AIFA RECOMMENDATIONS ON DRUGS for the home management of COVID-19 Vers.10 — Updated 10/03/2023	
SYMPTOMATIC DRUGS	
Symptomatic therapy	Acetaminophen or NSAIDs may be used in case of fever or joint or muscle pain (unless there is clear contraindication to use). Other symptomatic drugs may be used on clinical judgment.
DRUGS TO BE USED ONLY AT SPECIFIC STAGES OF THE DISEASE	
Antivirals Remdesivir — Veklury ® information for healthcare professionals https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19 Nirmatrelvir/ritonavir — Paxlovid ® Information for healthcare professionals https://www.ema.europa.eu/en/medicines/human/summaries-opinion/paxlovid	Two antivirals (remdesivir, nirmatrelvir/ritonavir) are currently authorised by EMA to treat adults with COVID-19 who do not require additional oxygen therapy and are at increased risk of progression to severe COVID-19 forms. The patient **should not be hospitalised** due to COVID-19, have a **mild-to-moderate** form and at least one of the following risk factors associated with the development of severe disease: • Oncological/oncohematological pathology in active phase • Chronic kidney failure • Chronic obstructive pulmonary disease and/or other chronic respiratory disease (e.g. people with asthma, pulmonary fibrosis or who need oxygen therapy for reasons other than SARS-CoV-2) • Primary or acquired immunodeficiency • Obesity (BMI ≥30) • Cardio-cerebrovascular disease (heart failure, coronary heart disease, cardiomyopathy, hypertension with concomitant organ damage, stroke) • Uncompensated diabetes mellitus (HbA1c> 9.0 % 75 mmol/mol) or with chronic complications • Age>65 years • Chronic Hepatopathy • Hemoglobinopathies • Neurodevelopmental disorders and neurodegenerative diseases **Remdesivir** is an antiviral drug (nucleotide analogue prodrug of adenosine), already authorised by EMA for the treatment of COVID-19 with pneumonia requiring additional oxygen therapy, which obtained in December 2021 authorisation for the extension of the indication related to the treatment of COVID-19 for people 'who do not require additional oxygen therapy and have an increased risk of progression to severe COVID-19".

Treatment should be initiated as soon as possible after the diagnosis of COVID-19 and within 7 days of the onset of symptoms.
The recommended dosage of remdesivir in adults is:

- day 1: single loading dose of remdesivir 200 mg administered by intravenous infusion
- from day 2 onwards: 100 mg given once daily as an intravenous infusion.

The total duration of treatment should be 3 days.
Patients should be monitored during treatment with remdesivir.
Administration of the drug in an outpatient setting should be monitored according to local practice. Use should take place under conditions where severe hypersensitivity reactions, including anaphylaxis, can be treated.
For the prescribing and monitoring of outcomes, an AIFA web log will be compiled.

Paxlovid® (**nirmatrelvir-ritonavir**) is the first oral antiviral drug to have been authorised by EMA for the treatment of COVID-19 in adults, not hospitalised and at high risk of developing a serious COVID-19 disease. The medicinal product contains two active substances, nirmatrelvir and ritonavir, present in two separate tablets: nirmatrelvir works by reducing the ability of SARS-CoV-2 to replicate in the body, while ritonavir (a drug that has long been used in the treatment of HIV infection) has no antiviral activity but works as a pharmacological booster by prolonging the action of nirmatrelvir.
Paxlovid® should be administered as soon as possible after the diagnosis of COVID-19, no later than 5 days after the onset of symptoms. Treatment consists of taking two nirmatrelvir tablets and one ritonavir tablet twice daily for 5 days.
For warnings and precautions of use see Summary of Product Characteristics — SmPC (https:// www.ema.europa.eu/en/documents/product-information /paxlovid-epar-product-information_en.pdf).
Prescribers need to accurately investigate the patient's pharmacological history as ritonavir has important drug interactions with many drugs, in relation to which warnings and recommendations have been included in Paxlovid product information. For further support in the evaluation of possible drug interactions, it is recommended to consult the website: https://www.covid19-druginteractions.org/ .
For Paxlovid there is a two-fold way of prescribing:

- by the COVID centre specialist through AIFA web register and direct distribution by Health Companies identified by the Regions
- by GPs through a dematerialised prescription and compilation of the AIFA web Therapeutic Plan and dispensing through proximity pharmacies through distribution "on behalf".

Monoclonal antibodies casirivimab/imdevimab — Ronapreve® (600/600 mg) information for healthcare professionals https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali sotrovimab — Xevudy ® information for healthcare professionals https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali tixagevimab/cilgavimab — Evushled® information for healthcare professionals https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali	The monoclonal antibodies available in Italy, authorised by EMA for the treatment of SARS-CoV-2 infection in people at high risk of progression to severe disease, are as follows: the casirivimab/imdevimab combination, sotrovimab, and the tixagevimab/cilgavimab combination. In the early stages of the outbreak, the bamlanivimab/etesevimab combination was made available, pursuant to Article 5.2 of Legislative Decree 219/2006 (Ministerial Decree of 6 February 2021 and 12 July 2021); its authorisation for emergency distribution ceased on 31 July 2022. The population eligible for treatment with the three treatments is as follows: people aged 12 years and older (and at least 40 kg), positive for SARS-CoV-2, non-hospitalised for COVID-19, not on COVID-19 oxygen therapy, with mild-to-moderate symptoms and who are at high risk of severe COVID-19. Possible risk factors include the following: • age > 65 years; • a Body Mass Index (BMI) ≥ 30, or > 95% percentile by age and gender; • chronic kidney failure, including peritoneal dialysis or haemodialysis; • uncontrolled diabetes mellitus (HbA1c ≥ 9.0 % or 75 mmol/mol) or with chronic complications; • primary or secondary immunodeficiency; • cardio-cerebrovascular disease (including hypertension with concomitant organ damage) • chronic obstructive pulmonary disease and/or other chronic respiratory disease (e.g. people with asthma, pulmonary fibrosis or who need oxygen therapy for reasons other than SARS-CoV-2); • Chronic Hepatopathy • Hemoglobinopathies • Neurodevelopmental disorders and neurodegenerative diseases. COVID-19 must be recently onset (however for no later than 7 days). Treatment is possible more than seven days after onset only in subjects with immunodeficiency who have: negative serology for SARS-CoV-2 and prolonged positivity to the molecular buffer. For all types of treatment, a single administration is provided at the following dosages: - casirivimab (600 mg) + imdevimab (600 mg) IV;the combination may be administered at the same subcutaneous dose if intravenous administration is not feasible and results in a delay in treatment. - sotrovimab (500 mg) IV - tixagevimab (300 mg)/cilgavimab (300 mg) IM, with two separate and sequential injections. For modalities and duration see information for healthcare professionals (https://www.aifa.gov.it/uso-degli-anticorpi-monoclonali).

	Administration should be monitored for up to one hour after the end of the infusion by a properly trained healthcare professional and able to handle any serious adverse reactions. For the prescription and monitoring of 30-day outcomes, an AIFA web log will be compiled. The effectiveness of monoclonal antibodies may be reduced against certain viral variants;this should also be taken into account in the therapeutic choice in relation to the local epidemiological situation, for which reference is made to the flash surveys periodically published by the ISS. Although no published clinical studies are available, there is evidence from in vitro studies assessing the neutralising efficacy of different monoclonal antibodies. For an up-to-date overview of in vitro efficacy against different variants it is recommended to consult Stanford University's website (***Stanford University's Coronavirus Antiviral & Resistance Databas*****and; https://covdb.stanford.edu/susceptibility-data/table-mab-susc/**), updated in real time and used as a reference also by the main international bodies. When interpreting these data, it should be considered that other intrinsic characteristics (such as those related to the effectiveness of different antibodies) could have an impact on clinical efficacy compared to the currently prevailing variants. In general, based on the advancement of knowledge, diagnostic availability, possible logistical and organisational difficulties and the epidemiological situation, it may be considered the opportunity to determine the viral variant involved in the infection before deciding on which antibody or combination of monoclonal antibodies to guide the therapeutic choice. It should be noted that these data are constantly evolving and that therefore the indication to the use of specific monoclonal antibodies may vary over time depending on the variant of SARS-CoV-2 prevailing in the country and its sensitivity to the different products available.
Corticosteroids AIFA Information sheet: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-	The use of corticosteroids is recommended in patients hospitalised with severe COVID-19 disease who need oxygen supplementation. This recommendation is because currently there is evidence of a clinical benefit of such drugs only in this patient/disease setting. It should also be stressed that at the early stage of the disease (where viral replication-related phenomena prevail) the use of cortisone could have a negative impact on the developed immune response.

of the-disease-covid19	**The use of corticosteroids at home can be considered in patients who have factors of risk of disease progression towards severe forms, in the presence of a worsening of pulsometer parameters requiring oxygen therapy and if it is not possible immediately hospitalisation for overloading of hospital facilities.** The study that showed reduced mortality with low doses of corticosteroids used dexamethasone at a dosage of 6 mg for up to 10 days. Any other corticosteroids should be used at equivalent dosages (methylprednisolone 32 mg, prednisone 40 mg, hydrocortisone 160 mg). Finally, it is important to remember that in many people with chronic diseases the use of cortisone can lead to important adverse events that risk complicating the course of the viral disease. As an example known to all, that of diabetic subjects in which both the presence of an infection and the use of cortisone can severely destabilise glycemic control.
Heparins AIFA Information sheet: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19	The use of **heparins (usually low molecular weight heparins)** in prophylaxis of thromboembolic events in the medical patient with acute respiratory infection and reduced mobility is recommended by the main guidelines and should continue throughout the period of immobility. Routine use of heparins is **not recommended** in non-hospitalised and unassailed individuals due to the infectious episode, as there is no evidence of a clinical benefit in this patient/disease setting. Prophylactic dosages of the various heparinic compounds available may be used in the case of an allotted subject. It is important to remember that SARS-CoV-2 infection is not a contraindication to continue oral anticoagulant therapy (with AVK or NAO) or antiaggregating even double therapy already underway.
MEDICINES NOT RECOMMENDED FOR THE TREATMENT OF COVID-19	
Molnupiravir — Lagevrio ®	**Molnupiravir**, an antiviral drug (prodrug metabolised to ribonucleosidic analogue N-hydroxycitidine), was initially made available through emergency distribution authorisation pursuant to Art.5.2 of DL 219/2006 (Ministerial Decree of 26 November 2021 and subsequent extensions). Following the negative opinion issued by the CHMP for the failure to demonstrate a clinical benefit in terms of reduced mortality and hospitalisations, the Agency suspended the use of the drug on 10/03/2023.

Antibiotics AIFA Information Sheet (relative to azithromycin): https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-of the-disease-covid19	**The use of antibiotics is not recommended for the treatment of SARS-CoV-2 infection.** Recent well-conducted randomised clinical trials (which in most cases assessed the effectiveness of azithromycin) have shown that the use of an antibiotic, alone or associated with other drugs, with particular reference to hydroxychloroquine, does not alter the clinical course of the disease. The use of an antibiotic can only be considered when the presence of a bacterial overlap is suspected, in relation to the general clinical picture of the patient. Unjustified use of antibiotics can also result in the onset and spread of bacterial resistance that could impair the response to future antibiotic therapies.
Hydroxychloroquine AIFA Information sheet: https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-of the-disease-covid19	**The use of chloroquine or hydroxychloroquine is not recommended for the purpose of preventing or treating infection.** The randomised clinical trials published to date conclude that the drug is substantially ineffective in the face of an increase in adverse events, albeit not serious. This makes the relationship between the benefits and risks of using this drug negative.
Lopinavir/ritonavir Darunavir/ritonavir or cobicistat AIFA Information sheet :https://www.aifa.gov.it/aggio rnamento-sui-farmaci-utilizzabili-per-il-trattamento-of the-disease-covid19	**The use of lopinavir/ritonavir or darunavir/ritonavir or cobicistat is not recommended for the purpose of preventing or treating infection.** The randomised clinical trials published to date all conclude for the ineffectiveness of these pharmacological approaches.
The recommendations provided reflect the existing literature and guidance and will be updated in relation to the rapid evolution of scientific evidence. For more details on the individual data sheets, you can consult the AIFA institutional website at the following link:: https://www.aifa.gov.it/aggiornamento- sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19 . Oxygen therapy, which is an essential therapeutic presence in the presence of respiratory failure and for which proper use refers to the specific recommendations, is excluded from the guidelines provided. In addition to these recommendations, it should be noted that people on chronic treatment (e.g. with antihypertensives, ACE inhibitors or statins) are recommended to continue their treatment until different provisions of their doctor. People undergoing chronic immunosuppressive treatment due to a previous solid organ transplant rather than diseases with immune-mediated pathogenesis may continue the ongoing pharmacological treatment unless otherwise indicated by the treating specialist.	