitalopram	0.93	-2.6	7.2	-1.3
venlafaxine	0.76	-0.3	3.5	-0.2
duloxetine	0.69	-1.4	2.8	2.9
sertraline	0.68	2.5	7.9	2.2
citalopram	0.42	-3.8	4.3	-2.0
trazodone	0.38	6.4	1.1	6.9
vortioxetine	0.33	>100	0.8	>100
mirtazapine	0.31	1.9	1.7	4.6
bupropion	0.16	-6.4	0.2	-4.8

Table 3.2.19d. Prescriptions of antidepressants patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	4.77	78.3	0.0	36.1	89.5	0.6	0.36
Equivalent	1.84	38.7	3.5	17.6	48.8	-6.0	0.29
Ex originator	2.92	61.3	-2.1	18.5	51.2	-1.5	0.43
Patent covered	1.32	21.7	14.8	4.2	10.5	11.9	0.85
Antidepressants	**6.09**	**100.0**	**2.9**	**40.4**	**100.0**	**1.7**	**0.41**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Figure 3.2.19d. Antidepressants, regional consumption variability (DDD/1000 inhab die weighed) by subgroup



(The line inside the box represents the median of the regional distribution; the extremes of the box represent the first and third quartiles; the mustache represents the minimum and the maximum).

Medications for genitourinary disorders

Figure 3.2.20a. Medication for genitourinary disorders, consumption trend (2013-2017)

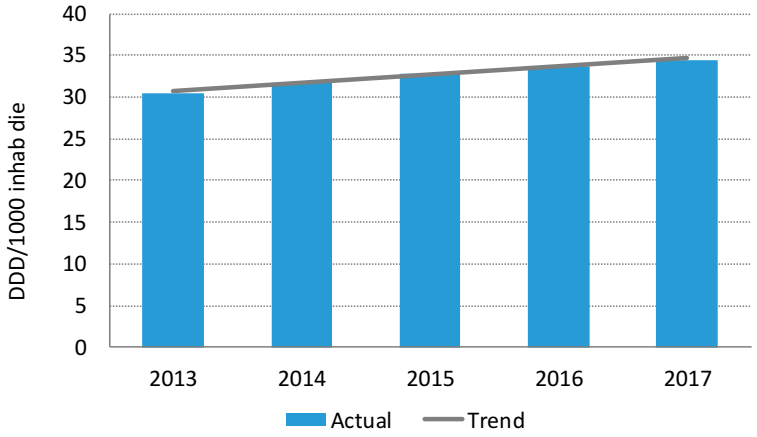


Table 3.2.20a. Medication for genitourinary disorders consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Alpha-blocking agents	21.7	22.5	23.2	23.8	24.4	2.7
5-alpha reductase inhibitors	8.8	9.2	9.6	10.0	10.1	1.3
Beta 3 selective agonist	0.0	0.0	0.0	0.0	0.0	8.8
Alpha-blocking agents in combination	0.0	0.0	0.0	0.0	0.0	>100
Medication for genitourinary disorders	**30.5**	**31.7**	**32.9**	**33.8**	**34.5**	**2.3**
dutasteride	6.0	6.5	7.0	7.3	7.4	1.3
tamsulosin	9.4	9.4	9.5	9.8	9.9	1.9
silodosin	2.6	3.4	4.0	4.5	4.9	8.4
alfuzosin	7.6	7.7	7.8	8.0	8.2	2.2
finasteride	2.8	2.7	2.7	2.7	2.7	1.2
terazosin	1.9	1.7	1.6	1.5	1.4	-5.8

Table 3.2.20c. Medication for genitourinary disorders prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Alpha-blocking agents	2.87	2.9	24.4	2.7
5-alpha reductase inhibitors	2.63	-17.0	10.1	1.3
Beta 3 selective agonist	0.00	6.6	0.0	8.8
Alpha blocking agents in combination	0.00	>100	0.0	>100
Medication for genitourinary disorders	**5.51**	**-7.6**	**34.5**	**2.3**
dutasteride	2.05	-20.9	7.4	1.3
tamsulosin	1.02	1.3	9.9	1.9
silodosin	0.91	8.1	4.9	8.4
alfuzosin	0.76	1.6	8.2	2.2
finasteride	0.58	0.9	2.7	1.2
terazosin	0.18	-5.9	1.4	-5.8

Table 3.2.20d. Prescriptions of drugs for genitourinary disorders, patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	3.00	54.6	20.7	25.1	72.7	15.3	0.33
Equivalent	0.97	32.3	10.1	9.8	38.9	-24.5	0.27
Ex originator	2.03	67.7	26.6	15.3	61.1	18.5	0.36
Patent covered	2.50	45.4	-28.0	9.4	27.3	-21.3	0.73
Medications for genitourinary disorders	**5.51**	**100.0**	**-7.6**	**34.5**	**100.0**	**2.3**	**0.44**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Antipsychotics

Figure 3.2.21a. Antipsychotics consumption trend (2013-2017)

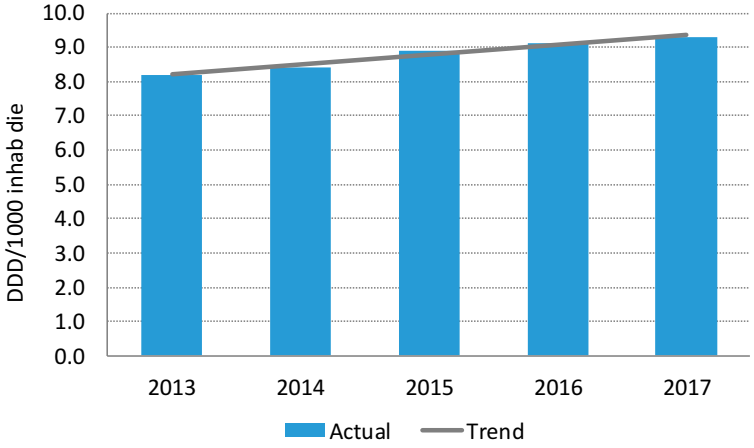


Table 3.2.21a. Antipsychotics, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and acive ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Atypical antipsychotics and others	5.3	5.6	6.2	6.4	6.7	4.7
Typical antipsychotics	2.9	2.9	2.7	2.7	2.6	-3.0
Antipsychotics	**8.2**	**8.4**	**8.9**	**9.1**	**9.3**	**2.4**
paliperidone	0.3	0.4	0.5	0.5	0.6	11.0
quetiapine	1.5	1.7	1.7	1.7	1.8	3.9
aripiprazole	0.6	0.3	0.8	0.9	1.0	16.9
risperidone	0.8	0.9	0.9	0.9	0.9	1.9
olanzapine	1.6	1.9	2.0	2.0	2.0	-1.8
clozapine	0.4	0.4	0.4	0.4	0.4	21.8
haloperidol	1.2	1.2	1.1	1.2	1.1	-6.2
asenapine	0.1	0.1	0.1	0.1	0.1	-21.7
amisulpride	0.1	0.1	0.1	0.1	0.1	-4.6
lithium	0.3	0.3	0.4	0.4	0.4	-2.8

Table 3.2.21c. Antipsychotics, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Atypical antipsychotics and others	3.90	-0.7	6.7	4.7
Typical antipsychotics	0.38	-3.6	2.6	-3.0
Antipsychotics	**4.29**	**-0.9**	**9.3**	**2.4**
paliperidone	1.23	12.6	0.6	11.0
quetiapine	0.79	-11.4	1.8	3.9
aripiprazole	0.79	2.2	1.0	16.9
risperidone	0.53	-9.0	0.9	1.9
olanzapine	0.35	2.0	2.0	-1.8
clozapine	0.14	1.4	0.4	21.8
haloperidol	0.08	-4.4	1.1	-6.2
asenapine	0.07	-26.3	0.1	-21.7
amisulpride	0.07	-4.9	0.1	-4.6
lithium	0.06	-3.0	0.4	-2.8

Table 3.2.21d. Prescription of antipsychotics patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	1.83	42.7	-10.2	6.4	68.6	3.7	0.78
Equivalent	1.11	60.6	7.7	4.9	75.8	144.6	0.63
Ex originator	0.72	39.4	-28.6	1.6	24.2	-21.7	1.27
Patent covered	2.45	57.3	7.4	2.9	31.4	-0.2	2.29
Antipsychotics	**4.29**	**100.0**	**-0.9**	**9.3**	**100.0**	**2.4**	**1.26**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Parkinson disease medications

Figure 3.2.22a. Parkinson disease medications consumption trend (2013-2017)

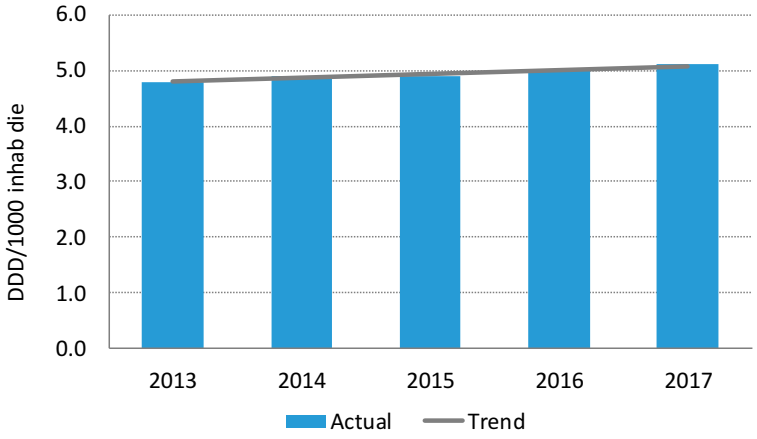


Table 3.2.22a. Parkinson disease medications, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Dopamine agonists	1.5	1.5	1.4	1.3	1.3	-1.5
Dopaderivatives agonists	2.2	2.2	2.3	2.3	2.3	1.2
MAO-B inhibitors	1.0	1.1	1.2	1.3	1.4	7.9
COMT inhibitors	0.0	0.0	0.0	0.0	0.0	-8.5
Amantadine	0.0	0.0	0.0	0.0	0.0	-4.6
Parkinson disease medications	**4.8**	**4.9**	**4.9**	**5.0**	**5.1**	**2.2**
rotigotine	0.3	0.3	0.4	0.4	0.4	1.2
levodopa/carbidopa	0.8	0.9	0.9	0.9	0.9	2.3
pramipexole	0.6	0.6	0.5	0.5	0.5	3.3
levodopa/benserazide	0.9	0.9	0.9	0.9	0.9	1.7
rasagiline	0.4	0.4	0.4	0.4	0.4	-13.5
safinamide				0.1	0.1	>100
melevodopa/carbidopa	0.2	0.2	0.2	0.3	0.3	0.9
ropinirole	0.6	0.5	0.5	0.4	0.4	-9.3
levodopa/carbidopa/entacapone	0.3	0.3	0.2	0.2	0.2	-4.7
selegiline	0.6	0.7	0.8	0.9	0.9	8.6

Table 3.2.22c. Parkinson disease medications, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Dopamine agonists	1.27	1.5	1.3	-1.5
Dopaderivatives agonists	1.22	-6.4	2.3	1.2
MAO-B inhibitors	0.65	-25.6	1.4	7.9
COMT inhibitors	0.04	-10.1	0.0	-8.5
Amantadine	0.00	-3.7	0.0	-4.6
Parkinson disease medications	**3.19**	**-8.5**	**5.1**	**2.2**
rotigotine	0.72	0.9	0.4	1.2
levodopa/carbidopa	0.62	-0.4	0.9	2.3
pramipexole	0.40	4.6	0.5	3.3
levodopa/benserazide	0.31	3.0	0.9	1.7
rasagiline	0.29	-56.1	0.4	-13.5
safinamide	0.26	>100	0.1	>100
melevodopa/carbidopa	0.17	3.9	0.3	0.9
ropinirole	0.14	-8.6	0.4	-9.3
levodopa/carbidopa/entacapone	0.12	-43.7	0.2	-4.7
selegiline	0.11	9.4	0.9	8.6

Table 3.2.22d. Prescription of Parkinson disease medications patent expired* in 2017

Categorie	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	1.31	41.2	20.0	2.9	57.1	12.8	1.24
Equivalent	0.27	20.4	12.8	0.6	20.7	-70.1	1.22
Ex originator	1.05	79.6	22.0	2.3	79.3	14.3	1.25
Patent covered	1.88	58.8	-21.5	2.2	42.9	-9.1	2.36
Parkinson disease medications	**3.19**	**100.0**	**-8.5**	**5.1**	**100.0**	**2.2**	**1.72**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Non-steroidal anti-inflammatory drugs (NSAIDs)

Figure 3.2.23a. Non-steroidal anti-inflammatory drugs (NSAIDs), consumption trend (2013-2017)

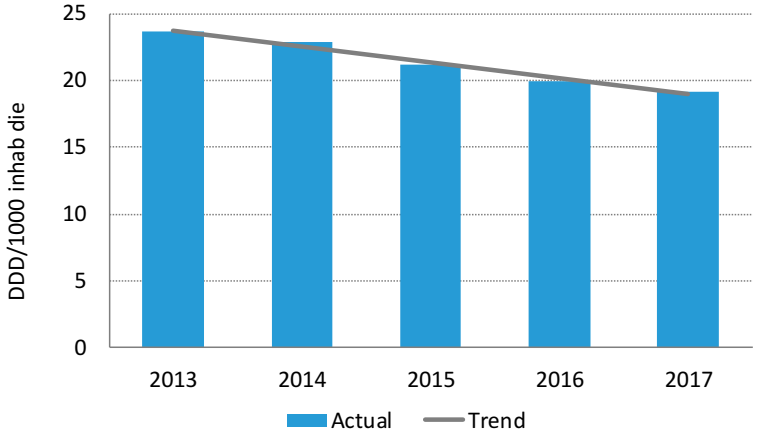


Table 3.2.23a. Non-steroidal anti-inflammatory drugs (NSAIDs), (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Traditional NSAIDs	15.0	14.6	13.7	13.0	12.6	-2.6
Coxib	4.9	4.7	4.4	4.1	3.8	-7.0
Nimesulide	3.1	2.9	2.6	2.3	2.2	-5.1
Ketorolac	0.7	0.7	0.6	0.6	0.6	2.2
NSAIDs	**23.7**	**22.9**	**21.2**	**19.9**	**19.2**	**-3.7**
etoricoxib	3.7	3.8	3.5	3.2	3.0	-6.4
diclofenac	4.3	4.2	4.0	4.0	4.1	3.3
ketoprofen	4.4	4.3	4.0	3.7	3.5	-4.6
ibuprofen	2.2	2.2	2.2	2.1	2.0	-1.7
nimesulide	3.1	2.9	2.6	2.3	2.2	-5.1
celecoxib	1.2	1.0	0.9	0.9	0.8	-9.1
ketorolac	0.7	0.7	0.6	0.6	0.6	2.2
aceclofenac	0.8	0.8	0.6	0.6	0.5	-9.1
piroxicam	0.7	0.7	0.6	0.5	0.5	-6.8
dexibuprofen	0.3	0.3	0.4	0.4	0.4	-8.7

Table 3.2.23c. Non-steroidal anti-inflammatory drugs (NSAIDs), prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Traditional NSAIDs	1.67	-4.0	12.6	-2.6
Coxib	0.94	-21.4	3.8	-7.0
Nimesulide	0.17	-5.3	2.2	-5.1
Ketorolac	0.11	0.1	0.6	2.2
NSAIDs	**2.89**	**-10.4**	**19.2**	**-3.7**
etoricoxib	0.79	-23.1	3.0	-6.4
diclofenac	0.58	1.4	4.1	3.3
ketoprofen	0.36	-5.9	3.5	-4.5
ibuprofen	0.29	-3.9	2.0	-1.7
nimesulide	0.17	-5.3	2.2	-5.1
celecoxib	0.14	-10.6	0.8	-9.1
ketorolac	0.11	0.1	0.6	2.2
aceclofenac	0.10	-10.1	0.5	-9.1
piroxicam	0.08	-6.6	0.5	-6.8
dexibuprofen	0.07	-8.9	0.4	-8.7

Table 3.2.23d. Prescription of non-steroidal anti-inflammatory drugs (NSAIDs) with patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	2.03	70.4	11.7	15.4	80.4	6.8	0.36
Equivalent	0.29	14.2	10.1	3.4	22.1	-69.8	0.23
Ex originator	1.74	85.8	12.0	12.0	77.9	6.8	0.40
Patent covered	0.85	29.6	-39.0	3.8	19.6	-31.4	0.62
NSAIDs	**2.89**	**100.0**	**-10.4**	**19.2**	**100.0**	**-3.7**	**0.41**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Thyroid disease medications

Figure 3.2.24a. Thyroid disease medications, consumption trend (2013-2017)

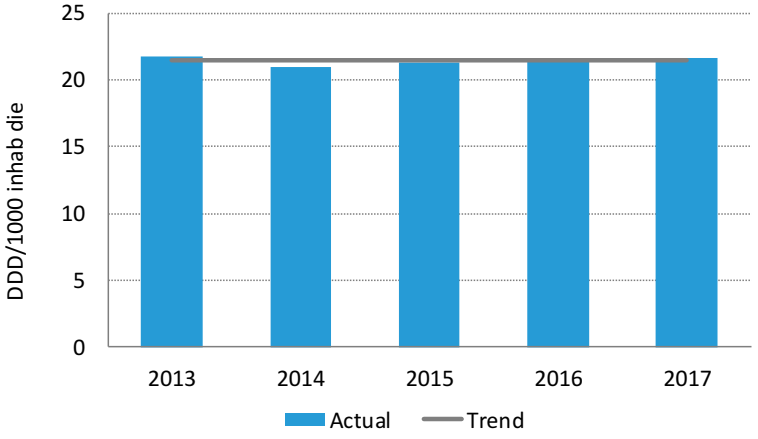


Table 3.2.24a. Thyroid disease medications, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Thyroid hormones	20.4	19.6	19.8	20.0	20.3	1.5
Anti-thyroid agents	1.5	1.5	1.4	1.4	1.4	-1.2
Thyroid disease medications	**21.8**	**21.0**	**21.3**	**21.4**	**21.6**	**1.3**
levothyroxine	20.3	19.5	19.8	19.9	20.2	1.5
thiamazole	1.5	1.5	1.4	1.4	1.4	-1.2
liothyronine	0.0	0.0	0.0	0.0	0.0	5.7

Table 3.2.24c. Thyroid disease medications, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Thyroid hormones	0.93	7.1	20.3	1.5
Anti-thyroid agents	0.05	-1.7	1.4	-1.2
Thyroid disease medications	**0.98**	**6.6**	**21.6**	**1.3**
levothyroxine	0.90	7.1	20.2	1.5
thiamazole	0.05	-1.7	1.4	-1.2
liothyronine	0.03	7.0	0.0	5.7

Table 3.2.24d. Prescription of thyroid disease medications patent expired* in 2017

Categories	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	0.65	65.6	0.3	19.1	88.1	0.2	0.09
Equivalent	0.01	1.7	1.2	0.5	2.5	-97.4	0.06
Ex originator	0.63	98.3	0.3	18.6	97.5	0.1	0.09
Patent covered	0.34	34.4	21.2	2.6	11.9	10.7	0.36
Thyroid disease medications	**0.98**	**100.0**	**6.6**	**21.6**	**100.0**	**1.3**	**0.12**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

Medications for cystic fibrosis

Table 3.2.25a. Medications for cystic fibrosis, per capita expenditure by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2015	2016	2017	Δ % 17-16
Medications for cystic fibrosis	**0.22**	**0.55**	**0.79**	**43.5**
ivacaftor	0.22	0.51	0.48	-6.5
lumacaftor/ivacaftor	-	0.04	0.31	695.0

Table 3.2.25b. Medications for cystic fibrosis, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Medications for cystic fibrosis	**0.79**	**43.5**	**0.0**	**82.8**
ivacaftor	0.48	-6.5	0.0	-1.8
lumacaftor/ivacaftor	0.31	>100	0.0	>100

Antidementia medications

Figure 3.2.26a. Antidementia medications, consumption trend (2013-2017)

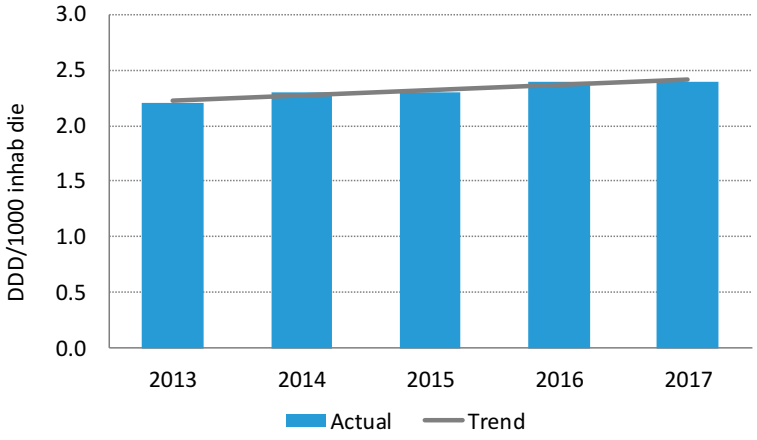


Table 3.2.26a. Antidementia medications, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2013-2017

Subgroups and active ingredients	2013	2014	2015	2016	2017	Δ % 17-16
Anticholinesterases	1.5	1.5	1.5	1.5	1.5	-0.6
Other antidementia medications	0.7	0.8	0.8	0.9	0.9	2.6
Antidementia medications	**2.2**	**2.3**	**2.3**	**2.4**	**2.4**	**0.6**
rivastigmine	0.6	0.7	0.7	0.6	0.6	-4.4
memantine	0.7	0.8	0.8	0.9	0.9	2.6
donepezil	0.7	0.8	0.8	0.8	0.8	3.3
galantamine	0.1	0.1	0.1	0.1	0.1	-11.4

Table 3.2.26d. Prescription of antidementia medications patent expired* in 2017

Categorie	Per capita expenditure	%	Δ % 17-16	DDD/1000 inhab die	%	Δ % 17-16	DDD average cost
Patent expired	0.45	81.7	-9.0	2.1	89.1	3.0	0.58
Equivalent	0.24	54.5	7.0	1.5	68.7	85.7	0.46
Ex originator	0.20	45.5	-22.8	0.7	31.3	-15.6	0.84
Patent covered	0.10	18.3	-48.2	0.3	10.9	-15.6	1.06
Antidementia medications	**0.55**	**100.0**	**-20.1**	**2.4**	**100.0**	**0.6**	**0.63**

* the monthly transparency lists published by the Italian Medicines Agency in 2017 were used

3.3 Off-patent medicines and biosimilars

The expenditure for off-patent medicines represents 59.0% of total NHS pharmaceutical expenditure and 79.4% of total NHS reimbursed consumption for the year 2017.
Generic products, that are off-patent medical products with exception of originators, represent 15.2% and 27.7% of NHS expenditure and consumption respectively (Figure 3.3.1 and Figure 3.3.2).
NHS expenditure for off-patent medicines is mainly due to medicines for cardiovascular (61.4%) and muscolo-skeletal (47.3%) systems (Table 3.3.1).
NHS expenditure and consumption for off-patent medicines has presented a growing trend also during 2017, while the NHS consumption and expenditure for generic medicines remain almost stable (Figure 3.3.3 e Figure 3.3.4).
Among the first twenty off-patent active ingredients, four are proton pump inhibitors, pantoprazole, lansoprazole, omeprazole and esomeprazole, accounting respectively for an expenditure of € 173.4, € 110.5, € 103.9 and € 93.9 million (Table 3.3.2).

Data for 2017, compared to 2016, have confirmed the increasing use of biosimilars that had already been available on the market for several years, such as epoetins (+65.1%), somatropin (+101.8%) and growth factors (+34.8%), which respectively contributed to reduction in expenditure by -8.0%, -4.4% and -6.9%, (Table 3.3.5).

It can be observed that, beside the consumption of biosimilars of infliximab and etanercept, which were already marketed with a positive trend in 2016, the consumption can be detected also of new biosimilars, such as the biosimilar of rituximab, which was marketed in 2017.

Figure 3.3.1. NHS outpatient pharmaceutical expenditure distinguished for patent coverage in the year 2017

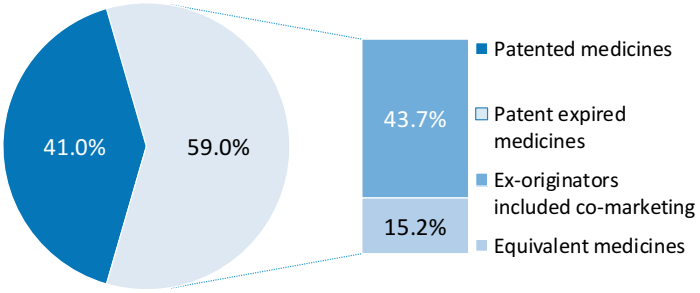
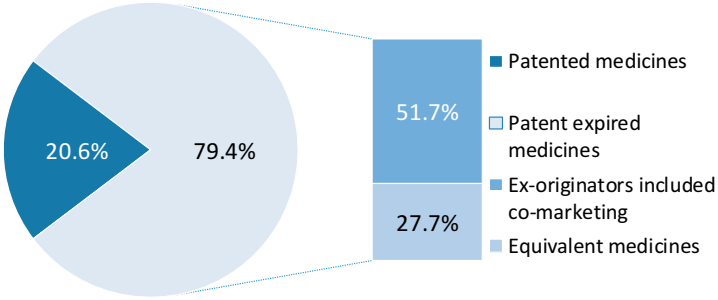


Figure 3.3.2. NHS outpatient pharmaceutical consumption distinguished for patent coverage in the year 2017



Medicines based on active ingredients with an expired patent are considered generic, with the exclusion of those who have received patent protection, pursuant to art.1bis, of the Decree Law of 27 May 2005, no. 87, converted, with amendments, by Law July 26, 2005, no. 149.

Table 3.3.1. Incidence of NHS outpatient pharmaceutical expenditure and consumption of patented expired drugs in 2017 by therapeutic area

ATC I level	NHS outpatient pharmaceutical expenditure		NHS outpatient pharmaceutical consumption (DDD)	
	% Patent expired by therapeutic category	% Generic drug by therapeutic category	% Patent expired by therapeutic category	% Generic drug by therapeutic category
A	43.0	13.8	71.1	31.0
B	6.8	1.9	49.6	13.7
C	61.4	14.4	87.3	30.8
D	18.4	4.0	6.5	0.9
G	37.8	9.6	64.9	23.9
H	15.9	1.6	70.8	4.8
J	14.9	3.3	76.9	20.0
L	5.2	1.0	47.7	23.0
M	47.3	9.4	74.5	24.2
N	41.7	13.1	66.8	31.3
P	5.0	0.9	7.0	3.1
R	12.7	1.7	38.5	8.3
S	11.7	1.4	36.9	7.6
V	3.4	0.9	5.1	2.6

Table 3.3.2. NHS outpatient pharmaceutical expenditure and consumption of Class A medicines, first twenty active ingredients patent expired* with greater expenditure: 2017-2016 comparison

ATC	Active active ingredient	Expenditure *(million)*	Δ % 17-16	% Generic medicines**	DDD/1000 inhab die	DDD average cost
A	pantoprazole	173.40	0.3	43.1	20.4	0.4
A	colecalciferol	151.86	25.9	5.5	7.8	0.9
C	atorvastatin	149.36	7.4	31.1	41.1	0.2
J	amoxicillin/clavulanic acid	111.66	-1.0	17.3	8.6	0.6
A	lansoprazole	110.50	-7.4	61.2	15.4	0.3
A	omeprazole	103.85	-4.9	28.8	16.9	0.3
A	esomeprazole	93.93	-1.0	32.8	12.5	0.3
C	bisoprolol	83.86	7.0	25.9	9.9	0.4
C	ramipril	77.96	-0.1	33.1	61.4	0.1
C	omega 3	70.81	5.1	2.1	3.9	0.8
N	pregabalin	67.04	-22.6	6.0	1.7	1.7
C	simvastatin	64.57	-3.0	46.3	14.3	0.2
C	amlodipine	59.96	-1.6	28.0	26.4	0.1
A	metformin	54.34	5.3	35.3	21.0	0.1
C	nebivolol	53.85	1.8	19.7	14.6	0.2
N	levetiracetam	50.78	5.5	33.3	1.8	1.3
J	ceftriaxone	48.59	-10.0	20.7	0.3	7.4
C	doxazosin	47.11	-1.6	27.3	7.4	0.3
B	acetylsalicylic acid	45.55	-0.3	10.9	43.3	0.1
A	mesalazine	43.32	2.2	11.2	3.2	0.6

*The transparency lists published by the AIFA were used in 2017
**Calculated on the total expenditure for expired patent medicines

Figure 3.3.3. Trend in the incidence of expenditure of expired patent medicines and generic drugs on the total Class A expenditure: comparison 2011-2017

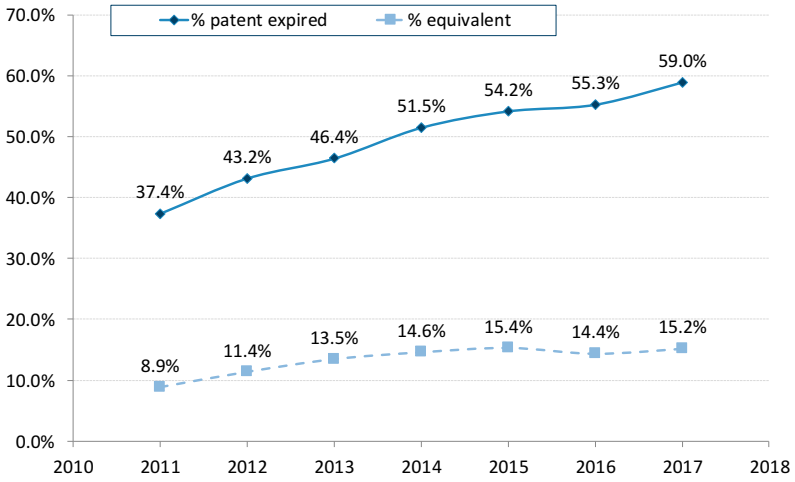
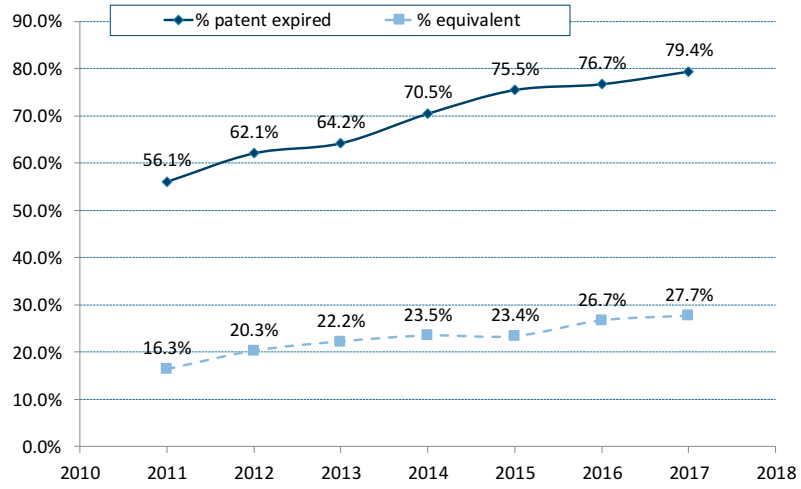


Figure 3.3.4. Trend in the incidence of consumption (doses) of expired patent medicines and generic drugs on the total consumption of Class A medicines: comparison 2011-2017



Biosimilars

Table 3.3.5. Biosimilars inpatient and outpatient NHS supply in 2017

Group Subgroup	Per capita expenditure	Inc %	Δ % 17-16	DDD/1000 inhab die	Inc %	Δ % 17-16
Epoetin	**3.66**		**-8.0**	**3.2**		**14.4**
Originator[1]	0.89	24.4	-17.5	0.7	20.6	-15.5
Biosimilar[2]	1.01	27.7	18.1	1.7	51.4	65.1
Other epoetins[3]	1.75	48.0	-13.9	0.9	28.1	-12.2
Growth factors	**0.95**		**-6.9**	**0.1**		**6.8**
Originator[4]	0.06	6.2	-19.6	0.0	2.2	-26.0
Biosimilar[5]	0.14	14.3	-11.1	0.0	38.7	34.8
Other growth factors[6]	0.75	79.5	-4.9	0.1	59.1	-4.6
Somatropin	**1.46**		**-4.4**	**0.3**		**5.5**
Originator[7]	0.28	19.2	-0.2	0.0	16.0	-2.7
Biosimilar[8]	0.18	12.3	27.3	0.1	18.0	>100
Other somatropin[9]	1.00	68.5	-9.6	0.2	66.0	-5.0
Insulin glargine	**2.86**		**-4.1**	**6.2**		**5.2**
Originator[10]	1.38	48.4	-19.7	3.4	55.2	-11.2
Biosimilar[11]	0.24	8.3	>100	0.7	10.5	>100
Other insulin glargine[12]	0.15	5.3	>100	0.4	5.7	>100
Other insulin long acting[13]	1.09	38.0	-4.7	1.8	28.5	2.9
Follitropin alpha	**1.12**		**-10.7**	**0.1**		**-5.2**
Originator[14]	0.48	43.1	-28.4	0.1	38.5	-21.8
Biosimilar[15]	0.05	4.8	>100	0.0	5.4	>100
Other Follitropin[16]	0.58	52.2	3.2	0.1	56.0	2.4
TNFα inhibitors	**10.94**		**2.4**	**1.1**		**6.8**
Originator Etanercept[17]	2.72	24.9	-14.2	0.2	21.7	-10.3
Biosimilar Etanercept[18]	0.30	2.8	>100	0.0	3.1	>100
Originator Infliximab[19]	0.86	7.9	-23.6	0.1	11.8	-24.2
Biosimilar Infliximab[20]	0.64	5.9	52.0	0.2	14.7	68.0
Other TNFα inhibitors[21]	6.41	58.6	7.7	0.6	48.7	8.2
Rituximab	**3.07**		**-1.8**	**0.6**		**6.7**
Originator[22]	2.99	97.4	-4.3	0.5	97.1	3.6
Biosimilar[23]	0.08	2.6		0.0	2.9	

[1] Eprex®; [2] Binocrit®; Retacrit®; [3] Aranesp®, Eporatio®, Mircera®, Neorecormon®; [4] Granulokine®; [5]Accofil®, Nivestim®, Tevagrastim®, Zarzio®; [6] Neulasta®, Myelostim®, Lonquex®, Granocyte®; [7] Genotropin®; [8] Omnitrope®; [9] Humatrope®, Norditropin®, Nutropinaq®, Saizen®, Zomacton®; [10] Lantus®; [11] Abasaglar®; [12] Toujeo®; [13] Tresiba®, Levemir®; [14] Gonal-F®; [15] Ovaleap®, Bemfola®; [16] Meriofert®, Puregon®, Elonva®, Pergoveris®, Fostimon®, Meropur®; [17] Enbrel®; [18]Benepali®; [19] Remicade®; [20] Inflectra®, Remsina®; [21] Humira®, Cimzia®, Simponi®; [22] Mabthera®; [23] Truxima®

Note: the biosimilar of rituximab has been marketed since September 2017

Figure 3.3.6. Incidence (%) of biosimilars on the expenditure of biosimilars and originators: 2013-2017

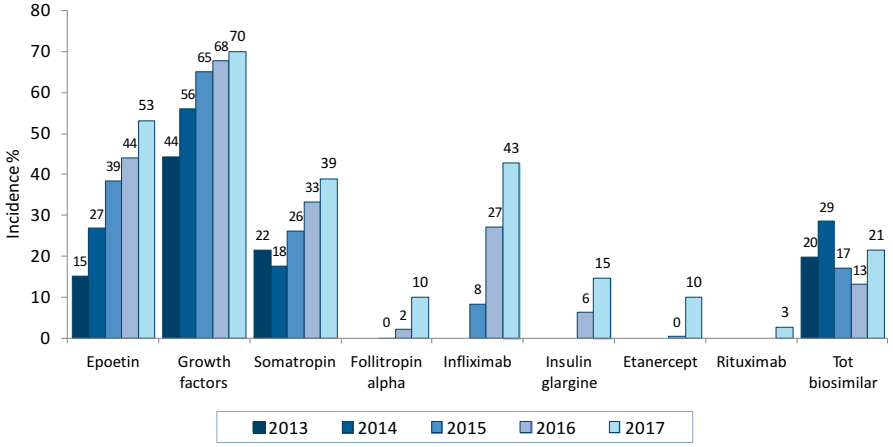


Figure 3.3.7. Incidence (%) of biosimilars on the consumption of biosimilars originators: 2013-2017

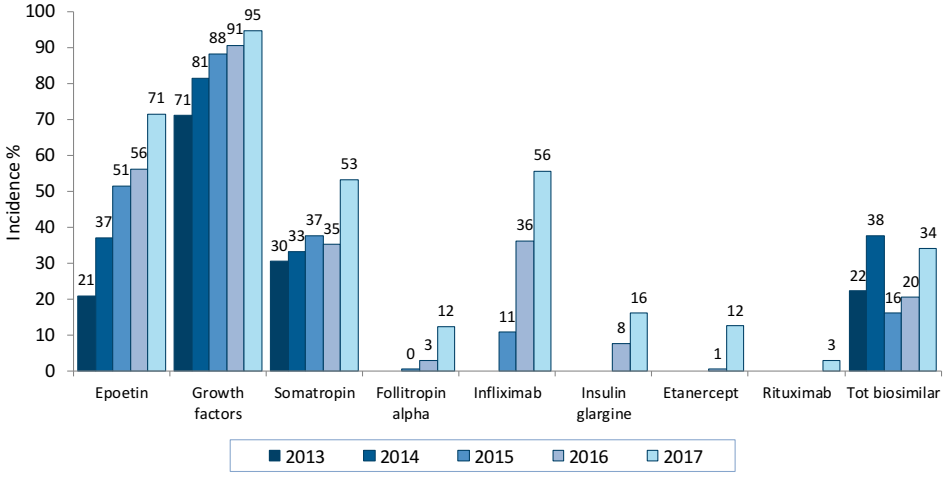


Table 3.3.6. Biosimilars inpatient and outpatient NHS supply in 2017: comparison between biosimilars and originators*

Group Subgroup	Per capita expenditure	Inc %	Δ % 17-16	DDD/1000 inhab die	Inc %	Δ % 17-16
Epoetin	**1.90**		**-1.7**	**2.31**		**29.7**
Originator[1]	0.89	46.9	-17.5	0.66	28.6	-15.5
Biosimilar[2]	1.01	53.1	18.1	1.65	71.4	65.1
Growth factors	**0.19**		**-13.8**	**0.04**		**29.1**
Originator[3]	0.06	30.0	-19.6	0.00	5.4	-26.0
Biosimilar[4]	0.14	70.0	-11.1	0.04	94.6	34.8
Somatropin	**0.46**		**9.0**	**0.09**		**34.1**
Originator[5]	0.28	61.0	-0.2	0.04	47.0	-2.7
Biosimilar[6]	0.18	39.0	27.3	0.05	53.0	>100
Follitropin alpha	**1.62**		**-11.9**	**4.09**		**-2.4**
Originator[7]	1.38	85.3	-19.7	3.44	84.0	-11.2
Biosimilar[8]	0.24	14.7	>100	0.65	16.0	>100
Insulin glargine	**0.54**		**-22.2**	**0.06**		**-13.3**
Originator[9]	0.48	90.0	-28.4	0.05	87.7	-21.8
Biosimilar[10]	0.05	10.0	>100	0.01	12.3	>100
Etanercept	**3.02**		**-5.0**	**0.28**		**1.9**
Originator[11]	2.72	90.0	-14.2	0.24	87.6	-10.3
Biosimilar[12]	0.30	10.0	>100	0.03	12.4	>100
Infliximab	**1.50**		**-3.0**	**0.30**		**9.1**
Originator[13]	0.86	57.3	-23.6	0.13	44.4	-24.2
Biosimilar[14]	0.64	42.7	52.0	0.17	55.6	68.0
Rituximab	**3.07**		**-1.8**	**0.55**		**6.7**
Originator[15]	2.99	97.4	-4.3	0.54	97.1	3.6
Biosimilar[16]	0.08	2.6	-	0.02	2.9	-

* the drug used as a comparator in the clinical study
[1] Eprex®; [2] Binocrit®, Retacrit®; [3] Granulokine®, [4] Accofil®, Nivestim®, Tevagrastim®, Zarzio®; [5] Genotropin®; [6] Omnitrope®; [7]Gonal-F®; [8] Ovaleap®, Bemfola®; [9]Lantus; [10] Abasaglar; [11] Enbrel® [12] Benepali® [13] Remicade® [14] Inflectra® Remsima®; [15] Mabthera; [16] Truxima®

Note: the biosimilar of rituximab has been marketed since September 2017

3.4 Medicines purchased directly by the citizen

In 2017 the citizen expenditure for class C medicines amounted to over 5.6 billions of euros: 51% (2.9 billions of euros) is due to Class C medicines with prescription and 49% (2.7 billions of euros) to self-medication products (SOP and OTC).

The +8.8% increase in Class C medicines with prescription, compared to 2016 datum, is mainly due to an increase (+8.5%) of consumption, while prices and mix effect remain stable (-0.1% and +0.3% respectively; Figure 3.4.1).

Paracetamol, accounting for 143 million euros, is the active ingredient with the highest expenditure (5.0% of the total expenditure). This medicine that is mainly used in the pediatric population for its analgesic and antipyretic action, shows a +10.7% increase compared to 2016. Tadalafil, lorazepam and alprazolam are the other active ingredients with an expenditure of more than 100 million euros, and with an increase compared to 2016, respectively of 5.3%, 4.0% and 8.5% (Table 3.4.2).

Benzodiazepines are the most purchased category, accounting for 18% of the total expenditure and for 26% of DDD of Class C medicines with prescription (Table 3.4.1). In the last four years, consumption remained substantially stable, reaching the value of 47.9 DDD in 2017. The benzodiazepines with anxiolytic and hypnotic effect represent over 90% of the category consumption and rank first and fifth position in terms of expenditure among Class C medications (+6.9% and +8.6% respectively, compared to 2016): lorazepam (1.83 euro per capita), alprazolam (1.73 euro per capita) and lormetazepam (0.87 euro per capita) are the three most prescribed active ingredients, while zolpidem showed the highest increase compared to 2016 (+16.5%) (Tables 3.4.1 and 3.4.2a). In addition, among the first twenty active ingredients at higher expense for Class C medications with prescription (Table 3.4.2), several active ingredients belong to this class: lorazepam, alprazolam, lormetazepam, bromazepam, delorazepam, triazolam.
Medications used for erectile dysfunction rank second with a total expenditure of 255 million euros, the consumption of these products increased from 2.9 DDD/1000 inhabitants day of 2014 to 3.2 DDD/1000 inhabitants day of 2017 (Table 3.4.7a). Tadalafil, which was marketed after sildenafil, is the most expensive active ingredient in 2017 (4.12 euros per capita), followed by sildenafil with 2.94 euros (Table 3.4.7c). Both these active ingredients show a DDD increase of over 18% compared to 2016.

Oral contraceptives are the third most purchased category (250 million euros), with a stable consumption in the last four years. The estro-progestogenic fixed associations cover the more than 80% of DDD consumption of this category, with an increase of almost +5% both in expenditure and consumption (expressed as DDD), compared to 2016.

Significant increases of consumption have also been detected for progestogens (+24.7%) and for emergency contraceptives (+24.5%).

The first four most expensive active ingredients are the estro-progestogen fixed associations: drospirenone / ethinyl estradiol (2.35 euro per capita; -2.8% compared to 2016); gestodene / ethinylestradiol (1.18 euros; -5.7% compared to 2016); levonorgestrel / ethinyl estradiol (0.84 euro, +13.8% compared to 2016) and dienogest / ethinyl estradiol (0.78 euro, +30.0% compared to 2016).
Among self-medication products, azelastine, a second generation antihistamine drug, with an expenditure of 627 million euros (+10% compared to 2016) represents a fifth of the total cost of self-medication, followed by two non-steroidal anti-inflammatory medicines: diclofenac with 195 million euros and ibuprofen with 159 million. Significant increases are reported in expenditure, compared to 2016, for flurbiprofen (+24.1%), a medical product used for the symptomatic treatment of irritative-inflammatory states also associated with oropharyngeal cavity pain and for dysosmia (+24.1%) (Table 3.4.3).

Figure 3.4.1. Trend of outpatient pharmaceutical expenditure during the period for Class C medicines with prescription: consumption effect, prices and mix

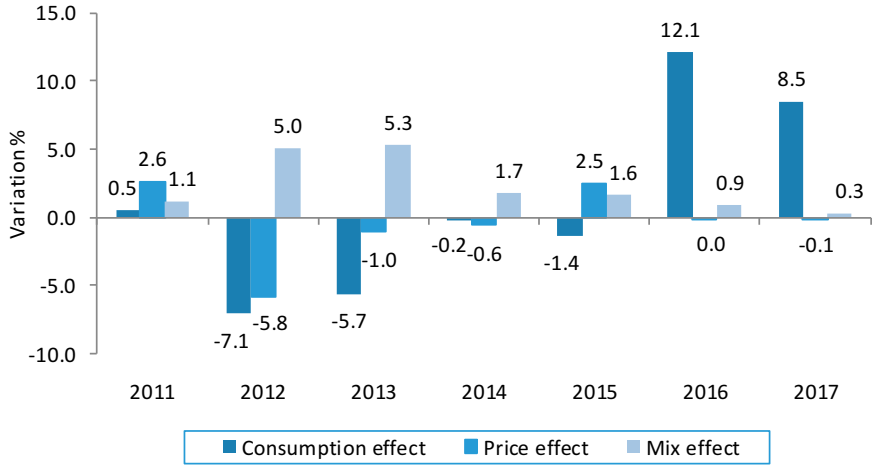


Table 3.4.1. First twenty therapeutic categories at greater expense of Class C medicines with prescription in 2017

ATC	Subgroup	DDD/1000 inhab die	Expenditure *(million)*	%*	Δ% 17-16
N	Benzodiazepine anxiolytic derivatives	25.0	348	12.1	6.7
G	Drugs used in erectile dysfunction	1.6	255	8.9	5.1
G	Estro-progestinic fixed associations	19.5	194	6.8	4.7
N	Anilides	4.8	150	5.2	11.0
N	Hypnotic benzodiazepine derivatives	18.6	121	4.2	8.4
D	Active corticosteroids, combination with antibiotics	4.0	74	2.6	12.8
S	Antimicrobial corticosteroids in combination	2.8	63	2.2	11.6
M	Other centrally-acting muscle relaxants	1.1	57	2.0	2.6
R	Corticosteroids	4.3	57	2.0	6.8
R	Mucolytic	5.5	57	2.0	6.0
N	Analogs of benzodiazepines	4.3	51	1.8	15.9
N	Other psychostimulants and nootropics	1.1	50	1.7	2.7
A	Laxatives with osmotic action	1.5	50	1.7	21.1
N	Antivertigo preparations	2.7	46	1.6	11.0
M	Bisphosphonates	0.0	43	1.5	8.5
B	Heparin	1.9	42	1.5	7.6
M	Other peripheral muscle relaxants	0.0	38	1.3	21.1
J	Other bacterial vaccines	2.4	35	1.2	4.9
D	Corticosteroids, active (group III)	3.3	34	1.2	-1.7
N	Benzamides	1.0	33	1.2	9.1

**calculated on total expenditure*

Table 3.4.2. First twenty active ingredients with a higher cost of Class C medicines with prescription in 2017

ATC	Active ingredient	DDD/1000 inhab die	Expenditure *(million)*	%*	Δ% 17-16
N	paracetamol	4.6	143	5.0	10.7
G	tadalafil	0.6	121	4.2	5.3
N	lorazepam	10.2	111	3.8	4.0
N	alprazolam	8.7	105	3.6	8.5
G	sildenafil	0.7	87	3.0	14.9
G	drospirenone/ethinyl estradiol	6.1	73	2.5	-3.0
D	gentamicin/betamethasone	3.5	64	2.2	11.3
N	lormetazepam	13.0	53	1.8	8.2
N	zolpidem	4.1	49	1.7	16.4
N	bromazepam	1.4	47	1.6	7.4
R	acetylcysteine	4.4	46	1.6	9.0
N	delorazepam	2.3	41	1.4	10.2
M	thiocolchicoside	0.6	39	1.4	0.1
N	triazolam	3.3	37	1.3	8.0
G	gestodene/ethinyl estradiol	6.2	37	1.3	-5.9
N	levoacetilcarnitin	0.7	35	1.2	7.8
N	betahistine	2.1	34	1.2	12.6
G	vardenafil	0.2	33	1.1	-11.4
G	etonogestrel/ethinyl estradiol	2.1	32	1.1	8.8
S	dexamethasone/tobramycin	1.4	31	1.1	8.5

** calculated on total expenditure*

Table 3.4.3. First twenty active ingredients of self-medication (SOP and OTC) at greater expenditure in 2017

ATC	Active ingredient	DDD/1000 inhab die	Expenditure *(million)*	%*	Δ % 17-16	% SOP	% OTC
R	azelastine	2.5	627	20.5	10.0	99.9	0.1
M	diclofenac	1.4	195	6.3	3.4	96.4	3.6
M	ibuprofen	0.4	159	5.2	6.0	78.9	21.1
A	probiotic	0.3	134	4.4	0.1	91.7	8.3
N	paracetamol	0.3	120	3.9	11.9	4.5	95.5
A	flurbiprofen	0.4	96	3.1	24.1	85.5	14.5
C	diosmin	0.4	94	3.1	22.0	-	100.0
M	ketoprofen	0.2	57	1.9	18.5	100.0	-
R	nafazolina	1.3	54	1.8	-1.7	100.0	-
R	ambroxol	0.1	52	1.7	-2.4	30.0	70.0
N	acetylsalicylic acid/ascorbic acid	0.1	49	1.6	2.7	100.0	0.0
A	glycerol	0.2	47	1.5	16.7	98.3	1.7
R	carbocysteine	0.2	37	1.2	10.0	88.4	11.6
A	loperamide	0.0	33	1.1	-7.1	78.7	21.3
G	clotrimazole	0.1	31	1.0	4.4	99.9	0.1
N	paracetamol/ascorbic acid/phenylephrine	0.1	30	1.0	-4.6	100.0	-
R	benzydamine	0.1	25	0.8	3.8	99.6	0.4
M	naproxen	0.1	21	0.7	12.8	90.9	9.2
D	povidone-iodine	0.2	21	0.7	-12.4	99.3	0.7
R	oxymetazoline	0.2	20	0.7	5.9	100.0	-

** calculated on total expenditure*

Figure 3.4.5a. Benzodiazepines outpatient consumption trend (2014-2017)

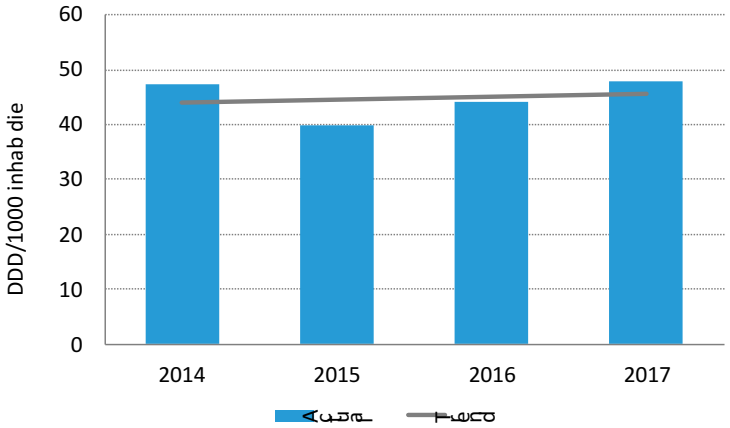


Table 3.4.5a. Benzodiazepines, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2014-2017

Subgroups and active ingredients	2014	2015	2016	2017	Δ % 17-16
Anxiolytics	25.2	21.2	23.4	25.0	7.0
Hypnotics	18.5	15.6	17.0	18.6	9.1
Sedatives	3.7	3.1	3.7	4.3	16.4
Benzodiazepines	**47.4**	**40.0**	**44.1**	**47.9**	**8.6**
lorazepam	10.8	9.2	9.8	10.2	4.9
alprazolam	8.1	7.0	8.0	8.7	8.9
lormetazepam	13.1	11.1	11.9	13.0	9.0
zolpidem	3.5	3.0	3.5	4.1	16.7
bromazepam	1.5	1.2	1.3	1.4	7.7
delorazepam	2.2	1.9	2.0	2.3	10.4
triazolam	3.1	2.7	3.0	3.3	8.6
diazepam	1.3	1.0	1.1	1.2	7.1
brotizolam	1.4	1.1	1.3	1.4	10.0
flurazepam	0.6	0.5	0.6	0.6	9.7

Table 3.4.5c. Benzodiazepines prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Anxiolytics	5.74	6.9	25.0	7.0
Hypnotics	2.00	8.6	18.6	9.1
Sedatives	0.85	16.1	4.3	16.4
Benzodiazepines	**8.59**	**8.1**	**47.9**	**8.6**
lorazepam	1.83	4.2	10.2	4.9
alprazolam	1.73	8.6	8.7	8.9
lormetazepam	0.87	8.3	13.0	9.0
zolpidem	0.81	16.5	4.1	16.7
bromazepam	0.77	7.6	1.4	7.7
delorazepam	0.68	10.3	2.3	10.4
triazolam	0.62	8.2	3.3	8.6
diazepam	0.32	5.7	1.2	7.1
brotizolam	0.28	8.5	1.4	10.0
flurazepam	0.13	9.0	0.6	9.7

All indicators of this section are calculated only in the female population

Figure 3.4.6a. Oral contraceptives outpatient consumption trend (2014-2017)

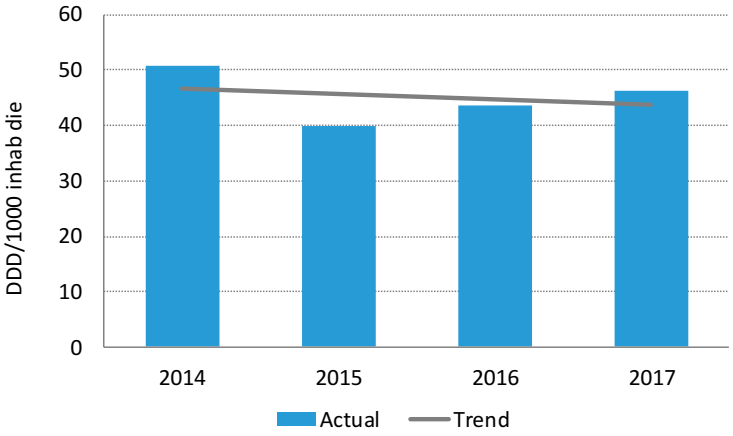


Table 3.4.6a. Oral contraceptives, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2014-2017

Subgroups and active ingredients	2014	2015	2016	2017	Δ % 17-16
Estro-progestinic fixed associations	42.4	33.2	36.1	37.9	4.8
Estrogen-progestin sequential preparations	6.4	5.1	5.4	5.7	6.9
Progestin	1.8	1.7	2.1	2.6	24.7
Emergency contraceptives	0.0	0.0	0.0	0.0	24.5
Oral contraceptives	**50.7**	**40.0**	**43.6**	**46.2**	**6.0**
drospirenone/ethinyl estradiol	16.3	12.1	12.0	11.8	-1.7
gestodene/ethinyl estradiol	16.1	11.9	12.5	12.1	-3.6
levonorgestrel/ethinyl estradiol	4.2	3.7	4.5	5.1	14.2
dienogest/ethinyl estradiol	1.7	2.2	3.3	4.3	30.6
dienogest/estradiol	2.7	2.4	2.9	3.4	18.2
estradiol/nomegestrol	1.6	1.5	1.8	2.2	18.3
desogestrel	1.7	1.6	1.9	2.4	26.3
ethinylestradiol/norelgestromin	1.5	1.1	1.2	1.4	14.5
desogestrel/ethinyl estradiol	2.6	1.8	1.7	1.7	-4.6
chlormadinone/ethinylestradiol	1.4	1.0	1.1	1.1	2.5

Table 3.4.6c. Oral contraceptives, prescription by therapeutic category and by active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Estro-progestinic fixed associations	6.24	4.9	37.9	4.8
Estrogen-progestin sequential preparations	0.99	12.0	5.7	6.9
Progestin	0.40	24.2	2.6	24.7
Emergency contraceptives	0.32	22.8	0.0	24.5
Oral contraceptives	**7.95**	**7.2**	**46.2**	**6.0**
drospirenone/ethinyl estradiol	2.35	-2.8	11.8	-1.7
gestodene/ethinyl estradiol	1.18	-5.7	12.1	-3.6
levonorgestrel/ethinyl estradiol	0.84	13.8	5.1	14.2
dienogest/ethinyl estradiol	0.78	30.0	4.3	30.6
dienogest/estradiol	0.76	17.8	3.4	18.2
estradiol/nomegestrol	0.47	18.3	2.2	18.3
desogestrel	0.39	24.8	2.4	26.3
ethinylestradiol/norelgestromin	0.29	14.5	1.4	14.5
desogestrel/ethinyl estradiol	0.24	-3.2	1.7	-4.6
chlormadinone/ethinylestradiol	0.21	2.4	1.1	2.5

All indicators of this section are calculated only in the male population

Figure 3.4.7a. Medicines used in erectile dysfunction time trend of territorial consumption (2014-2017)

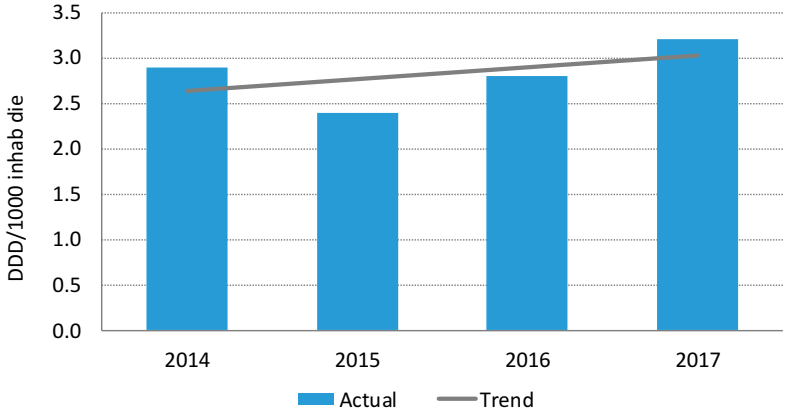


Table 3.4.7a. Medicines used in erectile dysfunction, consumption (DDD/1000 inhab die) by therapeutic category and by active ingredient: comparison 2014-2017

Subgroups and active ingredients	2014	2015	2016	2017	Δ % 17-16
Medicines used in erectile dysfunction	**2.9**	**2.4**	**2.8**	**3.2**	**13.0**
tadalafil	1.3	0.9	1.1	1.3	18.4
sildenafil	1.0	1.0	1.2	1.4	18.0
vardenafil	0.5	0.3	0.4	0.3	-11.7
avanafil	0.1	0.1	0.2	0.2	0.5
alprostadil	0.0	0.0	0.0	0.0	-20.0

Table 3.4.7c Medicines used in erectile dysfunction, prescription by therapeutic category and active ingredient in 2017

Subgroups and active ingredients	Per capita expenditure	Δ % 17-16	DDD/1000 inhab die	Δ % 17-16
Medicines used in erectile dysfunction	**8.68**	**5.2**	**3.2**	**13.0**
tadalafil	4.12	5.4	1.3	18.4
sildenafil	2.94	15.0	1.4	18.0
vardenafil	1.12	-11.4	0.3	-11.7
avanafil	0.35	-0.4	0.2	0.5
alprostadil	0.14	-13.9	0.0	-20.0

Section 4

AIFA medicines monitoring registries and managed entry agreements

4.1 AIFA Monitoring Registries

Introduction

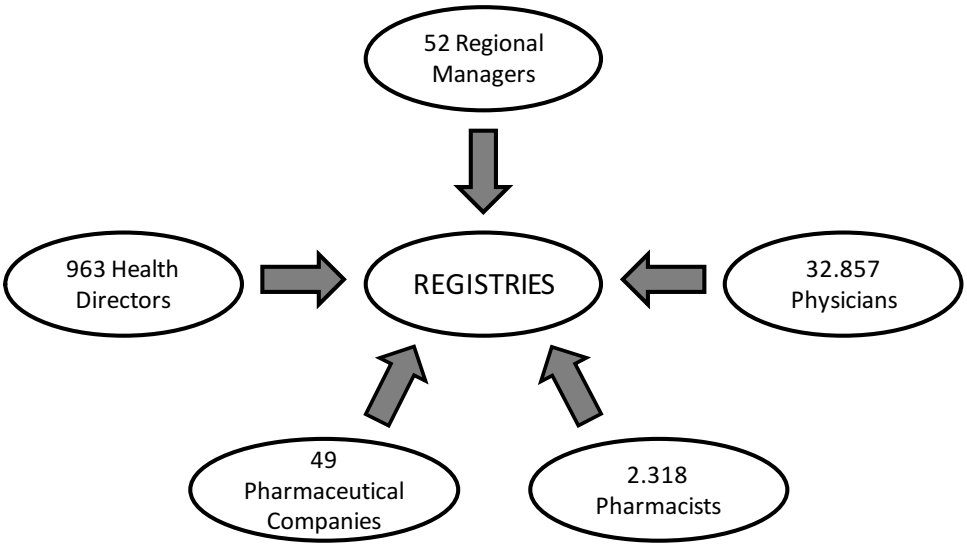
Monitoring registries are an advanced tool for the governance of prescribing appropriateness; they have been developed by the Italian Medicines Agency since 2005 and represent an additional regulatory tool, such as the Therapeutic Plans (TP) and the AIFA Notes.
Medicines are usually entered in Monitoring Registries immediately after their marketing authorization, or after the authorization of an extension of the therapeutic indication.
In special cases registers are also used to monitor medicines reimbursed by NHS according to Law 648/96. The initial regulatory experience was gathered through the Cancer Drugs Registry and was then extended to other therapeutic areas. In such cases AIFA deems this tool necessary to check prescribing appropriateness and NHS pharmaceutical expenditure.
AIFA Registries have become a well-established reality also in function of several laws passed over time, starting from Law no. 135 of 7 August 2012, which recognized Registries as an integral part of the National Health Service Information System (Art.15, paragraph 10). Subsequently, further regulations were introduced (Law 125/2015, Law 232/2016, Law 205/2017) which assigned different purposes to Registries: evaluating medicines' efficacy, acting as support for renegotiations, monitoring expenditure for innovative medicines and monitoring avoidable costs in the health care sector.
As reported in Figure 4.1.1, several stakeholders are involved in the registry process. In particular, within AIFA, the definition and the implementation of a registry firstly requires the definition of specific indicators of full treatment response and the identification of patients' subgroups who can obtain the maximum therapeutic benefit.
The registry platform management network includes about 3,500 health facilities, 52 regional managers, 963 Health Directors, 32,857 physicians and 2,318 pharmacists.
It is a very important network that allows Regions to regulate the organization of pharmaceutical assistance at a local level.
Currently, 49 Pharmaceutical Companies hold at least one monitoring registry, managed through the AIFA platform. This platform allows pharmaceutical companies to interact with the individual pharmacies, in compliance with Managed Entry Agreements (MEAs). In fact, the Registries platform allows the application of MEAs (for more details see section 4.2).

Moreover, AIFA Monitoring Registries satisfy the need for a rapid access to those medicines considered potentially very important for health, but also limiting the NHS expenditure through the implementation of reimbursement strategies, in order to guarantee the sustainability of NHS pharmaceutical expenditure, in particular for those medicines with very high marginal costs.

The role of registries is particularly relevant for recently authorized medicines that despite a positive benefit/risk ratio still have some uncertainty or in the case that the benefit/risk ratio might change according to the modality of use. Instead, in the case of an extension

approval of any of the already authorised and commercialised therapeutic indication, the registries allow the use of the medicine in strictly accordance with the new indication.
In fact, most of medicines included in the AIFA Registries received a centralized authorization (often accelerated and/or conditioned) which mainly concerns biological and/or high cost medicines for the NHS.
In particular, the definition and the implementation of a registry require, first of all, the definition of specific indicators of full treatment response and the identification of patients subpopulations that can obtain the maximum therapeutic benefit. The selection of indicators and their parametrisation according to the treatment outcome are a process carried out within the AIFA commissions, scientific-technical committee (Commisione tecnico scientifica - CTS) and price and reimbursement committee (Comitato Prezzi e Rimborso - CPR), together with the assessment of the economic implications arising from the medicinal product authorization. After that, the Commissions shall appoint the Monitoring Registers Office to implement and validate a dedicated medicine monitoring form.

Figure 4.1.1. Staff participating in the Registry Network in the year 2017



Structure of AIFA Monitoring Registries

The Monitoring Registries are designed to collect both clinical and administrative data and to make an automatic check of consistency and quality of data inputted.

Each AIFA Monitoring registry is based on data collected specifically for one single indication of a medicinal product. Physicians and pharmacists are due to insert information in the following order:

1. Patient demographic data (collected by a form common to all Registries and/or therapeutic plan)
2. Eligibility and clinical data
3. Prescription data (such as medicine name, dosage etc.)
4. Eligibility and clinical data at Re-evaluation visit
5. Eligibility and clinical data at Follow-up visit
6. End of treatment data
7. Pregnancy data (for medicine requiring a Risk Management Plan)

Italy is also provided with another online tool, the web-based *Therapeutic Plan* (TP), which similarly to Monitoring Registries, can be used only by specialized and authorized physicians. The number of web-based Therapeutic Plans (TP) implemented in the period 2014-2017 amounts to 16.

As of December 31, 2017, the total number of Monitoring Registries amounts to 212: 122 web-based, 61 in development and temporary available in paper format and 29 closed. In 2017, AIFA Scientific Technical Commitee has requested the Monitoring Registers Office to establish 41 new Monitoring Registries.

The complete updated list of AIFA Monitoring Registries is available through the following link: http://www.aifa.gov.it/content/lista-aggiornata-dei-registri-e-dei-piani-terapeutici-web-based

AIFA Monitoring Registries Data

An analysis of AIFA monitoring registries is presented in the following tables.

Table 4.1.1. Summary data of the monitoring registries present in the web platform: cumulative trend 2014-2017

	N.				Δ %
	2014	2015	2016	2017	17-16
Registries	106	126	132	151	14.4
PT web based	11	14	16	16	0.0
Treatments	442,896	799,565	1,195,621	1,644,119	37.5
Patients	363,355	660,724	992,868	1,463,548	47.4

Table 4.1.2. Number of treatments in 2015-2017 by I ATC

ATC I Level	Treatments initiated			Incidence %			Δ %	
	2015	2016	2017	2015	2016	2017	16-15	17-16
A	38	47	57	0.0	0.0	0.0	0.0	0.0
B	360,022	571,401	821,725	45.0	47.8	50.0	53.4	55.8
C	344	1,438	3,511	0.0	0.1	0.2	0.3	0.5
D	1,552	1,762	1,920	0.2	0.2	0.1	0.1	0.0
H	125	158	183	0.0	0.0	0.0	0.0	0.0
J	32,573	66,573	111,745	4.1	5.6	6.8	8.6	10.1
L	204,286	274,413	341,898	25.6	23.0	20.8	17.7	15.1
M	75,132	111,308	149,992	9.4	9.3	9.1	9.1	8.6
N	5,503	6,632	7,734	0.7	0.6	0.5	0.3	0.3
R	2,030	2,328	2,512	0.3	0.2	0.2	0.1	0.0
S	117,881	159,458	202,718	14.7	13.3	12.3	10.5	9.7
V	79	103	124	0.0	0.0	0.0	0.0	0.0
Total	**799,565**	**1,195,621**	**1,644,119**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**

Table 4.1.3. Number of patients in the ATC categories (I Level) for the period 2015-2017

ATC I Level	N° Patients			Incidence %			Δ %	
	2015	2016	2017	2015	2016	2017	16-15	17-16
A	38	47	57	0.0	0.0	0.0	0.0	0.0
B	359,990	571,369	821,693	45.8	48.4	50.6	53.8	56.2
C	344	1,437	3,510	0.0	0.1	0.2	0.3	0.5
D	1,549	1,759	1,917	0.2	0.2	0.1	0.1	0.0
H	125	158	183	0.0	0.0	0.0	0.0	0.0
J	32,573	66,573	111,745	4.1	5.6	6.9	8.7	10.1
L	202,808	272,507	339,553	25.8	23.1	20.9	17.7	15.1
M	75,023	111,138	149,798	9.5	9.4	9.2	9.2	8.7
N	5,503	6,632	7,734	0.7	0.6	0.5	0.3	0.3
R	2,028	2,326	2,510	0.3	0.2	0.2	0.1	0.0
S	106,288	145,492	186,261	13.5	12.3	11.5	10.0	9.2
V	79	103	124	0.0	0.0	0.0	0.0	0.0
Total	**786,348**	**1,179,541**	**1,625,085**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**

Table 4.1.4. Number of treatments initiated by ICD category (years 2015-2017)
ICD: International Classification of Diseases

ICD classification	Treatments initiated			Incidence %			Δ %	
	2015	2016	2017	2015	2016	2017	16-15	17-16
Diseases of the blood and hematopoietic organs	3,319	4,747	6,312	0.4	0.4	0.4	0.4	0.4
Diseases of the circulatory system	357,917	568,554	818,042	44.8	47.6	49.8	53.2	55.6
Diseases of the nervous system and sensory organs	132,111	181,593	232,717	16.5	15.2	14.2	12.5	11.4
Diseases of the musculoskeletal system and connective tissue	64,635	96,266	131,120	8.1	8.1	8.0	8.0	7.8
Diseases of the digestive system	1,349	2,315	3,076	0.2	0.2	0.2	0.2	0.2
Diseases of the respiratory system	4,082	5,095	6,007	0.5	0.4	0.4	0.3	0.2
Diseases of the skin and subcutaneous tissue	1,552	1,762	1,920	0.2	0.2	0.1	0.1	0.0
Diseases of the nutrition and metabolism endocrine glands and immune disorders	1,217	2,527	4,834	0.2	0.2	0.3	0.3	0.5
Infectious and parasitic diseases	31,861	65,576	110,553	4.0	5.5	6.7	8.5	10.0
Not classified	6,166	7,731	9,301	0.8	0.7	0.6	0.4	0.4
Tumors	195,356	259,455	320,237	24.4	21.7	19.5	16.2	13.6
Total	**799,565**	**1,195,621**	**1,644,119**	**100**	**100**	**100**	**100**	**100**

Table 4.1.5. Number of patients enrolled for ICD category (years 2015-2017)
ICD: International Classification of Diseases

ICD classification	Patients			Incidence %			Δ %	
	2015	2016	2017	2015	2016	2017	16-15	17-16
Diseases of the blood and hematopoietic organs	3,319	4,747	6,312	0.4	0.4	0.4	0.4	0.4
Diseases of the circulatory system	357,885	568,522	818,010	45.5	48.2	50.3	53.6	56.0
Diseases of the nervous system and sensory organs	119,549	166,262	214,491	15.2	14.1	13.2	11.9	10.8
Diseases of the musculoskeletal system and connective tissue	64,526	96,116	130,946	8.2	8.2	8.1	8.0	7.8
Diseases of the digestive system	1,349	2,315	3,076	0.2	0.2	0.2	0.3	0.2
Diseases of the respiratory system	4,080	5,093	6,005	0.5	0.4	0.4	0.3	0.2
Diseases of the skin and subcutaneous tissue	1,549	1,759	1,917	0.2	0.2	0.1	0.1	0.0
Diseases of the nutrition and metabolism endocrine glands and immune disorders	1,217	2,526	4,833	0.2	0.2	0.3	0.3	0.5
Infectious and parasitic diseases	31,861	65,576	110,553	4.1	5.6	6.8	8.6	10.1
Not classified	6,166	7,731	9,301	0.8	0.7	0.6	0.4	0.4
Tumors	194,847	258,894	319,641	24.8	22.0	19.7	16.3	13.6
Total	**786,348**	**1,179,541**	**1,625,085**	**100**	**100**	**100**	**100**	**100**

Demographic characteristics of patients included in AIFA Monitoring Registries and in web based Therapeutic Plans (TPs)

The percentage distribution of treatments included in Monitoring Registries and in web - based TPs, stratified by gender and age, is reported in the following tables. These data clearly show the high prevalence of patients aged over 60 years.
The distribution of treatments by age and gender is reported and distincted for Monitoring Registries and Therapeutic Plans in tables 4.1.6 and 4.1.7. Data of Registries show that the largest number of treatments was recorded in the 70-79 years age group, in both genders, while TPs data show that the highest number of treatments can be found in the 70-79 years age group for males and in over-80s age group for females.

Table 4.1.6. Year 2017 - Number of treatments by age group and gender in the Registries

Age (class)	Men		Women	
	N. Treatments	Inc. %	N. Treatments	Inc. %
<40	10,332	1.52	9,915	1.46
40-49	27,679	4.08	23,573	3.48
50-59	63,310	9.34	50,232	7.41
60-69	95,449	14.08	77,096	11.37
70-79	113,899	16.80	100,399	14.81
>80	48,171	7.11	57,870	8.54
Total	**358,840**	**52.93**	**319,085**	**47.07**

Table 4.1.7. Year 2017 - Number of treatments by age and gender in the Therapeutic Plans

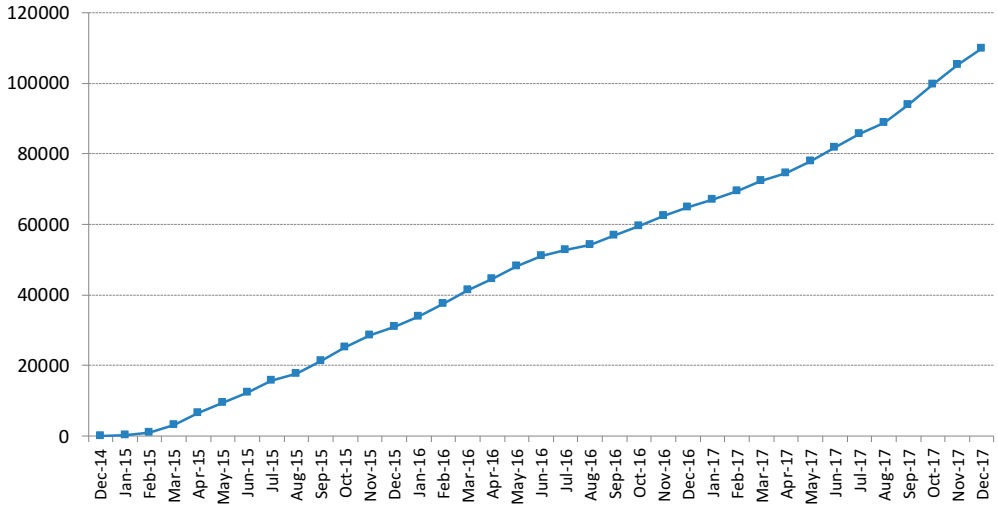
Age (class)	Men		Women	
	N. Treatments	Inc.%	N. Treatments	Inc.%
<40	4,472	0.46	4,174	0.43
40-49	10,798	1.12	9,456	0.98
50-59	30,364	3.14	27,699	2.87
60-69	83,189	8.61	83,856	8.68
70-79	157,032	16.25	192,938	19.97
>80	136,192	14.10	226,024	23.39
Total	**422,047**	**43.68**	**544,147**	**56.32**

Chronic C hepatitis

AIFA launched the monitoring registries for the 2nd generation of Direct Antiviral Antigens (DAAs) indicated for treatment of chronic hepatitis C (CHC) in December 2014. These registries aim to monitor appropriatness of prescription and implementation of MEAs. In total there are 9 DAAs Monitoring Registries as of 31 December 2017. The active ingredients with brand name, registry activation date and genotypic target are listed below. Figure 4.1.2 shows the time serie of treatments started (cumulative datum).

Active ingredient (Brand name)	Activation date of Registry	Genotype
sofosbuvir (Sovaldi)	6 dec 2014	All genotypes
simeprevir (Olysio)	24 feb 2015	1 e 4
daclatasvir (Daklinza)	5 may 2015	1, 2, 3 e 4
ledipasvir/sofosbuvir (Harvoni)	14 may 2015	1, 3, 4
ombitasvir/paritaprevir/ ritonavir (Viekirax) e dasabuvir (Exviera)	24 may 2015	1 e 4
elbasvir/grazoprevir (Zepatier)	4 feb 2017	1 e 4
sofosbuvir/velpatasvir (Epclusa)	27 apr 2017	All genotypes
glecaprevir/pibrentasvir (Maviret)	28 sep 2017	All genotypes

Figure 4.1.2. Number of treatments started (cumulative)



Novel oral anticoagulants (NOACs)

In Italy, the novel oral anticoagulants (NOACs), dabigatran, rivaroxaban, apixaban and edoxaban, have been reimbursed since 2013 for the prevention of cerebral stroke and systemic embolism in patients with non-valvular atrial fibrillation (FANV), and for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and prevention of recurrence of DVT and PE in adults The last NOAC approved for NHS reimbursement was edoxaban, in September 2016.

Tables of this paragraph report data related to the following therapeutic indications "Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischaemic attack".

In particular, in Italy, in order to be enrolled in the NOACs registries a patient was required to be older than 18 years and to meet one of the following main criteria:

- CHA2DS2VASc and the HAS-BLED scores ≥1 and >3, respectively (or both >3 for rivaroxaban);
- previous treatment with VKA with a time of therapeutic range (TTR) ≤70% (60% for rivaroxaban);
- anticoagulant treatment with VKA not feasible for objective difficulties to carry out INR monitoring;
- patients undergoing cardioversion (just for rivaroxaban as of December 2016).

Table 4.1.9. Baseline characteristics of patients treated with NOACs

	Apixaban		Edoxaban		Dabigatran		Rivaroxaban		Total	
	N	%	N	%	N	%	N	%	N	%
Patients, N°	225,457		47,397		207,252		245,584		725,690	
Age, aa median (range)	79 (18-109)		79 (18-104)		77 (18-102)		78 (18-106)		78 (18-109)	
Gender										
Women	118,703	52.6	24,850	52.4	97,418	47.0	122,722	50.0	363,693	50.1
Men	106,754	47.4	22,547	47.6	109,834	53.0	122,862	50.0	361,997	49.9
CHA2DS2VASc Score										
0	864	0.4	210	0.4	1,390	0.7	1,965	0.8	4,429	0.6
1	6,680	3.0	1,706	3.6	9,223	4.5	10,271	4.2	27,880	3.8
2	21,554	9.6	5,353	11.3	26,295	12.7	27,838	11.3	81,040	11.2
3	45,719	20.3	10,564	22.3	47,895	23.1	52,653	21.4	156,831	21.6
4	62,803	27.9	13,545	28.6	55,386	26.7	67,486	27.5	199,220	27.5
5	45,140	20.0	8,786	18.5	35,984	17.4	45,567	18.6	135,477	18.7
6	26,661	11.8	4,604	9.7	19,711	9.5	24,874	10.1	75,850	10.5
7	11,561	5.1	1,943	4.1	8,394	4.1	10,827	4.4	32,725	4.5
8	3,791	1.7	597	1.3	2,535	1.2	3,476	1.4	10,399	1.4
9	684	0.3	89	0.2	433	0.2	622	0.3	1,828	0.3
10	-	-	-	-	6	-	5	-	11	-
Total	**225,457**	**100.0**	**47,397**	**100.0**	**207,252**	**100.0**	**245,584**	**100.0**	**725,690**	**100.0**
HAS-BLED Score										
0	2,893	1.3	761	1.6	4,130	2.0	5,007	2.0	12,791	1.8
1	27,876	12.4	7,422	15.7	29,844	14.4	34,048	13.9	99,190	13.7
2	89,107	39.5	20,935	44.2	78,147	37.7	98,932	40.3	287,121	39.6
3	65,475	29.0	11,813	24.9	60,480	29.2	68,563	27.9	206,331	28.4
4	33,203	14.7	5,441	11.5	29,311	14.1	32,569	13.3	100,524	13.9
5	6,057	2.7	910	1.9	4,745	2.3	5,668	2.3	17,380	2.4
6	756	0.3	97	0.2	526	0.3	660	0.3	2,039	0.3
7	81	0.0	15	0.0	52	0.0	99	0.0	247	0.0
8	8	0.0	2	0.0	11	0.0	32	0.0	53	0.0
9	1	0.0	1	0.0	6	0.0	6	0.0	14	0.0
Total	**225,457**	**100.0**	**47,397**	**100.0**	**207,252**	**100.0**	**245,584**	**100.0**	**725,690**	**100.0**
Comorbidity										
Heart failure / left ventricular dysfunction	68,616	30.4	13,334	28.1	53,520	25.8	73,923	30.1	209,393	28.9
Hypertension	194,215	86.1	40,710	85.9	180,062	86.9	212,611	86.6	627,598	86.5
Diabetes mellitus	45,508	20.2	8,947	18.9	41,215	19.9	48,471	19.7	144,141	19.9
Previous Stroke	44,686	19.8	7,213	15.2	39,023	18.8	41,835	17.0	132,757	18.3
Vascular diseases	62,967	27.9	12,204	25.7	54,882	26.5	66,987	27.3	197,040	27.2
Impaired renal function	17,013	7.5	3,138	6.6	5,987	2.9	13,185	5.4	39,323	5.4
Impaired liver function	2,302	1.0	380	0.8	2,209	1.1	2,190	0.9	7,081	1.0
History of bleeding	31,597	14.0	5,060	10.7	22,546	10.9	24,247	9.9	83,450	11.5

PCSK-9 inhibitors for the treatment of hypercholesterolaemia

Evolocumab and alirocumab have been reimbursed for the treatment of hypercholesterolemia since 2017. These are monoclonal antibodies that inactivate proprotein convertase subtilsin-kexin type 9 (PCSK-9) involved in the recycling of LDL receptors to the cell surface.

In Italy, in the context of primary hypercholesterolaemia (heterozygote familial and non-familial) or mixed dyslipidaemia, PCSK9 inhibitors are reimbursed according to the following prescribing criteria:

In adult patients aged 12-80 years who do not reach pre-defined LDL-C levels despite at least 6 months of prior combination therapy with maximum tolerated dose of high-potency statin agent and ezetimibe or ezetimibe monotherapy in case of statin-intolerant patients both in primary and secondary CVD prevention:
- Primary CVD prevention in patients with familial heterozygote hypercholesterolaemia (HeFH) and LDL-C ≥130mg/dL;
- Secondary CVD prevention in patients with HeFH or non-familiar hypercholesterolaemia or mixed dyslipidaemia with LDL-C ≥100mg/dL.

Then evolocumab, consistently with the more extensive authorized indication, is also reimbursed in homozygous familial hypercholesterolemia for patients aged 12-80 years.

Tables of this paragraph report data related to reimbursed therapeutic indications.

Table 4.1.11. Baseline characteristics of patients treated with PCSK-9 inhibitors

	Evolocumab		Alirocumab		TOTAL	
	N	%	N	%	N	%
Patients, N.	1,516		1,092		2,608	
Age, aa median (range)	61 (18-80)		61 (18-80)		61 (18-80)	
Gender						
Women	517	34.1	359	32.9	876	33.6
Men	999	65.9	733	67.1	1,732	66.4
Type of hypercholesterolemia						
HoFH*	23	1.5	-	0.0	23	0.9
HeFH	483	31.9	402	36.8	885	33.9
noFH	644	42.5	475	43.5	1,119	42.9
MD	366	24.1	215	19.7	581	22.3
Use in CVD prevention						
Primary prevention	224	14.8	179	16.4	403	15.4
Secondary prevention	1,292	85.2	913	83.6	2,205	84.6
Relevant comorbidity §						
Cardiovascular disease	1,125	74.2	789	72.3	1,914	73.4
Cerebrovascular disease	126	8.3	102	9.3	228	8.7
Peripheral arterial disease	249	16.4	149	13.6	398	15.3
Diabetes mellitus	251	16.6	188	17.2	439	16.8
Hypertension	961	63.4	605	55.4	1,566	60.0
None	130	8.6	125	11.4	255	9.8
Smoking habit						
Present	208	13.7	129	11.8	337	12.9
Previous	584	38.5	366	33.5	950	36.4
Absent	724	47.8	597	54.7	1,321	50.7
Use of statins						
Intolerance to statins	759	50.1	517	47.3	1,276	48.9
Basal statin treatment^:						
atorvastin	365	24.1	240	22.0	605	23.2
rosuvastatin	383	25.3	335	30.7	718	27.5

HoFH= Homozygous familial hypercholesterolemia; HeFH= familial hypercholesterolemia heterozygous
noFH= Non-familial hypercholesterolemia; MD= mixed dyslipidemia.
* only evolocumab has indication in the HoFH
§ you can select multiple items
^ for 9 treatments there is no information on the statins used in combination

4.2 Economical impact of Managed Entry Agreements (MEAs)

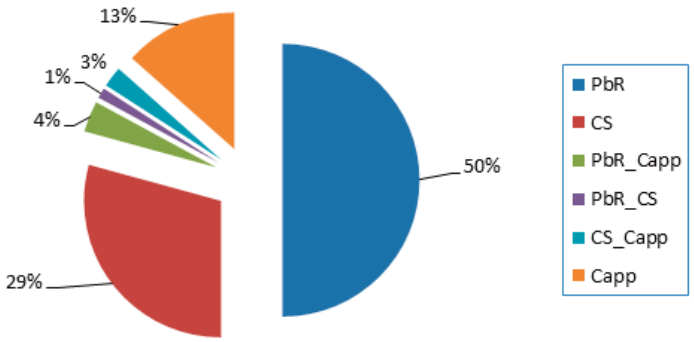
Italy has been one of the first European Country to adopt Managed Entry Agreements (MEAs), in order to foster access to new medicines with high cost and high level of uncertainty on clinical benefit at launch. AIFA can negotiate with pharmaceutical companies different types of MEAs: at patient level and at population level MEAs. The first type is monitored through AIFA monitoring Monitoring Registries, while the second one is monitored through information flows which collect data on NHS reimbursed expenditure and consumption such as the OSMED flow.

Managed Entry Agreements motitored through AIFA monitoring registries (Patient level):

MEAs that are monitored through AIFA Monitoring Registries are classified according to an international taxonomy, in two main categories: a) performance-based Risk-Sharing schemes and b) financial-based schemes. The first category includes Payment by result (PbR) and risk sharing (RS) models, while the second one includes Cost sharing (CS) and Capping models.

- The **CS** model provides for a discount on the price of first courses of therapy or for the total duration, for all patients eligible for treatment. This tool is usually implemented in case of uncertainty both on financial impact and on clinical efficacy of a medical product.
- The **Capping** model provides that the pharmaceutical company pays therapy costs when the quantities established by the agreement are exceeded.
- The **RS** model, in comparison to the CS model, provides for a discount to be applied to non-responder patients.
- The **PbR** model extends the RS and provides for the full refund from the pharmaceutical company for all non-responder patients (100% payback of therapeutic failures). Usually the PbR model is implemented when the benefit/risk ratio has a higher level of uncertainty and the definition of non-responder patient is based on results of pivotal clinical trials.

Figure 4.2.1. Percentage distribution of the types of risk sharing agreement (as of 31/12/2017)

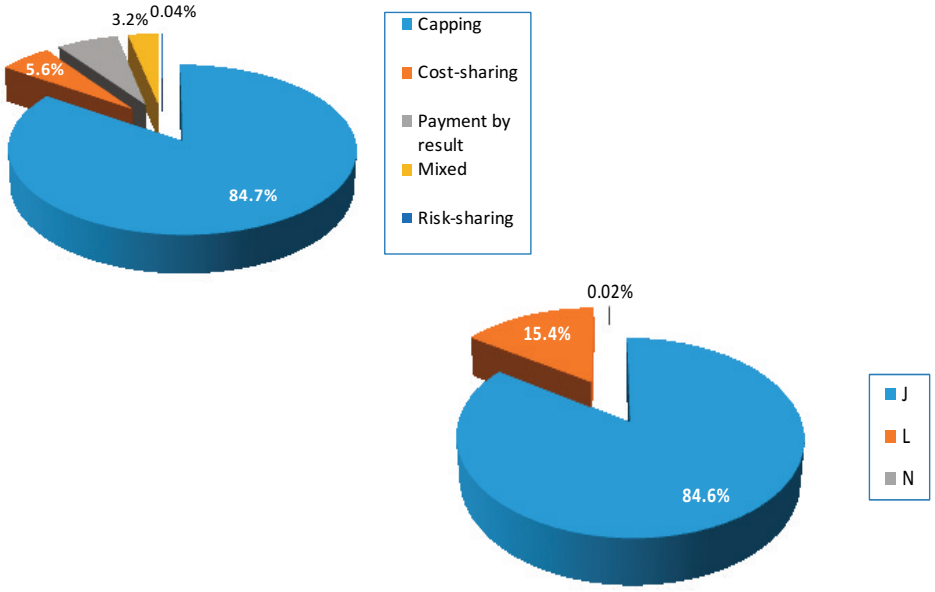


The distribution of each MEA for 2017 is reported in Figure 4.2.1. The most applied model is the payment by result agreement, accounting for 100% of the outcome-based agreements. In fact, no risk sharing model was implemented in 2017. This finding reflects the AIFA directive of refunding the treatment costs only for responder patients. The cost sharing and capping agreements rank below. Cases are also present of contextual application of MEAs relating to distinct categories (outcome-based and financial-based agreements) for the management of both clinical and financial uncertainty.

At a national level, the total reimbursement issuing from implementation of MEAs amounted to 531,841,836 euros in 2017. 90% of this value derives from implementation of financial based schemes: 84.7% is due to Capping agreements and 5.6% is due to Cost-sharing agreements. The payment by result and risk-sharing agreements account only for 6.5% of the total reimbursement. The remaining share of 3.2% is due to the contextual application of financial-based and outcome-based MEAs.

The 2017 reimbursement percentages for the ATC level are instead spread over 3 categories: 84.6% of the reimbursement is due to: general antimicrobials for systemic use (J), 15.4% to antineoplastic medicines and immunomodulators (L) and 0.02% to medicines of the nervous system (N).

Figure 4.2.2. Payback 2017, percentages by agreement and by I ATC



Managed Entry Agreements monitored through information flows collecting data on NHS reimbursed expenditure and consumption (population level).

These are financial agreements which can be mainly classified into: a) spendig caps by product and b) price/volume agreements.

a) Spending caps by product are used to promote the appropriate use of medicines. When an expenditure cap is settled, the Price and Reimbursement Committee finalizes the agreement with the pharmaceutical company, both in relation to the price of the medicine and in relation to the maximum sustainable NHS expenditure in the first 12/24 months of marketing. This parameter is based on the estimated number of patients expected in Italy for the reimbursed therapeutic indication, according to epidemiological data. Consequently, at the end of the period defined by the contract, if the monitoring of pharmaceutical expenditure shows that the amount is higher than the agreed ceiling, AIFA communicates to the pharmaceutical company the value of the pay-back shelf for the benefit of Italian regions.

b) Price/volume agreements provide for progressive discounts on the price of a medicine based on the volumes achieved during the contract period. These discounts can be obtained through a reduction in the medicine price or, if provided for in the agreement, through a payback to the Regions.

Moreover, AIFA, in some cases, can negotiate confidential discounts with pharmaceutical companies which, however, do not entail a payback for the Regions, but involve a direct price reduction in favour of NHS healthcare facilities. It should be noted that the aforementioned confidentiality is only limited to the discount and not to the presence or absence of this type of negotiating agreement.

The Table 4.2.2 reports medicines which were subject to verification procedures for the application of spending caps and price-volume agreements and obtained reimbursement.

A total of 15 medical products were involved, for a total of € 433.6 million. Moreover the sums paid by companies to the Regions pursuant to Art. 21, paragraph 23-bis, of the Decree Law. no. 113/2016, converted with amendments by Law no. 160/2016 have to be added to this value. Law no. 160/2016 laid down that AIFA concludes negotiations still pending as of 31 December 2015 because of disputes arising from the application of Article 48, paragraph 33, of the Decree-Law of 30 September 2003, n. 269, converted, with modifications, of L no. 326/2003. AIFA, therefore, started the negotiations with the pharmaceutical companies involved, ensuring the regions a total amount of 119.6 million euros (Table 4.2.5).

Table 4.2.2 List of medicinal products subject to verification procedures for the application of spending caps and price-volume agreements and obtained reimbursement

Medicinal products	Type of agreement	€
Sycrest	Spending cap	699,445
Gravax	Spending cap	1,476,381
Kalydeco	Spending cap	3,062,320
Herceptin	Spending cap	59,045,013
Lojuxta	Spending cap	289,374
Crestor	Spending cap	7,000,000
Oralair	Spending cap	918,437
Tresiba	Spending cap	30,746,468
Daparox	Spending cap	1,229,985
Raoctemra	Spending cap	6,132,371
Duodopa	Spending cap	5,647,663
Sovaldi	Price/volume	148,587,358
Harvoni	Price/volume	155,080,647
Eliquis	Price/volume	6,316,715
Pradaxa	Price/volume	7,340,472

In 2017 a total amount of 45.4 million euros was paid by pharmaceutical companies for Class A medical products and 70.8 million euros for Class H medicines, as consequence of the implementation of product cost ceilings. The reimbursements obtained due to the implementation of the price/volume agreements amounted to € 317 million in 2017 and refer to 4 specialties.

Section 5

Orphan drugs

Orphan drugs

"Orphan" drugs are medicines used for the diagnosis, prevention and treatment of rare diseases. In Europe, a disease is considered rare when it affects no more than five people per 10.000 inhabitants. Generally, "orphan" drugs require research and development investments that may not be profitable for the manufacturer. For this reason, orphan medicinal products are excluded from the pay-back procedures foreseen in the hospital pharmaceutical expenditure regulation (Article 15, paragraph 8, points i and i-bis of Law no. 135 of 2012, amended by Law no. 147 of December 27, 2013 2014 Stability Act). To date, more than seven thousands rare diseases have been discovered, thus representing a significant social issue, which involves millions of people: according to estimates, patients affected in Europe are over thirty million, 2-3 million of which in Italy.

European legislation

The first regulation concerning orphan medicinal products, the *Orphan Drug Act*, was introduced in the USA in 1983. In the European Union, the issue of orphan drugs was addressed by Regulation (EC) no. 141 of 2000 of the European Parliament and of the Council of the European Union and later Regulation (EC) no. 847 of 2000 of the European Parliament and of the Council. The aforementioned regulations define criteria and procedures for orphan drug designation, and provide for awards and incentives. The orphan status is granted by the Committee of Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA). The marketing authorization (MA) of an orphan medicinal product is achieved through a centralised procedure. In some cases, for the purpose of accelerating marketing of an orphan product, a medicine may be granted an authorisation, even though the clinical trials have not yet been completed. Such authorisation under conditional approval is eventually renewed on an annual basis. For a product to be granted conditional marketing authorisation, the following conditions are to be respected:

- Positive benefit/risk ratio;
- The applicant shall be later required to provide more comprehensive clinical data;
- Fulfilment of an unmet medical need;
- The benefits to public health for the immediate availability outweigh the risks inherent to the fact that additional data are still required.

Once the evaluation is completed, if the EMA's Committee for Medicinal Products for Human Use (CHMP) issues a favourable opinion as to whether to grant the authorisation, the European Commission formally issues the authorisation. Furthermore, pursuant to Article 14, paragraph 8 of EC Regulation n. 726 of 2004, in exceptional circumstances and following consultation with the applicant, the authorisation may be granted due to a requirement for the applicant to introduce specific procedures, in particular concerning safety of the medicinal product, notification to the competent authorities of any adverse reaction relating to its use, and action to be taken (when the indications for which the

product is intended are encountered so rarely that the applicant cannot be reasonably expected to provide comprehensive evidence).
Continuation of the authorisation shall be linked to the annual reassessment of these conditions.

Italian legislation

In order to facilitate orphan drugs access, several regulations were issued. In particular, the 2014 Stability Act introduced a mechanism of economic protection for marketing authorization holders (MAHs) of orphan medicinal products. Indeed, when the national pharmaceutical expenditure ceiling is exceeded, MAHs of orphan medicinal products are excluded from the payback mechanism, which is conversely distributed among all other MAHs in proportion to their pharmaceutical sales volumes. Pursuant to Article 15, paragraph 8, points i, and i-bis of Decree-Law no. 95 of 2012, converted with amendments into Law no. 135 of 2012, then modified by Article 1, paragraph 228, of Law no. 147 of December 27, 2013, AIFA's Board of Directors (on February 27, 2014) approved the list of orphan medicinal products for the treatment of rare diseases and the related chosen criteria, as prescribed by law. On the basis of this list, AIFA identifies orphan medicinal products which will benefit from the provisions of 2013 hospital pharmaceutical expenditure legislation. The list was approved by AIFA's Board of Directors and was drafted on the basis of the following criteria:

1. medicines qualified as orphan products in accordance with Regulation (EC) no. 141 of 2000 of the European Parliament and of the Council of December 16, 1999 (including orphan drugs, whose 10 years market exclusivity expired) and Article 8 of Regulation December 31, 2013;
2. medicines, referring to paragraph 1, are included in the list only if they hold a marketing authorisation in Italy. The following are therefore excluded:
   a. orphan medicinal products not reimbursed by the NHS as referred to points c) and c-bis of Article 8, paragraph 10, of Law n. 537 of December 24, 1993;
   b. orphan drug packages reimbursed by the NHS, as referred to point c) and c-bis of Article 8, paragraph 10, of Law n. 537 of December 24, 1993;
   c. any orphan medicinal product previously authorized and whose authorisation was then suspended or withdrawn as of December 31, 2013;
   d. any medicinal product initially inserted in the Community Register of orphan medicinal products for human use and which have then lost the orphan designation, as a result of the MAH's request or following COMP (EMA) re-evaluation;
3. any medicinal product which, pursuant to Article 15, paragraph 8, point I – bis of Decree-Law no. 95 of 2012, converted into Law no. 135 of 2012, then modified by Article 1, paragraph 228, of Law n. 147 of December 27, 2013, is included in the European Medicines Agency Note EMEA/7381/01/en. dated March 30, 2001 – if not excluded according to the criteria described in paragraph 2, points a) to d);
4. any medicinal product holding a marketing authorization for the treatment of a rare disease or condition included in the Orphanet register (*http://www.orpha.net/*),

although not included in the Community Register of orphan medicinal products pursuant to (EC) Regulation n. 141 of 2000 of the European Parliament and of the EU Council of December 16, 1999. Moreover are excluded:

a. any product authorised for the treatment of non-rare diseases or non-rare conditions;
b. products authorized for the treatment of rare diseases or conditions, for which MAHs had notsubmitted as of December 31, 2013 the requests to benefit from provisions of Article 15, paragraph 8, point i) of Decree-Law no. 95 of 2012, converted into Law no. 135 of 2012 and later amended by Article 1, paragraph 228, of Law no. 147 of December 27, 2013.

In order to increase orphan drugs availability nationwide, the *Balduzzi Law* (Law no. 189/ 2012, Article 12, paragraph 3) provides for the possibility for MAHs to apply to AIFA for pricing & reimbursement procedure as soon as the CHMP positive opinion is released and therefore, before the marketing authorization is formally granted by the European Commission. Moreover, following Decree Law no. 69 of June 21, 2013, and Law no. 98 of August 9, 2013 (Article 44), AIFA provides orphan drugs pricing and reimbursement dossiers (together with those concerning medicines of exceptional therapeutic relevance) with a priority over other pending applications. In such cases, the assessment period is reduced from 180 days to 100 days (so-called "fast track authorisation").

Access to rare disease treatments

In Italy, access to treatment for patients suffering from a rare disease is guaranteed through various legislative instruments. The centralised procedure represents the standard access route; whenever an orphan drug has no marketing authorisation, patient access is ensured through the following:

- Law n. 648/ 1996, allowing the use of a medicine on a national basis;
- Law n. 326/2003, Article 48 (also known as 5% AIFA Fund) and Ministerial Decree of September 7, 2017 (also known as “compassionate use”) in addition to Law n. 94/1998 (formerly *Legge Di Bella*) that, unlike Law no. 648, regulate pharmaceutical prescription for individual patient on a nominal basis.

Law no. 648/1996

This law allows the supply of certain medicines reimbursed by the NHS, in order to respond to pathological conditions for which no alternative therapeutic option is available (see Table 1.9.1). In order to include a medicine into the lists laid down by Law no. 648, one of the following conditions shall be met:

- innovative medicines holding a marketing authorisation granted in any European country, but not in Italy;
- medicinal products not yet authorised, but undergoing clinical trials, and for which results are available concerning phase two clinical studies;

- medicines to be used for a different therapeutic indication compared to the one already authorised in Italy, and which have undergone a phase two clinical trial.

The inclusion of a pharmaceutical product into Law no. 648 list is performed by AIFA on the basis of a documented request from patients' associations, scientific societies, health facilities, universities or following recommendations of AIFA's Scientific-Technical Committee (CTS). The list of orphan drugs included in Law no. 648/1996 can be downloaded from AIFA website at the following link: http://www.agenziafarmaco.gov.it/it/content/legge-64896.
Following the entry into force of Law no.79 of 2014, it was established that the supply of medicines used for a therapeutic indication different from the authorised one, through the list provided by Law no. 648/96 (100% reimbursement by the NHS), is allowed even if therapeutic alternatives are available, according to affordability and appropriateness parameters. Bosentan constitutes an example of orphan drug that has benefited from this provision.

Law n. 326/ 2003 (Article 48): 5% AIFA Fund

The 50% of the AIFA Fund is dedicated to the purchase of orphan drugs intended for the treatment of rare diseases and medicinal products not yet authorized, but representing a chance for the treatment of serious conditions (i). The remaining 50% of the Fund is used to carry out scientific researches (independent research) on the use of pharmaceutical products (i.e. comparative trials on medicines aimed at demonstrating their additional therapeutic value, or studies aimed at demonstrating the appropriateness of use of medicines, or focusing on scientific information). This Fund is fed by the 5% of pharmaceutical companies' annual expenditure issuing from promotional activities intended for physicians (seminars, workshops, etc.) (Article 48, paragraph 19, point a, Decree-Law no. 269 of September 30, 2003, converted into Law. no. 326 of November 24, 2003).
In 2017, this Fund amounted approximately to €17.8 million.
As regards the purchase of the above-mentioned pharmaceutical products (i), requests to access the Fund are submitted to AIFA, through the Italian regions, by local reference centres or designated structures treating patients affected by a rare disease.
The following documents are required in order to access the Fund: a formal request, supporting scientific literature (if any) and a brief clinical report including a description of the therapeutic plan for each patient. The application shall be supported by specific information, such as: dose per treatment cycles, number of cycles and the price of the medicine. The application is assessed by the AIFA's Scientific-Technical Committee which issues an opinion after having verified the existence of the conditions provided by law. On the basis of the supporting documents submitted as proof of costs incurred for the patient's treatment, AIFA reimburses the invoices submitted. The total expenditure for patients accessing the AIFA Fund amounted to € 13,465,742 in 2017 (see Table 1.9.1).

Ministerial Decree of September 7, 2017 "Therapeutic use of a medicine undergoing clinical trials" (compassionate use)

Despite considerable medical progress achieved in the diagnosis and treatment of many diseases, there are still several therapeutic areas (so-called "niches") associated to unmet medical needs which represent both a challenge and a major goal for health care providers. The Italian Ministerial Decree of September 7, 2017 establishes procedures for "Therapeutic use of medicines undergoing clinical trials" (so-called "compassionate use of medicinal products"). The provisions of compassionate use represent a pathway for patients to access medicinal products for the treatment of serious, life-threatening conditions, or rare diseases, for which no satisfactory authorised alternative therapy exists. Ethic Committees are responsible for granting authorisation for access to experimental medicines, it being understood that the pharmaceutical company shall provide a declaration of willingness to supply the medicine free of charge. This Decree represents the transposition of the "Guideline on Compassionate use of Medical Products, pursuant to Article 83 of Regulation (EC) no. 726/2004", as laid down in Art. 158, paragraph 10, Decree-Law no. 219/2006.

Law no. 94/1998, Art. 3, paragraph 2 (formerly *Legge Di Bella*)

This legislation allows medical prescription of an off-label medicine. The prescription of an off-label medicine is granted under the responsibility of the prescribing physician, and followed by an informed consent of the patient, if the patient cannot be beneficially treated with available treatments approved for the same therapeutic indication. For such a prescription to be issued, documents on the use of a medicine are required from successfully concluded phase two clinical trials (Finance Law 2008).

Table 5.1. Number of patients who have accessed the AIFA fund and related expenditure for the year 2017

Active ingredient Brand Name	Therapeutic indication	No. patients	€
Parathyroid hormone (rDNA) (Natpar)	Additional treatment in adult patients with chronic hypoparathyroidism not adequately controlled by standard therapy plain	8	345,575
Asfotase alpha (Strensiq)	Long-term enzyme replacement therapy in patients with pediatric onset hypophosphatia for the treatment of bone disease manifestations	5	3,870,720
Sebelipasi alpha (Kanuma)	Long-term enzyme replacement therapy (TES) in patients of all ages with lysosomal acid lipase deficiency (LAL)	10	4,015,378
Idebenone (Raxone)	Treatment of visual impairment in adult and adolescent patients with hereditary optic neuropathy of Leber (LHON)	2	27,882
	Treatment of Duchenne Muscular Dystrophy (unauthorized indication)	11	177,206
Eculizumab (Soliris)	Treatment of the membranoproliferative glomerulonephritis (indication not authorized)	9	2,330,268
Metreleptin	Treatment of congenital or acquired lipodystrophy	4	606,254
Cerliponase alpha (Brineura)	Treatment of neuronal type 2 ceroidolipofuscinosis pathology (CLN2), also known as tripeptidyl-peptidase 1 (TPP-1) deficiency	1	600,000
Teduglutide (Revestive)	Treatment of patients 1 year of age and over who have short bowel syndrome (SBS). Patients should be in stable condition after a period of bowel adaptation following surgery	2	225,937
Megestrol acetate	Ovarian cancer of granulosa cells (unauthorized indication)	1	801
Genetically modified allogeneic T lymphocytes (Zalmoxis)	Additional treatment in haploidentical transplantation of haematopoietic stem cell (HSCT) in adult patients with high-risk haematological malignant neoplasms	1	569,000
Dinutuximab beta (Qarziba)	Treatment of high-risk neuroblastoma in patients from 12 months of age	4	593,400
Belinostat	Treatment of T-cell peripheral lymphoma	1	79,800
Pirfenidone (Esbriet)	Treatment of Idiopathic pulmonary fibrosis (Idiopathic Pulmonary Fibrosis - IPF) mild to moderate	1*	23,517

* patient under the age of 40

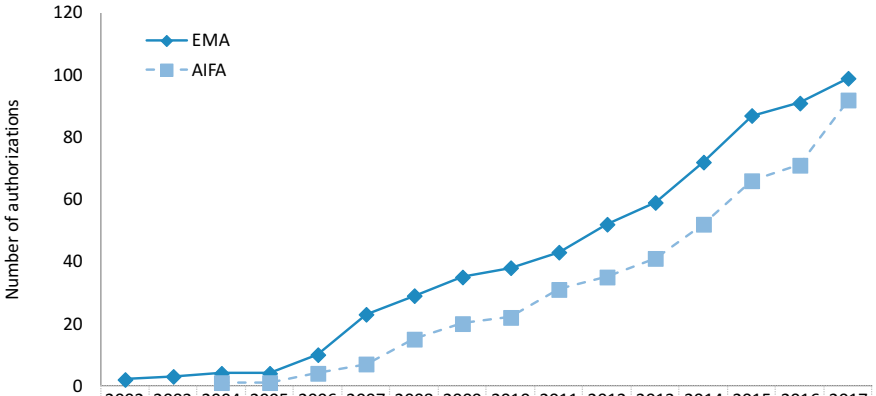
Table 5.2. Synoptic overview of the main requirements for access to the orphan drug designation on the basis of the various regulations in force

Requirement	Law 648/1996	Law 326/2003	D.M. 7 sep 2017	Law 94/1998
Lack of a valid therapeutic alternative	Yes	Not explicit	Yes	Yes
Informed consent of the patient	Yes	Not explicit	Yes	Yes
Scientific documentation to support	Results of phase II studies (for investigational drugs)	Clinical report of the patient	Phase III studies, or in special cases of disease conditions that put the patient in danger of life Phase II clinical trials. In the case of rare diseases or rare cancers, Phase I clinical trials, already completed, that have documented the activity and safety of the medicinal product (not applicable to advanced therapies)	At least results of phase II studies, positively concluded
Taking responsability of the doctor	Yes	Not explicit	Yes	Yes
Data transmission Monitoring	AIFA and Regional Councilorship (only for the "classic" or "historical" list)	-	Notification of documentation relating to requests for medicinal products formulated pursuant to the D.M. 7/9/2017 and approved by the local Ethics Committee	-
Contributing to the cost of therapy	NHS	AIFA	Free supply from the Pharmaceutical Company	Citizen, except in case of hospitalization

Orphan drugs expenditure and consumption in Italy

In 2017 the European Medicines Agency authorized 14 medicines for the treatment of rare diseases. In general orphan drugs are mainly focused on oncology, central nervous system and metabolic therapeutic areas.
Furthermore, in the last 16 years, out of 99 orphan drugs authorised by EMA, 92 (including 7 products classified as C-nn) were marketed in Italy as of 31 December 2017. In the case of 1 medicine a P&R application has never been submitted by the pharmaceutical company and, as for the remaining 4 medicines, they were in any case available to patients through alternative channels (e.g. Law no. 648/96, Law no. 326/2003, etc.) encouraged by AIFA.

Figure 5.1. Comparison between EMA authorized orphan drugs and ones marketed in Italy (cumulative data 2002-2017)



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
EMA	2	3	4	4	10	23	29	35	38	43	52	59	72	87	91	99
AIFA			1	1	4	7	15	20	22	31	35	41	52	66	71	92

Moreover, according to criteria approved by AIFA's Board of Directors , the list of orphan drugs reimbursed by the Italian NHS has increased from 85 (C-nn class medicine excluded) to 94 authorised orphan drugs, due to the inclusion of orphan-like products, as well as to the addition of orphan drugs, whose market exclusivity granted by the EMA had expired, so being removed from the Community register.

During the period 2013-2017 the expenditure and consumption data concerning orphan drugs had been elaborated on the basis of the new lists approved by AIFA's Board of Directors (Resolution no. 10 of February 27, 2014). Due to the use of these new lists, data resulting from current analysis are not comparable with those referring to previous years.
In 2017, orphan drugs expenditure (inpatient + outpatient settings) amounted to €1,6 billion, corresponding to 7.2% of the total NHS pharmaceutical expenditure. The share in expenditure of orphan drugs not reimbursed by the NHS on the total expenditure of orphan drugs (reimbursed + not reimbursed by the NHS) is 0.85% (it was 0.11% in 2014).
In 2017, consumption of orphan drugs, evaluated in both settings, amounted to 12.7 million DDD, corresponding to 0.05% of overall pharmaceutical consumption. As regards therapeutic classes, 55% of orphan drug expenditure concerned antineoplastic agents and immuno-modulators, followed by gastrointestinal tract and metabolism medicines (18%) and cardiovascular system medicines (8%).
Alongside, 49% of orphan drug consumption was covered by antineoplastic agents and immuno-modulators, followed by cardiovascular system medicines (about 13%) and nervous system medicines (11%) (Table 1.9.6 and Figure 1.9.1).

Table 5.3. Expenditure and consumption trends for orphan drugs, 2010-2017*

Year	2010	2011	2012	2013	2014	2015	2016	2017
Expenditure for orphan drugs (millions)	657	800	671	917	1,060	1,212	1,393	1,599
Incidence % orphan drugs on pharmaceutical expenditure	3.50	4.20	3.50	4.67	5.31	5.49	6.13	7.20
Consumption (DDD) orphan drugs (millions)	6.6	7.5	5.9	7.5	8.5	10.3	11.4	12.7
Incidence % orphan drugs on consumption	0.03	0.03	0.02	0.03	0.03	0.04	0.04	0.05

*Expenditure and consumption data have been prepared for the years 2013-2017 on the basis of the new classification approved by the AIFA Board of Directors (resolution No. 10 of 27 February 2014); these results are not comparable with those relating to previous years.

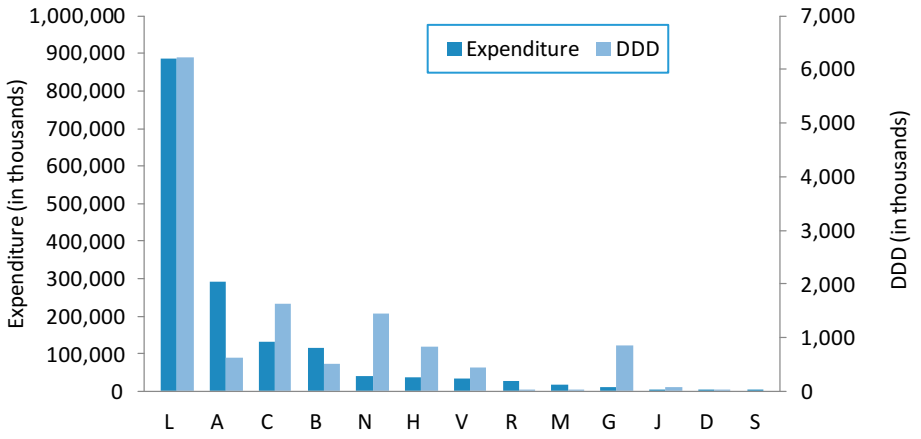
Table 5.4. Orphan drugs accessing the fund of innovative cancer drugs and innovative non-cancer drugs: expenditure and consumption for 2017

Drug	2017	
	Expenditure	DDD
Imbruvica	81,353,750	522,570
Kalydeco	28,928,070	42,392
Spinraza	8,008,000	12,480
Total	**118,289,820**	**577,442**

Note: Regarding Strimvelis, although two patients are treated according to AIFA Registries, the drug does not appear in the flow data of public health facilities, as dispensed by an Accredited Private Health Facility.

In 2017 four orphan drugs, which had also been recognized as innovative medicines, resulted in €118.3 millions expenditure. Imbruvica is the medicine on top of the list for expenditure and consumption, while Spinraza is the last one since it has been marketed only since October 2017. The following tables report data on consumption and expenditure of orphan drugs sorted by ATC I level and therapeutic area.

Figure 5.2. Expenditure and consumption of orphan drugs in Italy for the ATC level, year 2017

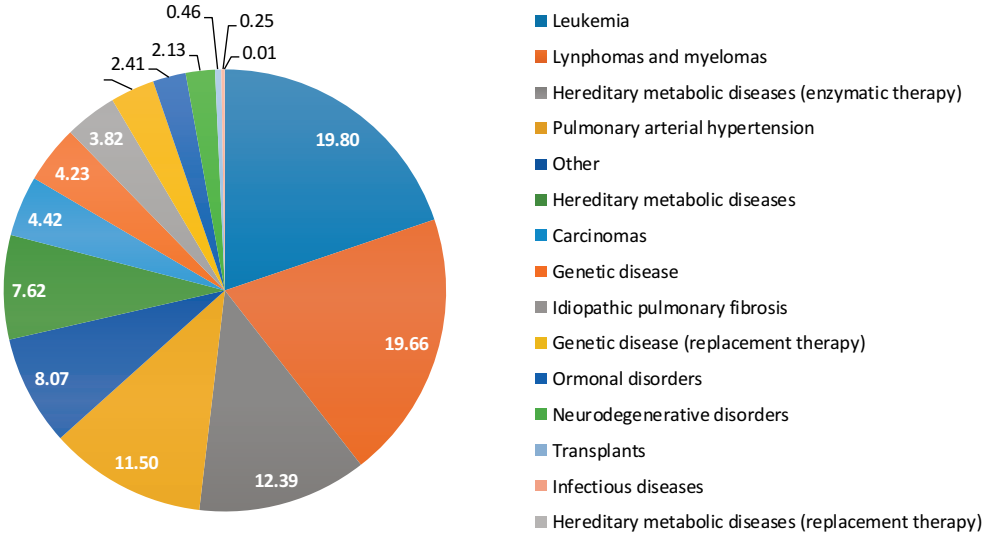


L = Antineoplastic and immunomodulating agents
A = Alimentary tract and metabolism
C = Cardiovascular system
B = Blood and blood forming organs
H = Systemic hormonal preparations, excl.sex hormones and insulins
V = Various
R = Respiratory system
M = Musculo-skeletal system
N = Nervous system
G = Genito urinary system and sex hormones
J = Antiinfectives for sistemi use
D = Dermatologicals
S = Sensory organs

Table 5.6. Expenditure and consumption of orphan drugs in Italy by therapeutic area, year 2017 (Table and Figure)

Therapeutic area	Expenditure	DDD	Per capita expenditure	DDD/1000 inhab die	Inc. % exp on tot orphan drugs
Leukemia	316,652,741	1,997,194	5.23	0.09	19.8
Lymphomas and myelomas	314,397,501	2,246,252	5.19	0.10	19.7
Hereditary metabolic diseases (enzymatic therapy)	198,099,739	184,535	3.27	0.01	12.4
Pulmonary arterial hypertension	183,986,454	2,568,985	3.04	0.12	11.5
Other	129,100,988	518,179	2.13	0.02	8.1
Hereditary metabolic diseases	121,792,425	720,106	2.01	0.03	7.6
Carcinomas	70,757,224	474,685	1.17	0.02	4.4
Genetic diseases	67,607,906	1,109,903	1.12	0.05	4.2
Idiopathic pulmonary fibrosis	61,067,100	781,744	1.01	0.04	3.8
Genetic diseases (replacement therapy)	51,678,246	124,272	0.85	0.01	3.2
Hormonal disorders	38,534,533	858,432	0.64	0.04	2.4
Neurodegenerative disorders	34,098,684	1,004,683	0.56	0.05	2.1
Transplants	7,309,995	86,509	0.12	0.00	0.5
Infectious diseases	3,954,793	37,281	0.07	0.00	0.2
Hereditary metabolic diseases (replacement therapy)	163,187	222	0.00	0.00	0.0
Total	**1,599,201,515**	**12,712,980**	**26.39**	**0.57**	**100.0**

* Calculated on the total expenditure of orphan drugs nationwide



In 2017 the five active ingredients with major impact on expenditure were: lenalidomide (12.6%), eculizumab (6.5%), ibrutinib (5%), dasatinib (4.5%) and bosentan (4.3%). As regards consumption, 39% of DDD dispensed was due to the following active ingredients: lenalidomide (12.2%), sildenafil (6.8%), bosentan (6.5%) and pirfenidone (4.7%).

Section 6

Innovative medicines

6.1 Innovative medicines

The assessment of pharmaceutical innovation is a complex and dynamic process. The complexity in defining potential pharmaceutical innovation is the result of the heterogeneity of available treatment options, as well as of the mutable perception of priorities and expectations towards a new medicine in relation to the health and social context. The dynamism of pharmaceutical innovation evaluation mainly depends on the continuous evolution of scientific knowledge and the consolidation of scientific evidence.
The Italian Medicines Agency (AIFA), which has the dual function of a regulatory and a reimbursement authority, has recently established new criteria to define innovative medicinal products (AIFA' Determination n. 519/2017, 31 March 2017, updated by the determination n. 1535/2017, 12 September 2017). Indeed, the decision making process to grant the innovative status is based on the evaluation of the unmet medical need, the added therapeutic value compared to existing therapeutic options and the overall quality of clinical evidence, which is assessed based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation, http://www.gradeworkinggroup.org/) system. Following this evaluation, if a medicinal product is granted the status of "full innovativeness" for a specific therapeutic indication, its manufacturer can access dedicated yearly funds amounting to 500 million Euros each, depending on the type of medicine (one fund for oncology, the other for all other innovative medicinal products). Alternatively, the product can be granted the status of "conditional innovativeness" which allows immediate access to all Regional formularies, with no additional re-assessments at the local level. The third possible outcome is that no innovativeness is recognized.
The 2017 Financial Law establishes that recognition of innovation and related benefits have a maximum duration of thirty-six months. Moreover the innovation status can be reconsidered in the case of new evidences becoming available. If it is not confirmed the associated benefits shall lapse, with the consequence of starting a new negotiation of the price and reimbursement.
In order to guarantee the maximum level of transparency, a full report explaining the rationale for the Agency Committee's decision is made publicly available on AIFA's website (http://www.agenziafarmaco.gov.it/content/elenco-aggiornato-innovative-
0), as of January 2018.

6.2 Expenditure and consumption of innovative medical products

The following tables show an analysis of expenditure and consumption for innovative medical products in the period 2015-2017. For each medical product, expenditure and consumption were considered only for the period of effectiveness of the status of innovation (innovativeness and conditioned innovation). The data refer to the total value of expenditure and consumption of the medicinal product and not only to the indication to which the innovation was recognized if several indications are reimbursed. Table 6.1 lists the medicines considered in the analysis and the respective dates of effectiveness and expiry of the innovation requirement.

Table 6.1. List of innovative medicines in the period 2015-2017

ATC IV	Drug	Active ingredient	Class	Effective date (G.U.)	Expiry date requirement
L01XC	Yervoy	Ipilimumab	H	09/03/2013	08/03/2016
M09AB	Xiapex	Collagenasi di clostridium histolyticum	H	14/03/2013	13/03/2016
L02BX	Zytiga	Abiraterone	H	06/04/2013	05/04/2016
L01XC	Perjeta	Pertuzumab	H	08/07/2014	07/07/2017
L01XC	Adcetris	Brentuximab vedotin	H	08/07/2014	07/07/2017
L04AX	Revlimid	Lenalidomide	H	30/09/2014	29/09/2017
J04AK	Sirturo	Bedaquilina	H	01/10/2014	30/09/2017
L01XC	Kadcyla	Trastuzumab emtansine	H	11/10/2014	10/10/2017
J05AX	Tivicay	Dolutegravir	H	02/11/2014	01/11/2017
J05AX	Sovaldi	Sofosbuvir	A	20/12/2014	01/06/2017
L01CD	Abraxane	Nab paclitaxel	H	21/02/2015	20/02/2018
J05AE	Olysio	Simeprevir	A	24/02/2015	23/02/2018
L01XE	Xalkori	Crizotinib	H	11/04/2015	10/04/2018
J05AX	Daklinza	Daclatasvir	A	05/05/2015	04/05/2018
R07AX	Kalydeco	Ivacaftor	A	05/05/2015	04/05/2018
J05AX	Harvoni	Ledipasvir/sofosbuvir	A	14/05/2015	01/06/2017
J05AX	Exviera	Dasabuvir	A	24/05/2015	23/05/2018
J05AX	Viekirax	Ombitasvir/paritaprevir/ritonavir	A	24/05/2015	23/05/2018
V10XX	Xofigo	Radio ra 223 dicloruro	H	11/06/2015	10/06/2018
L04AX	Imnovid	Pomalidomide	H	20/08/2015	19/08/2018
L01XX	Zydelig	Idelalisib	H	11/09/2015	10/09/2018
L01XE	Imbruvica	Ibrutinib	H	05/01/2016	04/01/2019
L01XC	Opdivo	Nivolumab	H	25/03/2016	24/03/2019
L01XC	Keytruda	Pembrolizumab	H	11/05/2016	11/05/2019
L03	Strimvelis	Autologous CD34+ cells	H	16/08/2016	15/08/2019
J05AX	Zepatier	Elbasvir/grazoprevir	A	04/02/2017	03/02/2020
L01XC	Blincyto	Blinatumomab	H	24/02/2017	23/02/2020
C09DX	Entresto	Sacubitril/valsartan	A	12/03/2017	11/03/2020
J05AX	Epclusa	Sofosbuvir/velpatasvir	A	27/04/2017	26/04/2020
L01XC	Lartruvo	Olaratumab	H	05/08/2017	04/08/2020
L01XX	Venclyxto	Venetoclax	H	12/08/2017	11/08/2020
J05AP	Maviret	Glecaprevir/pibrentasvir	A	28/09/2017	26/04/2020
M09AX	Spinraza	Nusinersen	H	28/09/2017	27/09/2018

Table 6.2. Expenditure and consumption trends for innovative medicines (years 2015-2017) purchased by public health facilities

	2015	2016	2017	Δ % 17-16
Innovative expenditure*	2,226	2,636	1,635	-38.0
Inc. % NHS expenditure	10.09	11.73	7.36	
DDD*	9.2	12.0	13.4	11.7
Inc. % DDD NHS	0.033	0.048	0.054	

* millions

Note: The expense does not take into account the paybacks paid by pharmaceutical companies for the application of conditional reimbursement agreements

Table 6.3. Expenditure and consumption for innovative medicines (innovation and conditioned innovation) purchased by public health facilities for medicinal specialties (years 2015-2017)

Drug	2015			2016			2017		
	Expenditure *(million)*	**DDD** *(thousand)*	**Inc.% ****	**Expenditure** *(million)*	**DDD** *(thousand)*	**Inc. % ****	**Expenditure** *(million)*	**DDD** *(thousand)*	**Inc. % ****
Abraxane	7.1	475.1	0.3	22.7	600.8	0.9	23.1	650.4	1.4
Blincyto	-	-	-	-	-	-	4.0	1.9	0.2
Daklinza	119.4	524.9	5.4	189.5	1,018.9	7.2	56.9	477.9	3.5
Entresto	-	-	-	-	-	-	5.2	1,193.4	0.3
Epclusa	-	-	-	-	-	-	156.7	1,423.8	9.6
Exviera	9.8	411.3	0.4	10.8	588.7	0.4	4.5	488.0	0.3
Imbruvica	-	-	-	38.2	245.8	1.5	81.4	522.6	5.0
Imnovid	5.8	21.3	0.3	34.1	111.5	1.3	38.3	122.6	2.3
Kalydeco	13.6	19.3	0.6	31.0	43.3	1.2	28.9	42.4	1.8
Keytruda	-	-	-	11.1	46.3	0.4	61.2	478.3	3.7
Lartruvo	-	-	-	-	-	-	0.9	3.4	0.1
Maviret	-	-	-	-	-	-	26.5	189.5	1.6
Olysio	130.7	570.6	5.9	5.9	49.1	0.2	0.5	4.8	0.0
Opdivo	0.0	0.1	0.0	62.0	286.5	2.4	181.7	1,009.5	11.1
Spinraza	-	-	-	-	-	-	8.0	12.5	0.5
Venclyxto	-	-	-	-	-	-	0.9	5.2	0.1
Viekirax	131.8	475.5	5.9	146.0	685.8	5.5	57.4	542.6	3.5
Xalkori	9.8	60.6	0.4	19.2	113.9	0.7	24.3	141.2	1.5
Xofigo	2.0	0.6	0.1	6.1	2.1	0.2	7.9	2.7	0.5
Zepatier	-	-	-	-	-	-	87.7	751.8	5.4
Zydelig	1.2	11.6	0.1	10.7	100.2	0.4	12.6	115.1	0.8
Xiapex*	0.9	1.1	0.0	0.2	0.2	0.0	-	-	-
Yervoy*	56.8	96.4	2.6	7.4	12.5	0.3	-	-	-
Zytiga*	95.5	949.8	4.3	26.9	267.2	1.0	-	-	-
Harvoni^	433.3	813.0	19.5	940.1	1,763.9	35.7	252.1	473.0	15.4
Sovaldi^	893.1	1,843.2	40.1	689.6	1,423.2	26.2	221.1	456.3	13.5
Adcetris^	19.2	52.2	0.9	23.0	58.8	0.9	11.3	34.3	0.7
Perjeta^	52.7	368.1	2.4	78.3	550.0	3.0	49.2	343.3	3.0
Kadcyla^	57.8	215.8	2.6	57.4	246.0	2.2	42.6	182.2	2.6
Revlimid^	164.5	1,054.2	7.4	184.6	1,208.1	7.0	149.2	1,144.0	9.1
Sirturo^	0.3	2.6	0.0	0.6	5.7	0.0	0.1	1.3	0.0
Tivicay^	20.9	1,269.0	0.9	40.4	2,616.9	1.5	40.9	2,617.0	2.5
Total	**2,226.4**	**9,236.6**	**100.0**	**2,635.6**	**12,045.4**	**100.0**	**1,635.3**	**13,431.0**	**100.0**

* innovation requirement expired in 2016;
** calculated on the total expense of innovative drugs
^ innovation requirement expired in 2017

Table 6.5. List of medicines accessing to the Innovative Funds as of 31 December 2017 (2017 Budget Law)

Innovative non-oncological	Innovative oncologic
Sovaldi	Abraxane
Olysio	Perjeta
Kalydeco	Zydelig
Daklinza	Imbruvica
Harvoni	Opdivo
Exviera	Keytruda
Viekirax	
Epclusa	
Zepatier	
Strimvelis	
Spinraza	
Maviret	

Keytruda was first sold on July 2017. With Determina AIFA of 22 May 2017 (GU n.126 of 01/06/2017) the Sovaldi and Harvoni medicines are reclassified in Class C starting from 2 June 2017, therefore they don't contribute any more to the pharmaceutical spending of the NHS; as of this date they are also excluded from the Innovative Fund. With regard to Strimvelis, although two patients are treated according to the AIFA Registries, this medicine does not appear in the flow data of public health facilities, as dispensed by an Accredited Private Health Facility.

Appendix 1

Regulation of pharmaceutical assistance in Italy

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1. Medicines reimbursement and distribution

Decision-making processes concerning pricing and reimbursement of pharmaceuticals and provision methods vary across European countries. In Italy, this competence is ascribed to AIFA. Medicines included in the National Pharmaceutical Formulary and completely reimbursed by NHS are classified as Class A (Class H when medicines are dispensed in hospital setting or equivalents), (Art. 8, paragraph 10, point A, Law no. 537 of December 24, 1993). Otherwise, medicines are classified as Class C when not reimbursed by NHS (with the exception of subjects with a lifetime war pension) (Law no. 203 July 19, 2000).
NHS reimbursed medicines include essential products, intended for care of chronic diseases, reimbursed for each authorized therapeutic indication. In some cases, reimbursement is granted through AIFA Notes, which restrict reimbursement only to some indications. Therefore, Class A products, whose therapeutic indications are not included in AIFA Notes, are entirely paid by patients.
On the contrary, Class C medicines are not considered to be essential and can be dispensed to citizens with or without a medical prescription (respectively Class C with prescriptions and Class C without obligation of prescription, C - SOP). Among non-reimbursed pharmaceuticals, those classified as Class C-(a) (Art. 8, paragraph 10, point C – (a), Law no. 537 of December 24, 1993, as amended) are defined as over-the-counter (OTC). These products can be dispensed without prescription and can be promoted directly by pharmaceutical companies.
Through Ministerial decree April, 18, 2012, (implementation of regulations of Art. 32, paragraph 1, Legislative Decree no. 201 of December 6, 2011, as amended) AIFA has updated the delivery method of C–medications. The decree established medications for which the medical prescription obligation had to persist and those for which the delivery method was converted in C-SOP, so allowing the distribution in other settings besides conventional Pharmacies, such as malls and Para-Pharmacies. The Ministerial decree of April 18, 2012 was then updated, implementing the list of C-SOP medicines with medications reclassified as C-SOP by AIFA's scientific technical committee (CTS) (Ministerial Decree of November 15, 2012 as amendend.
Table 1.3.1 shows the number of C-SOP medications approved within December 2014, including medications approved by CTS.

Moreover, Legislative Decree no. 158 of September, 2012 modified with amendments, into Law no. 189 of November 8, 2012 (so-called "Decreto Balduzzi"), established that medications which are granted Market Authorization through centralized or mutual recognition or decentralized, or national procedure as well as of parallel import, are automatically classified in the new group of "C- without negotiation" (C-NN). After that, the pharmaceutical company shall request the reimbursement from the NHS and price negotiation, the latter of which is allowed only after the submission of a specific dossier according to CIPE (Interministerial Committee for Economic Planning) indications (CIPE deliberation no.3 of February 1, 2001).

When a pharmaceutical company submits to AIFA the pricing and reimbursement dossier, competent offices and advisory committees perform a preliminary assessment to evaluate

and establish the reimbursement class of the pharmaceutical product. At the end of the decision making process, once the pricing and reimbursement committee (CPR) has concluded the negotiation procedure, the final decision concerning reimbursement classification, provision methods and price, is ratified by AIFA's Board of Directors and published in the Official Gazette of the Italian Republic (*Gazzetta Ufficiale*).
In terms of provision methods (According to Article no. 87 of Decree-Law no. 219 of April 24, 2006 as amended), medicines are classified as follows:

a) requiring a medical prescription (RR)
b) requiring a new medical prescription each time (RNR)
c) requiring a special medical prescription (RMS – Consolidated Law on narcotics (Presidential Decree no. 309 of October 9, 1990 as amended)
d) under a restricted medical prescription, including:
    1) medicines dispensable only with a prescription released by Hospitals or Specialists (RRL and RNRL)
    2) medicines to be used exclusively in hospitals or analogous healthcare facilities (OSP)
    3) medicines to be used/administered exclusively by specialists (USPL)
e) medicines not requiring a medical prescription:
    1) over the counter medicines (OTC)
    2) medicines not requiring a medical prescription (SOP).

The repeatable prescription (RR) is the most common type of prescription. It has a six-month validity period, during which the patient can use the prescription for a maximum of ten times. A peculiar case is represented by the prescription of psychotropic medicines (tranquilizers, sedatives, hypnotics), having a thirty days' validity and repeatable for no more than three times.
The repeated limited prescription (RNR) is necessary for all medications with a potential risk of acute or chronic toxicity, addiction and tolerance, or abuse. This kind of prescription is more restrictive than the previous one (RR), as the procurement of the medicine requires the issuing of a new prescription. The validity is of thirty days and is restricted to the number of packages indicated (in case of compounded preparations not including narcotics, the prescription has a three-month validity). A peculiar case is represented by the isotretinoin, whose prescription and delivery is allowed only within teratogenic risk prevention programs and with a seven-day validity RNR prescription.
The RRL and RNRL prescriptions are used for medicines dispensable only by specific healthcare facilities and/or specialists. These types of prescriptions include:

a) medicines for exclusive hospital use (Art. 92, Legislative decree no. 219/2006)
b) medicines provided only if prescribed by a specific specialist or hospital (Art. 93, Legislative decree no. 219/2006)
c) medicines for exclusive use of specialist and care settings (Art. 94, Legislative decree no. 219/2006)

Some medicines cannot be sold directly to patients, even if available in pharmacies, but can only be provided to specialists, who can purchase them directly from pharmaceutical companies and wholesalers.

AIFA Resolution of January 13, 2010, available on the Official Gazette's supplement no. 21, updated the supply methods of OSPs. The previous supply systems, OSP1 and OSP2, were abrogated and a new system came into effect as of February 16, 2010.
Medicines previously defined as OSP1 became OSP (see above), without additional changes. The OSP2 system supply was modified into RR, RNR, RRL or RNRL. At a later stage, in accordance with Article no. 11, paragraph 7 of Decree-Law no. 78 of May 31, 2010, transposed with amendments, into Law no. 122 of July 30, 2010, many Class H medicines delivered by a RR, RNR, RRL or RNRL prescription were reclassified as Class A-PTH (AIFA Resolution of November 2, 2010).
Class A-PHT includes those medicines dispensed through direct distribution for the purpose of ensuring hospital-community continuity of care.

3. Medicines distribution chain margins and discounts in favour of the NHS

According to Law no. 662/1996 and its amendments, distribution margins of pharmaceutical companies, wholesalers and pharmacies are fixed respectively at 66.65%, 3.0% and 30.35% of the retail price, net of VAT. Moreover, Law no. 135 of August 7, 2012, as amended, establishes an additional 2.25% discount to be applied at the expense of pharmacies in favor of the NHS. This discount pertains to both off-patent and patented medicines, while it is not applied to:

- rural pharmacies with national assistance (pharmacies located in towns with less than 3,000 inhabitants) and sales volumes below €387,342.67, net of VAT, per year;
- rural and urban pharmacies, without national assistance, and sales volumes below €258,228.45, net of VAT, per year.

Moreover, pharmaceutical companies are required to remit to Regions an additional discount of 1.83% of the retail price, net of VAT.
According to Decree-Law no. 39 of April 28, 2009, as amended, distribution margins of generics are calculated as follows: 58.65% for pharmaceutical companies, 6.65% for wholesalers and 26.70% for pharmacists. In addition, a remaining 8% is shared between pharmacists and wholesalers, according to market agreements.
The pharmacies' discounts in favor of the NHS, as of January 1, 2013, are reported in table 3.1.

Table 3.1. Discounts applied to pharmacies in favor of the NHS (these turnover thresholds have been in force till December 31, 2017)

Price range	**Rate for urban and rural pharmacies without national assistance**		**Rate for rural pharmacies with national assistance**	
Price (€)	With sales volume >€ 258,228.45	With sales volume <€ 258,228.45	With sales volume >€ 387,342.67	With sales volume <€ 387,342.67
Range 0 - 25.82	3.75%	1.50%	3.75%	flat-rate 1.5%
Range 25.83 - 51.65	6.0%	2.40%	6.0%	flat-rate 1.5%
Range 51.66 - 103.28	9.0%	3.60%	9.0%	flat-rate 1.5%
Range 103.29 - 154.94	12.50%	5.0%	12.50%	flat-rate 1.5%
Over 154.94	19.0%	7.60%	19.0%	flat-rate 1.5%
Further discount	2.25%	-	2.25%	-

4. Pharmaceutical price

As of January 1st, 2004, prices of all medicines reimbursed by the NHS are set through negotiation procedure between AIFA and pharmaceutical companies, following methods and criteria previously adopted for medicines approved only under European procedures.
During negotiations, the parameters taken into account are those defined by the CIPE (Interministerial Committee for Economic Planning) Resolution no. 3 of 2001:

- economic impact on the NHS;
- prices in other EU countries;
- cost of treatment per day compared to the cost of medicines with similar effectiveness;
- benefit/risk ratio compared to medicines with the same therapeutic indication;
- cost/effectiveness ratio when other treatment options are available;
- level of innovation.

According to the new AIFA Regulation of October 2009, the pricing and reimbursement process occurs in four stages, which can be summarized as follows:

1. pharmaceutical company applies for the pricing and reimbursement procedure by submitting the dossier to AIFA;
2. CTS provides its judgment concerning the reimbursement condition according to clinical-therapeutic evaluations;
3. CPR evaluates the dossier and then meets the pharmaceutical company for the negotiation procedure;
4. results of the negotiation are submitted to the Board of Directors for a final evaluation.

The CTS and CPR express their decisions within 180 days from the application and the ex-factory price is published in the Official Gazette of the Italian Republic.

Decree-Law no. 69 of June 21, 2013 (converted with amendments into Law no. 98 of August 9, 2013) establishes as a priority the assessment of orphan drugs, medicines to be used in hospital setting or with exceptional therapeutic value and considered of social relevance, compared to other pending procedures, and sets a 100 day time limit for the assessment of these products. The Committees may be convened in extraordinary sessions in order to ensure the time limit for the procedure to be respected. The price of Class A medicines, dispensed by community pharmacies, is published in the Official Gazette and is equal to the retail price per single package, inclusive of citizen co-payment, as well as pharmacists' and pharmaceutical companies' mandatory discounts and VAT. Consequently, the price of the NHS reimbursed medicines corresponds to the retail price net of discounts, citizen co-payment and VAT.
The price of Class H and A medicines distributed by public health facilities corresponds to the ex-factory price, VAT inclusive, resulting from procurement tenders or from HLUs (or Regions) negotiations with pharmaceutical company.
Pharmaceutical companies establish prices of Class C pharmaceuticals, which are then notified to AIFA without publication in the Official Gazette. Increases in the price of Class C medicines are allowed only in the month of January of odd-numbered years (Decree-Law no. 87 of May 27, 2005, modified, with amendments, into Law no. 149 of July 26, 2005), while reductions are always allowed.

Article 9-(b), paragraph 11 of the Decree-Law19 June 2015, no. 78 (D.L. *Local Authorities*), with the introduction of paragraph 33-(a), provided that when a biotechnological product loses the patent protection and a price negotiation procedure of a biosimilar or of a therapeutically similar medication is not started, AIFA starts a new price negotiation procedure with the marketing authorization holder in order to obtain a reduction of the NHS reimbursement price. Furthermore, the insertion of paragraph 33-(b) provided that AIFA starts a new negotiation procedure with the marketing authorization holder, in the case of medications monitored through an AIFA Monitoring Register, in order to reduce the price if the benefits were proved lower than those identified in the negotiation agreement, after two years from the granting of the marketing authorization.

Appendix 2

Data source and methods

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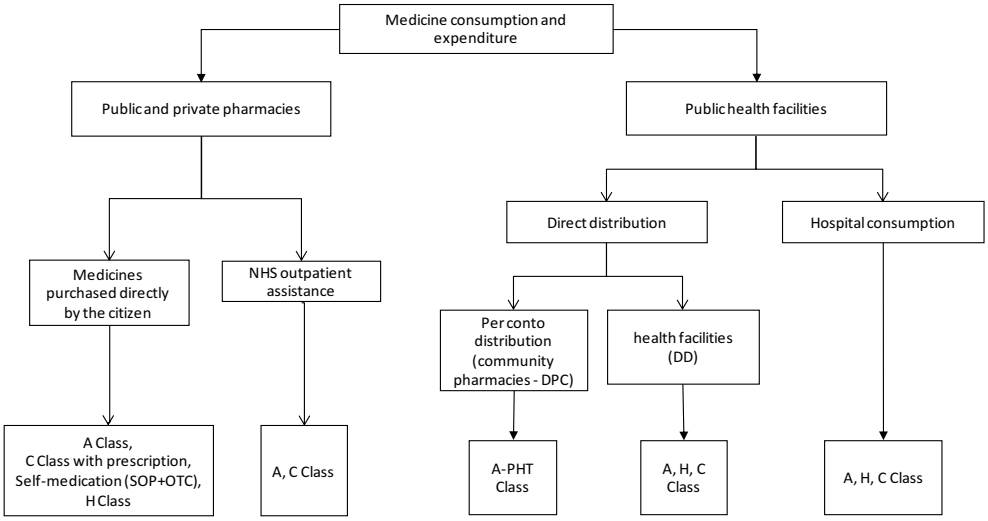
1. Medicines consumption and expenditure data

This Report provides a summary of data on consumption and expenditure of medicines supplied by the National Health Service (NHS) in conventional, direct and *per conto* and hospital distribution. A schematic synthesis of data included in this Report is provided in Figure 1.1. Moreover this Report describes consumption and expenditure of Class C medicines purchased directly by the citizen, in addition to the private purchase of class A-H medicines.

Figure 1.1. Summary of Report data



The description of medicines' consumption made available by the Report is based on the analysis and integration of data collected through different information flows:

1. OsMed Flow. This represents the information flow of pharmaceutical services provided through public and private pharmacies, affiliated with the NHS. This flow collects data of medical prescription and includes the medicines reimbursed by NHS.

2. The purchase by public health facilities. The information of this flow is fed by pharmaceutical companies and by the intermediate distribution and detects the packages moved along the distribution chain, up to the final distribution points: pharmacies, hospitals, clinics, malls, etc. The data analyzed by the Report refer to medicines purchased by public health facilities for the inpatient and outpatient consumption.

3. Medicines purchased directly by the citizen. This flow provides information about consumption and expenditure of Class C medicines purchased directly by the citizen as well as information on private purchases of class A-H medicines.

4. Direct and per conto distribution. This flow provides information on medicines supplied by the NHS and distributed to patients either directly by health facilities (e.g. 1st - 1st cycle of treatment after hospital discharge and specialist outpatient visits), or alternatively, by community pharmacies, by virtue of specific agreements between pharmacist and local health unit (so called per conto distribution).

5. Pharmaceutical prescriptions. This flow is provided for by paragraph 5 of article 50 of the Decree Law no. 269 of 30th September 2003, converted, with amendments, into Law 24 November 2003, no. 326 as amended (Health Card). Health care services, such as local health facilities, hospitals, Scientific Institute for Research and Healthcare, university hospitals, public and private pharmacies, outpatient specialist offices and other centers and accredited health facilities, are due to telematically transmit the NHS pharmaceutical prescriptions to the Ministry of Economy and Finance (MEF) of the recipes charged to the NHS. (Health Card). Data used for the analysis according to age and gender derive from this flow and refer to 6 Italian Regions of North, Centre and South of Italy (Lombardy, Veneto, Lazio, Tuscany, Campania and Apulia) representing more than 55% of Italian population.