AGENZIA ITALIANA DEL FARMACO

Questions and answers on COVID-19 vaccines

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General information on COVID-19 vaccination

As of December 2020, the European Medicines Agency (EMA) has recommended the provisional granting of conditional marketing authorizations for COVID-19 vaccines. AIFA acknowledges the European decisions and therefore authorises the use of such vaccines in Italy.

1. What is the mechanism of action of COVID-19 vaccines?

The SARS-CoV-2 coronavirus, responsible for COVID-19, uses a protein (called 'Spike') which protrudes from its envelope to enter the human cells, where it then reproduces. The vaccines currently available have been developed to induce an immune response capable of blocking the Spike protein, thus preventing the virus from infecting cells. These vaccines introduce into some cells of the human body not the SARS-CoV-2 coronavirus, but the genetic information necessary to produce the Spike protein for a short time. The presence of this foreign protein will stimulate the immune system to react against it by producing antibodies that will prevent the virus from entering and infecting cells through binding to the Spike protein. The presence of the foreign Spike protein will also activate T lymphocytes driving antibody production and killing virus-infected cells. Some of these lymphocytes survive for several months ('memory lymphocytes') and allow the immune system of the immunized person to rapidly activate an extraordinary reaction against a possible SARS-CoV-2 invasion.

2. Was the clinical trial shortened to have these vaccines available quickly?

The studies that led to the development of COVID-19 vaccines did not skip any of the phases of verification of the efficacy and safety required for the development of a medicine; on the contrary, these studies saw the participation of a very large number of volunteers, about ten times higher than that of similar studies for the development of other vaccines. The rapid development and approval is due to new technologies, to the huge resources made available very quickly and to a new evaluation process by the regulatory agencies, which evaluated the results as they were obtained and not when all the studies were completed - as was previously the case.

3. How long does the protection induced by such vaccines last?

At present, the exact duration of the protection offered by the vaccine is unknown. Clinical trials to establish it are still ongoing. Most clinical trials on authorised vaccines require vaccinated people to be monitored for 2 years to gather more information on the duration of protection. Data from observational studies show a progressive decline in vaccine protection from approximately 5-6 months after completion of the initial vaccination course, so that the booster dose is expected to be administered during this period. To date, even vaccinated people are required to comply with the protective measures provided for.

4. Can vaccinated people still transmit the infection to others?

The aim of the registration studies was to assess the vaccines efficacy in protecting from the COVID-19 disease. Studies are ongoing to determine whether asymptomatically infected vaccinated people can infect others. Since it is possible that, despite protective immunity, in some cases the virus may persist in the nasal mucosa, vaccinated people and those who are in contact with them must

continue to take protective measures against COVID-19.

5. Do vaccines protect just the vaccinated person or his/her family too?

Vaccines protect the vaccinated person, but if many people are vaccinated, they can reduce the circulation of the virus, thus protecting also those who are not vaccinated. Vaccination protects those who are vaccinated, but it also helps protect the community where they live.

6. Variants of SARS-CoV-2 virus have been reported: will vaccines be effective also against such variants?

SARS-CoV-2 virus is subject to frequent mutations. The vaccine-induced immune response protects against most of these variants although protection might be less effective against some of them.

7. Why is it not possible to choose the vaccine?

Vaccination against COVID-19 is a right for all, however the risk of contracting the virus and developing the disease in a severe form is not the same for everyone and the availability of doses is currently not the same for all vaccines. Therefore, with an aim to ensure maximum fairness, it is necessary to comply with the Strategic plan for COVID-19 vaccination developed by the Ministry of Health.

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Recipients of COVID-19 vaccination

1. Who is entitled to vaccination?

All persons residing or otherwise present on the Italian territory, with or without a residence permit or identity documents, including holders of the STP (Stranieri Temporaneamente Presenti) or ENI (European Non Iscritto) code, holders of the numerical tax code Codice Fiscale or those without one, holders of an expired health card and those who fall into the categories periodically updated by the Vaccination Plan.

2. Can anyone be vaccinated who has already had a COVID-19 infection, confirmed by a molecular test?

In subjects who have had prior (symptomatic or asymptomatic) SARS-CoV-2 infection, the administration of a single dose of SARS-CoV-2/COVID-19 vaccine may be considered, provided that vaccination is carried out preferably within 6 months from the infection and no later than 12 months after its resolution.
Subjects with immunodeficiency conditions (either primary or secondary following pharmacological treatments) who have had a previous SARS-COV-2 infection are recommended to follow the planned vaccination schedule.

3. Shall people be administered the second dose of vaccine if they are infected with SARS-CoV-2 after receiving the first dose?

In people who have contracted a SARS-CoV-2 infection after being administered the first dose of a vaccine with a two-dose vaccine schedule, the following guidelines apply:

- in case of confirmed infection (defined by the date of the first positive molecular test) within the fourteenth day from administration of the first dose of vaccine, the completion is recommended of the vaccination schedule with a second dose to be carried out within six months (180 days) from the documented infection (date of the first positive molecular test) (after this period of time, the vaccination schedule can still be completed, as soon as possible, with the second dose only);
- in case of confirmed infection (defined by the date of the first positive molecular test) after the fourteenth day from the administration of the first dose of vaccine, the vaccination schedule is to be considered completed as the infection itself is equivalent to the administration of the second dose. However, the possible administration of a second dose is not contraindicated.

4. How is the absence of contraindications to vaccination detected?

Before vaccination, healthcare staff ask the vaccine a series of simple but precise questions, using a standardized form to assess whether the vaccination can be carried out or postponed. In addition, the healthcare professional checks for any contraindications or special precautions.

5. Who can I contact if I have a reaction after vaccine administration?

Adverse reactions to the vaccine can be reported to general practitioners or to any health professional, in agreement with the pharmacovigilance system in place. Moreover, anyone can report an adverse reaction to the vaccine by using any of tools provided on the AIFA website. For further details, please refer to FAQs on Pharmacovigilance on COVID-19 vaccines and monthly reports on adverse reactions.

6. Can people who have experienced a severe allergic or non-allergic adverse reaction to the first administration of Covid-19 vaccine receive the second dose?

NO, people having previously experienced severe, allergic and non-allergic reactions, to the first dose, should NOT be administered the second dose, but should contact a referral centre with experience on reactions to vaccinations, to receive specialist information.

NB. A "serious adverse reaction" means that it required hospitalization or prolonged treatment, or that it was a danger to life.

7. Can pregnant women be vaccinated with COVID-19 vaccines?

Laboratory studies on animal models using COVID-19 vaccines during pregnancy showed no harmful effects. In addition, several large post-authorisation observational studies showed no significant

adverse events in pregnant women or in the newborn. Therefore, COVID-19 vaccines are not contraindicated during pregnancy. Pregnant women, especially in case of other risk factors such as diabetes, cardiovascular diseases and obesity, could be more exposed to risk of developing complications, including serious, in case of SARS-CoV-2 infection.
According to Ministry of Health's Circular of 24 September 2021, vaccination against SARS-CoV-2/COVID-19 with mRNA vaccines is recommended for pregnant women in the second and third trimesters. For the first trimester, vaccination may be considered after assessing the potential benefits and risks with the reference healthcare professional.
Through the Italian Obstetric Surveillance System, the Italian National Health Institute (Istituto Superiore di Sanità) has published a document aimed at supporting healthcare professionals and pregnant and breastfeeding women in the decision regarding vaccination ("Indicazioni ad interim su Vaccinazione contro il COVID-19 in gravidanza e allattamento" - Interim guidance on COVID-19 vaccination during pregnancy and lactation). The updated guidance also takes into account new evidence relating to the increased spread and morbidity associated with the Delta variant, the spread of infection and the lowering of the average age of infected individuals.

8. Can breastfeeding women be vaccinated with COVID-19 vaccines?

As regards breastfeeding, although there are still no specific studies on breastfeeding, and since SARS-CoV-2 antibodies have been found in the milk of vaccinated women, it can be assumed that the infant might acquire additional protection against infection, the level of which is not known at the moment.
Since the mRNA in Comirnaty and Spikevax is rapidly degraded without entering the cell nucleus and breast milk, as well as the viral vectors contained in Vaxzevria and Jcovden (ex COVID-19 Vaccine Janssen) are not able to replicate, it is biologically and clinically unlikely that there will be any risks for breast-fed infants.

9. Can women of childbearing potential be vaccinated with COVID-19 vaccines?

Studies performed on animal models did not reveal any direct or indirect harmful effects on reproductive capacity following vaccination. In addition, preliminary literature data show no adverse effects of COVID-19 vaccination on female fertility. Therefore, vaccination is also indicated in women of childbearing potential, including in case they are planning to become pregnant.

10. Can children and adolescents be vaccinated with COVID-19 vaccines?

Comirnaty (Pfizer/BioNTech) has been initially authorised for people aged 16 years and over, and has been subsequently approved for use in adolescents aged 12-15 years and, starting from 1 December, also in children aged 5-11 years. Spikevax (Moderna) has been initially authorised for people aged 18 years and over, and then has been approved for use also in adolescents aged 12-17 years.

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COVID-19 vaccination for adolescents aged over 12 years

1. What is the therapeutic indication of Comirnaty and Spikevax in adolescents aged 12-17 years?

Following an in-depth assessment, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) concluded that data on the use of Comirnaty and Spikevax in adolescents aged 12 to 17 years meet the established efficacy, safety and quality criteria. Therefore, the benefit/risk ratio is considered positive also for this age group (i.e. the benefits associated with vaccination clearly outweigh the potential risks associated with the use of the vaccine).

2. Who can benefit most from vaccination?

Those girls and boys who, due to diseases or pre-existing conditions, have an increased risk of progressing to serious COVID-19, will benefit most from the vaccination. In addition, the extension of vaccination to this population could be used to create a potential barrier of protection around those who cannot be vaccinated or may have a suboptimal immune response to the vaccine.

3. Will vaccination in adolescents aged 12-17 years occur differently from people aged over 18 years?

No, the method for administering the vaccines does not differ among age groups. In adolescents aged 12-15 years, each dose of Comirnaty is 0.3 mL and the vaccination course consists of two intramuscular injections administered at least 3 weeks apart and no more than 6 weeks apart. Each dose of Spikevax is 0.5 mL and the vaccination course consists of two intramuscular injections administered at least 4 weeks apart and no more than 6 weeks apart.

4. Are there any contraindications to vaccination?

Vaccination with Comirnaty and Spikevax is contraindicated in all people with hypersensitivity to the active substance or to any of the excipients contained in the medicinal product.
The second dose of the vaccine should not be given to those people who have experienced anaphylaxis (serious allergic reaction) at the first dose of Comirnaty or Spikevax.

5. What precautions should be taken into account for vaccination?

Vaccination should be postponed in people suffering from acute serious/debilitating febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.
The vaccine should be given with caution in people suffering from thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration.
The efficacy, safety and immunogenicity of the vaccine has not been assessed in immunocompromised people, including those receiving immunosuppressant therapy. The efficacy of the vaccines may be lower in immunosuppressed individuals.

6. When is maximum vaccine protection achieved after vaccination?

As with adults, for adolescents aged 12-15 years too it is necessary to wait until 7 days after the second dose of the vaccine.

7. What are the possible side effects for adolescents?

The safety profile of Comirnaty and Spikevax in adolescents was similar to that seen in young adults. The most frequent adverse reactions in adolescents were injection site pain, tiredness, headache, muscle and joint pain, chills and fever. Adverse reactions are usually mild or moderate in intensity and resolve within a few days after vaccination.
In adolescents aged 12-17 years no new side effects were observed that had not been reported in older age groups.
The assessment of vaccine safety is carried out according to the usual pharmacovigilance activities.

8. Have pharmacovigilance activities shown any safety signals that may be relevant to this age group?

Some events of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the heart membranes) have been reported after the administration of mRNA vaccines.
Most of these events occurred in the two weeks following vaccination, more often after the second dose and in younger men. Following vaccination, any signs indicative of myocarditis or pericarditis should be monitored, such as shortness of breath, palpitations or chest pain. If these occur, immediate medical attention should be sought.

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) continues to monitor events and evaluate new data, including the results of clinical and literature studies, to update the information on the safety and efficacy of vaccines, as necessary.

9. How was the efficacy of vaccines assessed in adolescents?

As for Comirnaty, efficacy was assessed by analysing SARS-CoV-2 neutralising antibody titers one month after administration of the second dose. This showed that the antibody response observed in the 12-15 age group was not inferior to that observed in the 16-25 age group.
Additionally, to assess the efficacy of Comirnaty in adolescents aged 12-15 without evidence of prior infection at baseline, the ability of the vaccine to prevent the first outbreak of COVID-19 from 7 days after the second dose was analysed. There were no cases among participants (n=1,005) who received the vaccine, whereas 16 cases were identified among those who received placebo (n=978).

As for Spikevax, efficacy was assessed by analysing SARS-CoV-2 neutralising antibody titers one month after administration of the second dose. Data showed that the antibody response observed in the 12-17 age group was not inferior to that observed in the 18-25 age group.
Additionally, to assess the efficacy of Spikevax in adolescents aged 12-17 years, a secondary efficacy analysis was performed in 3,181 participants who received 2 doses of either Spikevax (n=2,139) or placebo (n=1,042) and had a negative baseline prior infection. No symptomatic COVID-19 cases were identified in people who received Spikevax, whereas 4 symptomatic cases were identified in those who received placebo.

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Conditions for vaccination

1. Can people with chronic diseases, diabetes, cancers and cardiovascular diseases be vaccinated?
Since these people are most at risk of developing a serious condition in case of SARS-CoV-2 infection, it is important that they should be vaccinated.

2. Can people with respiratory allergies (rhinitis, conjunctivitis, bronchial asthma) be vaccinated?
People who suffer or have suffered from respiratory allergy can be vaccinated, remaining under observation, like everyone, for 15 minutes after the injection. Any ongoing antiallergic treatment, including specific immunotherapy, shall not be suspended. During specific immunotherapy, the vaccine should be administered with a 48 hours interval.

3. Can people with severe persistent bronchial asthma be vaccinated?
For those suffering from severe persistent bronchial asthma, well controlled by therapy, vaccination is recommended remaining under supervision for 60 minutes. In the case of uncontrolled asthma, the administration of the vaccine should be postponed until the clinical situation is again under control. If asthma cannot be controlled by therapy, the vaccine shall be administered in a protected environment (hospital), remaining under medical supervision for 60 minutes.

4. Can people with food allergies be vaccinated?
People with food allergies can be vaccinated by remaining under observation, like everyone, for 15 minutes after the injection. Should you have previously experienced severe allergic reactions (anaphylaxis) to food, you shall remain under medical supervision for 60 minutes.

5. Can people with allergies to drugs or to their excipients be vaccinated?
People with drug allergies can be vaccinated remaining under observation, like anyone else, for 15 minutes after the injection. Should you have previously experienced severe allergic reactions (anaphylaxis) to medicines, you shall remain under medical supervision for at least 60 minutes. People with suspected SERIOUS allergy to polyethylene glycol (PEG), macrogol and polysorbate excipients, shall be referred to an allergist before being administered the COVID-19 vaccine.

6. Can people with contact allergies (dermatitis) be vaccinated?
People having previously experienced contact dermatitis can be vaccinated.

7. Can people with latex allergies be vaccinated?
Yes, because all COVID-19 vaccines currently in use do not contain latex. However, it is necessary to inform the vaccination centre that you are allergic to latex so that the vaccination is carried out with latex free material. In case of severe allergic reaction (anaphylaxis) from latex the observation time after vaccination is extended to 60 minutes.

8. Can people with mastocytosis be vaccinated?
For vaccination of people with mastocytosis it is recommended, as with routine vaccines, oral anti-histamine coverage from 1 day before to 5 days after vaccination, and to remain under medical

supervision for at least 60 minutes after the injection. In case of previous anaphylactic reactions to any or unknown substance, the vaccine should be administered in a protected environment (hospital).

9. Can people with celiac disease or organ-specific autoimmune diseases (e.g., Hashimoto's thyroiditis) be vaccinated?

People suffering from celiac disease or organ-specific autoimmune diseases can be vaccinated, as these diseases are not a contraindication to vaccination.

10. Can people with autoimmune diseases or documented immunodeficiency be vaccinated?

People with autoimmune diseases or documented immunodeficiency with no contraindications can receive the vaccine. The ongoing therapy for the underlying disease should not be discontinued. With reference to certain specific medicines only, it should be adjusted or their administration should be postponed compared with the pharmacological treatment, according to the indications of the treating specialist.

These people are strongly recommended to complete the primary vaccination course and have an additional dose administered, as they may be at high risk of developing COVID-19 and may not respond as well to the vaccine. No specific safety issues are detected.

NB: For further indications on management of subjects with severe allergies, autoimmune diseases and immunodeficiencies, it is advisable to refer to the recommendations of the periodically updated Learned Societies.

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Additional dose for organ transplant recipients and immunocompromised individuals

1. Why should an additional dose be administered to organ transplant recipients and immunocompromised individuals?

Solid organ transplant recipients and immunocompromised individuals show a reduced antibody response after a complete primary vaccination course (2 doses of Comirnaty, Spikevax, Vaxzevria and 1 dose of Jcovden (ex COVID-19 Vaccine Janssen). Therefore, they are considered at risk of severe COVID-19. In these people, an additional dose of mRNA vaccine can significantly improve the immune response and thus the protection against COVID-19.

2. Who should receive an additional dose?

To complete the primary vaccination course, an additional dose of mRNA COVID-19 vaccine may be considered in adults and adolescents >12 years of age with clinically relevant immunocompromised conditions.

These include individuals who have received a solid organ transplant and those with comparable immunocompromised conditions based on clinical evaluation.

3. Which vaccines are used for the additional dose?

In all cases, the additional dose is based on one of the two mRNA vaccines authorised in Italy (Comirnaty and Spikevax). This applies even in case an adenoviral vaccine (Vaxzevria and Jcovden, ex COVID-19 Vaccine Janssen) was used for the first vaccination. In addition, if the same mRNA vaccine used for the first two doses is not available, an additional "heterologous" dose with a different type of mRNA vaccine may be used.

Based on current knowledge, the recommended dosage for the additional dose is equal to the dosage authorised for each single dose of the primary vaccination course (i.e. 30 micrograms for Cominarty and 100 micrograms for Spikevax).

4. How long after completing the primary vaccination course may the additional dose be administered?

The additional dose may be administered after at least 28 days following the last dose of the primary vaccination course (second dose of Comirnaty, Spikevax, Vaxzevria and single dose of Jcovden, COVID-19 Vaccine Janssen).

5. Is it safe to receive an additional dose of vaccine? Are there sufficient data that prove it?

Preliminary data on the tolerability of a third dose of a mRNA vaccine or of an additional dose after vaccination with Jcovden (ex COVID-19 Vaccine Janssen), from studies carried out on a limited number of subjects, and show a safety profile similar to that observed after the first or the second dose. This applies both in terms of type and frequency of local (injection site pain and redness) and systemic (tiredness, headache, chills, muscle and joint pain, fever) undesirable events.

In addition, pharmacovigilance in the COVID-19 vaccines post-authorisation phase provides for a system for collecting all suspected adverse reactions reports and continuous monitoring of adverse reactions in order to identify possible warning signals and implement appropriate risk minimisation measures.

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Booster dose in the general population

Who should receive a booster dose?

In order to maintain an effective immune response after completing the primary vaccination course (two doses of Comirnaty, Spikevax, Vaxzevria and one dose of Jcovden, ex COVID-19 Vaccine Janssen), a booster dose may be administered to:

- people aged 60 years and older;
- staff and guests of residential centres for the elderly;
- healthcare professionals and other professionals in the healthcare sector who carry out their activities in healthcare facilities, socio-healthcare and social welfare facilities, as currently indicated;

- highly vulnerable people due to underlying/concurrent conditions, aged 18 years and older;

As of 1 December 2021, a booster dose is administered to all people aged 18 years and older. In addition, as of 5 January 2022, a booster dose of Comirnaty (30 micrograms) is recommended also for the 12-17 age group.

For the booster dose, an mRNA vaccine authorised in Italy (Comirnaty or Spikevax) can be used. This applies even in case an adenoviral vaccine (Vaxzevria or Jcovden, ex COVID-19 Vaccine Janssen) was used for the first vaccination course. In addition, if the same mRNA vaccine used for the first two doses is not available, a booster dose with a different mRNA vaccine may be used ("heterologous vaccination"). Compared to the doses used for the primary vaccination course, an equal dose of Comirnaty (30 micrograms) and half a dose of Spikevax (50 micrograms) is expected to be administered based on the studies conducted.

The administration of a booster dose is possible after a minimum interval of at least four months (120 days) after completion of the primary vaccination course, or after administration of the single/last dose or diagnosis of confirmed infection in case of people vaccinated before or after SARS-CoV-2 infection.

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Individuals vaccinated abroad with COVID-19 vaccines not authorised by EMA and AIFA

What should individuals vaccinated abroad with COVID-19 vaccines not authorised by EMA and AIFA do?

There is currently no information available both on the level of vaccine effectiveness and on the progress of protection over time offered by COVID-19 vaccines currently in use in other countries, but not authorised in Europe. However, in order to ensure greater protection against severe forms of COVID-19, and at the same time reduce the circulation of the virus, such people are advised to have a booster dose administered with a mRNA vaccine from 28 days up to 6 months after completing the primary course. The dosages used will be those for the booster dose (Comirnaty 30 micrograms and Spikevax 50 micrograms). After the six-month period of the primary course, as well as if the primary course is not completed, consideration should be given to the possibility of starting a new vaccination course.

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Currently available COVID-19 vaccines

mRNA vaccines

1. How do mRNA vaccines work?

The two vaccines based on ribonucleic acid molecules (mRNA vaccines), approved for the COVID-19 vaccination campaign, work by delivering a small segment of mRNA into some cells of the vaccinated person. This mRNA segment contains the instructions for temporarily producing the spike protein, a protein found on the surface of coronavirus SARS-Cov-2.
In these vaccines, the small viral mRNA segment is embedded in microscopic lipid particles that, by merging with human cells, deliver such segment into the cells. Here, the viral mRNA segment starts the temporary production of the spike proteins. The person's immune system will recognise these proteins as foreign and will activate lymphocytes and produce antibodies.
After the vaccination, some of the lymphocytes that acted against the spike protein will survive for several months. The presence of these 'memory lymphocytes' will enable the person's immune system to rapidly activate a formidable response against a possible invasion of the virus responsible for COVID-19.

2. Can mRNA vaccines cause COVID-19 or other genetic modifications?

These vaccines do not use active viruses, but only a genetic component. No whole or live viruses are involved, therefore vaccines cannot cause the disease. As for all mRNAs produced by cells, the mRNA from the vaccine does not stay in the body but is broken down naturally few days after vaccination.

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Pfizer/BioNTech's mRNA BNT162b2 (Comirnaty)

1. What is it and what is it used for?

Comirnaty is an mRNA vaccine and is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus. It is administered to adults and children aged 5 years and older. Comirnaty 30 micrograms/dose is used both for the primary vaccination course and for the booster dose. The vaccine does not contain the virus itself and cannot cause the disease.

2. How is it administered?

Comirnaty is given as two injections, usually into the muscle of the upper arm, 21 days apart. The dose to be administered to each person is 0.3 mL. Should it be necessary to delay the second dose by a few days, AIFA's Technical Scientific Committee states that a 42-day interval should not be exceeded in any case. In order to achieve optimum protection, it is always necessary to complete the vaccination cycle with the second dose.

3. What does it contain?

Comirnaty contains a molecule called messenger RNA, enclosed in liposomes formed by ALC-0315

and ALC-0159, to facilitate entry into cells.
The inactive ingredients (excipients) are: ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315), 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159), 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC), cholesterol, potassium chloride, potassium dihydrogen phosphate, sodium chloride, disodium phosphate dihydrate, sucrose, water for injections.

4. How were clinical trials conducted?

A very large clinical trial showed that Comirnaty was effective at preventing COVID-19 in people from 16 years of age. The efficacy and safety profile of the vaccine was assessed during clinical trials that were conducted in six countries: United States, Germany, Brazil, Argentina, South Africa and Turkey. More than 44,000 people participated in these trials. Half received the vaccine and half were given a placebo, a product that is identical to the vaccine in all its aspects, but that is not active. Efficacy was calculated in over 36,000 people from 16 years of age (including people over 75 years of age) who had no sign of previous infection.
The study showed a 95% reduction in the number of symptomatic COVID-19 cases in the people who received the vaccine (8 cases out of 18,198 had COVID-19 symptoms) compared with people who received a placebo (162 cases out of 18,325 had COVID-19 symptoms).

5. How effective is it?

The results of these trials have shown that two doses of Comirnaty given 21 days apart may prevent 95% of adults aged 16 years and over from developing COVID-19, with results broadly similar across genders, racial and ethnic groups.
The 95% reduction refers to the difference between the 162 cases reported in the group of 18,325 people who received a placebo and the only 8 cases reported in the group of 18,198 people who received the vaccine.

6. Is protection effective immediately after injection?

No, the efficacy has been shown one week after the second dose.

7. What adverse reactions were observed during the trials?

The most common adverse reactions (affecting more than 1 in 10 people) with Comirnaty were usually mild or moderate and resolved within a few days after vaccination. These included pain and swelling at the injection site, tiredness, headache, muscle and joint pain, chills and fever. Redness at the injection site and nausea occurred in less than 1 in 10 people. Itching at the injection site, pain in extremities, enlarged lymph nodes, difficulty sleeping, feeling unwell were uncommon adverse reactions (affecting less than 1 in 100 people). Weakness in muscles on one side of face (acute peripheral facial paralysis or palsy) occurred rarely, in less than 1 in 1,000 people.

8. What serious adverse reactions were observed during the trials?

The only serious adverse reaction occurring more frequently in vaccinated people than in people who received the placebo was the enlargement of lymph nodes. However, this is a benign condition

which resolves naturally.
Overall, systemic reactions were more common and pronounced after the second dose.
Reports of adverse reactions, from the least serious to the most severe, including allergic reactions, are being collected in countries where mass administration of the vaccine has already started. Countries administering the vaccine to the entire population are collecting and assessing any adverse reaction reported to the relevant pharmacovigilance system in order to define the risk profile of the vaccine. For further information, please refer to FAQs on Pharmacovigilance on COVID-19 vaccines and reports on adverse reactions.

9. What adverse reactions were observed during the Comirnaty vaccination campaign?

The most frequent adverse reactions observed during the current vaccination campaign are non-serious, mild or moderate and, although annoying, resolve in a few hours or days, often without the need for symptomatic treatment (painkillers and the like). Some very rare adverse reactions, such as myocarditis/pericarditis or capillary leak syndrome, are constantly monitored and evaluated. Any new relevant information concerning these adverse reactions is included in the Summary of Product Characteristics and Package Leaflet.
The total rate of reports received for this vaccine is indicated in the periodic adverse reaction reports published on the dedicated section of the AIFA website.

10. How is Comirnaty prepared?

The 30 microgram multidose vial, both in the ready-to-use formulation and in the one to be diluted, contains a total of 6 doses. The 10 microgram multidose vial (concentrate to be diluted) contains ten doses. Any residues from different vials, even those belonging to the same lot number, should never be mixed.

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COVID-19 Vaccine Moderna mRNA-1273 (Spikevax)

1. What is it and what is it used for?

Spikevax is an mRNA vaccine and is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in people aged 12 years and above. For the primary vaccination course, the dose of Spikevax is equal to 100 micrograms, whereas for the booster, half a dose (50 micrograms) is used. The vaccine does not contain the virus itself and cannot cause the disease.

2. How is it administered?

The vaccine is given as two injections, each of 0.5 mL, usually into the muscle of the upper arm, 28 days apart. Should it be necessary to delay the second dose by a few days, AIFA's Technical Scientific Committee states that a 42-day interval should not be exceeded in any case. In order to achieve optimum protection, it is always necessary to complete the vaccination cycle with the second dose.

3. What does it contain?

Spikevax contains a molecule called messenger RNA, enclosed in very small lipid particles (liposomes).
The inactive ingredients (excipients) are: lipid SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000 DMG), tromethamol, tromethamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. How were clinical trials conducted?

A very large clinical trial showed that Spikevax was effective at preventing COVID-19 in people from 18 years of age. The efficacy and safety profile of the vaccine was assessed during clinical trials conducted at 99 centres across the United States. 30,420 people aged 18 years and above were enrolled.
Participants were divided into two groups: 15,210 received the vaccine and as many were given a placebo, a product that is identical to the vaccine in all its aspects, but that is not active. More than half (58.6%) of participants were 18 to 64 years of age, 24.8% of participants were 65 years of age and older, and 16.7% were below 65 years of age but had comorbidities that increased the risk of severe COVID-19. 47.3% were women.
Overall, 11 cases of COVID-19 were reported in the people who received the vaccine, compared with 185 cases reported in the group who had been given the placebo and who was used as the control group. This means that the vaccine showed a 94.1% efficacy in reducing the rate of symptomatic SARS-CoV-2 infection compared with the placebo.

5. How effective is it?

The results of these trials have shown that two doses of Spikevax given 28 days apart were able to prevent 94.1% of adults aged 18 years and over from developing COVID-19. The reported cases were 11 among vaccinated people and 185 in the placebo group. The results were substantially similar across age, gender and ethnic groups.
All serious COVID-19 cases (30 in total, with 1 death) occurring among study participants were recorded in the control group, confirming the vaccine's ability to prevent the severe form of the SARS-CoV-2 disease.

6. Is protection effective immediately after injection?

No, the efficacy has been shown two weeks after the second dose.

7. What adverse reactions were observed during the trials?

The most frequently reported adverse reactions were pain at the injection site (92%), fatigue (70%), headache (64.7%), muscle pain (61.5%), chills (45.4%), nausea/vomiting (23%), enlargement

of lymph nodes of the arm where the injection was received (19.8%), fever (15.5%), injection site swelling (14.7%) and redness (10%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. They occurred more frequently after the second dose and in younger participants (aged 18 to 65 years) compared with those aged 65 years and older.

8. What serious adverse reactions were observed during the trials?

The frequency of the most severe adverse events was comparable between the control group (1.3%) and that receiving the vaccine (1.5%). In less than 0.5% of cases, in both groups, adverse events were such as to prevent the administration of the second dose. No respiratory disorders were reported in relation to the vaccine.
For further information, please refer to FAQs on Pharmacovigilance on COVID-19 vaccines and reports on adverse reactions.

9. What adverse reactions were observed during the Spikevax vaccination campaign?

The most frequent adverse reactions observed during the current vaccination campaign are non-serious, mild or moderate and, although annoying, resolve in a few hours or days, often without the need for symptomatic treatment (painkillers and the like). Some very rare adverse reactions, such as myocarditis/pericarditis or capillary leak syndrome, are constantly monitored and evaluated. Any new relevant information concerning these adverse reactions is included in the Summary of Product Characteristics and Package Leaflet.
The total rate of reports received for this vaccine is indicated in the periodic adverse reaction reports published on the dedicated section of the AIFA website.

10. How is Spikevax prepared?

The multidose vial contains 6.3 mL and does not require dilution. Therefore, it is ready for use and allows for the administration of 10 doses, although an eleventh full dose can be obtained using appropriate syringes.
Any residue from different vials, even belonging to the same batch number, should never be mixed.

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Viral vector vaccines

1. What is the mechanism of action of DNA vaccines that use adenoviruses as transporters?

Some vaccines approved for the COVID-19 vaccination campaign use adenoviruses to send the DNA fragment containing the instructions for producing the Spike protein present on the surface of the COVID-19 virus into human cells. The adenoviruses used as transporters have been rendered unable to replicate and therefore cannot spread throughout the body.
After vaccination, these adenovirus transporters enter some cells of the vaccinated person where the DNA fragment carried by the virus initiates the temporary production of the Spike protein.
The presence of this foreign protein will stimulate the immune system to react by producing antibodies which, by binding to the Spike protein, will prevent the COVID-19 virus from entering the cells. The presence of the foreign Spike protein will also activate T lymphocytes that drive antibody production and kill virus-infected cells.
After vaccination, some of the lymphocytes that reacted against the Spike protein survive for several months. The presence of these "memory lymphocytes" will allow the vaccinated person's immune system to rapidly activate a formidable response against a possible invasion by the COVID-19 virus.
These vaccines do not use whole, active or inactivated viruses or fragments of the virus, but only a small segment of DNA that contains the instructions for making the Spike protein. The production of the foreign Spike protein will end within a short time.

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COVID-19 Vaccine AstraZeneca (Vaxzevria)

1. What is it and what is it used for?

Vaxzevria vaccine is a vaccine intended to prevent COVID-19 disease in people aged 18 and over. It is the third vaccine authorised by AIFA in Italy (30 January 2021). In Italy it is currently recommended preferably for the population aged 60 and over.

2. How is it administered?

Vaxzevria is administered as two injections, into the muscle of the upper arm. People who have been vaccinated with the first dose of Vaxzevria should receive the second dose of the same vaccine to complete the vaccination course during the 12th week and at least ten weeks after the first dose.

3. What does it contain?

The vaccine is composed of a chimpanzee adenovirus unable to replicate itself (ChAdOx1 - Chimpanzee Adenovirus Oxford 1) and modified to carry the genetic information intended to

produce the Spike protein of the SARS-CoV-2 virus. It is a genetically modified organism. The viral vector technology used for this vaccine has already been successfully tested and is used to prevent other diseases.
The inactive ingredients (excipients) are: L-histidine, L-histidine hydrochloride monohydrate, Magnesium chloride hexahydrate, Polysorbate 80 (E 433), Ethanol, Sucrose, Sodium chloride, Disodium edetate (dihydrate), water for injections. The vaccine does not contain preservatives.

4. What is the expected interval between the administration of the first and second dose?

The temporary authorisation of Vaxzevria by the EMA and AIFA provides that the second dose of the vaccine should be administered between 28 and 84 days after the first administration. However, new data collected from ongoing studies seem to offer the opportunity to indicate a longer interval between the first and second dose. In particular, the new data published in February 2021 as a preprint in the 'Lancet' magazine indicate an efficacy equal to 82% when the second dose is administered during the twelfth week.
This is why AIFA considers it useful to indicate the administration of the second dose of the Vaxzevria vaccine ideally during the twelfth week and in any case at least ten weeks after the first dose.

5. How were clinical trials conducted?

The evaluation of the clinical efficacy of Vaxzevria is based on the interim analysis of data from two ongoing clinical trials that included people over 18 years of age: study COV002 phase II/III and study COV003 phase III, conducted in the UK and Brazil respectively. 87% of the participants were aged between 18 and 64, 13% were aged 65 or older. 55.1% of the subjects were women. The studies did not involve people with severe or uncontrolled diseases, with severe immunosuppression, pregnant women, and people who already had COVID-19 disease.
A total of 6,106 participants received two doses of Vaxzevria, while 6,090 participants in the control group received either a meningococcal vaccine or a saline solution.
Due to logistical constraints, the interval between dose 1 and dose 2 ranged from 3 to 23 weeks with 86.1% of participants receiving the two doses within a 4 to 12 week interval.

6. How effective is it?

In subjects vaccinated with the approved dosage regimen (2 doses 4-12 weeks apart), 64 cases of COVID-19 were observed out of 5,258 vaccinated individuals and 154 cases out of 5,210 in the control group. Overall, the vaccine efficacy of Vaxzevria was found to be 59.5% in preventing symptomatic disease. In participants with one or more comorbidities, vaccine efficacy was very similar (58.3%).
In participants who received the second dose 12 weeks after the first, the efficacy 14 days after the second dose was 82.4% (see question "What is the expected interval between the administration of the first and second dose?").

In all participants who received at least one dose of the vaccine, no cases of hospitalisation were observed from 22 days after the first dose (0%, out of 8,032), compared to 14 cases (0.2%, out of 8,026), one of which was fatal, reported for the control group.

7. Is protection effective immediately after injection?

Protection begins approximately 3 weeks after the administration of the first dose of Vaxzevria and persists for up to 12 weeks. However, protection may be incomplete for up to 15 days after the second dose. Moreover, as with all vaccines, vaccination with Vaxzevria may not protect all vaccinated individuals.

8. What adverse reactions were observed during the trials?

Most of the reported adverse reactions were mild to moderate in severity and events usually resolved within a few days after vaccination.
Compared to what was observed in younger participants, adverse reactions, which are commonly expected with the administration of a vaccine, were generally less frequent and milder in participants over the age of 65.
In clinical studies, serious adverse reactions after administration of Vaxzevria were very rare.

9. What adverse reactions were observed during the Vaxzevria vaccination campaign?

The most frequent adverse reactions observed with Vaxzevria are non-serious, mild or moderate and, although annoying, resolve in a few hours or days, often without the need for symptomatic treatment. The total rate of reports received for this vaccine and the type of events are indicated in the monthly adverse reaction reports published on the dedicated section of the AIFA website.
In most cases, such adverse reactions include fever, local reactions at the site of inoculation, tiredness/asthenia, headache and musculoskeletal pain, often in combination with each other and with rising temperature.
Adverse events observed in the post-marketing phase are very rare. These include cases of venous thrombosis associated with thrombocytopenia, mainly at unusual sites such as cerebral venous sinuses and splanchnic veins. Most of these events occurred in the first three weeks following the first dose and predominantly in people under the age of 60. Therefore, the Ministry of Health has recommended preferential use in people aged over 60 years.
Outside these specific events of thrombosis with thrombocytopenia, pharmacovigilance data and clinical studies have shown that the vaccine does not increase the overall risk of thromboembolic events.
Rare cases of thrombocytopenia including immune thrombocytopenia, usually within the first four weeks after vaccination, have also been reported from the constant monitoring of the vaccine safety at national and European level.
Very rarely these cases occurred with very low platelet levels (< 20,000 per µL) and/or were associated with bleeding. Some of these cases occurred in subjects with a history of immune thrombocytopenia. Subjects diagnosed with thrombocytopenia occurring within three weeks of

vaccination with Vaxzevria should be actively assessed for signs of thrombosis.
In addition, cases of Guillain-Barré syndrome have been reported very rarely after vaccination with Vaxzevria, and their relationship with the vaccine was considered possible. Finally, in the first days following vaccination with Vaxzevria, cases of capillary loss syndrome (CLS) have been reported very rarely. This is a rare disorder characterised by oedema, hypotension and hypoalbuminaemia. Since some cases occurred in people who had had a diagnosis of CLS in the past, it was recommended not to administer Vaxzevria in people with a clinical history of this syndrome.
During the periodic reassessments of the safety of this vaccine, the PRAC established that the benefits of the vaccine in preventing COVID-19 outweigh risks to a great extent.

10. How is Vaxzevria prepared?

The multidose vial can contain 8 or 10 doses, although one or more additional full doses of 0.5 mL can be obtained using appropriate syringes. In no case is dilution required: the suspension is ready for use. Any residue from different vials, even belonging to the same batch number, should never be mixed.
Vaxzevria contains genetically modified organisms, as allowed by the derogation from certain provisions of Directive 2001/18/EC, approved by the European Parliament in July 2020. Any unused vaccine or waste material derived from this medicine should be disposed of in compliance with the guidance for genetically modified organisms or biohazardous waste. Spills should be disinfected using agents with activity against adenovirus.

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Jcovden (ex COVID-19 Vaccine Janssen)

1. What is it and what is it used for?
Jcovden (ex COVID-19 Vaccine Janssen) is a viral vector vaccine intended to prevent SARS-CoV-2 disease (COVID-19) in people aged 18 years and older. It is designed to prepare the immune system to recognize and counteract SARS-CoV-2.

2. How is it administered?
Jcovden (ex COVID-19 Vaccine Janssen) is administered as a single 0.5 ml dose by intramuscular injection only, into the upper arm.

3. What does it contain?
The active substance is the modified adenovirus (Ad26.COV2-S) encoding the SARS-CoV-2 spike protein. It is a genetically modified organism. The inactive ingredients (excipients) are: 2-hydroxypropyl-β-cyclodextrin (HBCD), citric acid monohydrate, ethanol, hydrochloric acid, polysorbate-80, sodium chloride, sodium hydroxide, trisodium citrate dihydrate, water for

injections. This vaccine does not contain adjuvants, preservatives, materials of animal origin or foetal tissue.

4. How were the clinical trials conducted?

The evaluation of the clinical efficacy of Jcovden (ex COVID-19 Vaccine Janssen) is based on the interim analysis of an ongoing randomised, double-blind, placebo-controlled phase 3 study (COV3001) conducted in the United States, South Africa and Latin American countries to assess the efficacy, safety, and immunogenicity of a single-dose of Jcovden (ex COVID-19 Vaccine Janssen) for the prevention of COVID-19 in adults aged 18 years and older.

A total of 21.895 adults received Jcovden (ex COVID-19 Vaccine Janssen) while 21.888 adults received placebo, that is a product identical in all respects to the vaccine, but not active. Participants were followed for a median of 58 days (range: 1-124 days) after vaccination

Out of the total number of participants, the efficacy was however evaluated on a population of 39.321 (of which 19.630 received the vaccine and 19.691 received the placebo). 79.7% of individuals who received the vaccine were 18 to 64 years old, 20.3% aged 65 or older. 44.3% of individuals were female; 39.9% of individuals had at least one pre-existing comorbidity associated with increased risk of progression to severe COVID-19.

5. How effective is it?

Fourteen days after vaccination, 116 cases of COVID-19 out of 19,630 vaccinated individuals were observed compared to 348 out of 19,691 in the control group. Therefore, Jcovden (ex COVID-19 Vaccine Janssen) efficacy against occurrence of moderate to severe symptomatic COVID-19 disease was 66.9%. The result includes people aged 60 years and over.

The efficacy observed was 66.1 % 28 days after vaccination (66 cases observed among individuals receiving Jcovden (ex COVID-19 Vaccine Janssen) compared to 193 cases in the placebo group). Furthermore, 14 days after vaccination, 14 severe cases in the vaccine group and 60 cases in the control group were observed (76.7 % efficacy in preventing severe/critical disease), whereas 28 days after vaccination 5 cases in the vaccine group and 34 in the placebo group were observed (85.4 % efficacy).

Of the severe cases with onset at least 14 days after vaccination- 14 in vaccine group and 60 in the placebo group- 2 and 6 respectively were hospitalised. Three individuals died (all in the placebo group). Overall, the efficacy of the vaccine was similar in the different subgroups based on age, comorbidity, gender and ethnicity.

6. Is protection effective immediately after injection?

Protection with Jcovden (ex COVID-19 Vaccine Janssen) starts around 14 days after vaccination.

7. What adverse reactions were observed during the trials?

Most adverse reactions reported were mild to moderate in severity and usually the events resolved within a few days.

Compared to younger participants, adverse reactions, which are commonly expected after vaccination, were reported less frequently and were generally milder in adults aged 65 years and

older. Rare side effects (that occurred in less than 1 in 1,000 people) have been hypersensitivity (allergy) and skin allergic reaction (urticaria).

Serious adverse reactions following administration of the Jcovden (ex COVID-19 Vaccine Janssen) during clinical trials have been very rare.

8. What adverse reactions were observed during the Jcovden (ex Janssen vaccine) vaccination campaign?

The most frequent adverse reactions observed with Jcovden (ex COVID-19 Vaccine Janssen) are non-serious, mild and, although annoying, resolve in a few hours or days, often without the need for symptomatic treatment. The total rate of reports received for this vaccine and the type of event are indicated in the monthly adverse reaction reports published on the dedicated section of the AIFA website. In most cases, such adverse reactions include fever, local reactions at the injection site, tiredness/asthenia, headache, myalgia and arthralgia.

Serious adverse events observed in the post-marketing phase are very rare. As already observed with Vaxzevria, cases of venous thrombosis with thrombocytopenia have been reported, especially in atypical sites such as intracranial venous sinuses and splanchnic veins, predominantly in subjects under 60 years of age and in women. Following these reports, the Ministry of Health has recommended preferential use in people aged over 60 years.

Cases of venous thromboembolism and immune thrombocytopenia with very low platelet levels have been reported very rarely following vaccination with Jcovden (ex COVID-19 Vaccine Janssen), generally within the first four weeks after administration. These risks should be carefully evaluated prior to vaccination in subjects at increased risk of venous thromboembolism or a history of immune thrombocytopenia. EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has concluded that the benefits of the Jcovden (ex Janssen vaccine) outweigh the risks and confirmed its authorisation for the entire population over 18 years.

In addition, cases of Guillain-Barré syndrome have been reported very rarely after vaccination with Jcovden (ex COVID-19 Vaccine Janssen), and their relationship with the vaccine was considered possible. Finally, very rare cases of capillary loss syndrome (CLS) have been reported in the first days after vaccination with Jcovden (ex COVID-19 Janssen vaccines). Therefore, the vaccine is currently contraindicated in subjects who have previously had episodes of CLS.

9. How is Jcovden (Janssen vaccine) prepared and stored?

The vaccine can be stored for 2 years at -25 °C to -15 °C if the package remains intact. Once removed from the freezer, the unopened vaccine vial may be stored refrigerated at 2°C to 8°C, protected from light, for a single period of up to 3 months, not exceeding the printed expiry date. Once thawed, the vaccine should not be re-frozen.

After opening the vaccine can be stored between 2°C-8°C for a maximum of 6 hours or remain at room temperature (maximally 25°C) up to 3 hours after first puncture of the vial.

The multidose vial contains 5 doses of 0.5 ml, no dilution is required. Any residues from different vials, even those belonging to the same batch number, shall not be mixed.

Jcovden (ex COVID-19 Vaccine Janssen) contains genetically modified organisms, in accordance with the derogation from certain provisions of Directive 2001/18/EC, approved by the European

Parliament in July 2020. Any unused vaccine or waste materials derived from this medicine should be disposed of in compliance with the guidelines for GMOs or biohazardous waste. Potential spills should be disinfected with agents with viricidal activity against adenovirus.

Protein subunit vaccines

1. What is the mechanism of action?

Protein subunit vaccines are composed of "protein fragments" of the virus. In the production of this type of anti-COVID-19 vaccine, a portion of DNA containing the information necessary to produce the spike protein is inserted inside a baculovirus.
Subsequently the baculovirus will infect some cells in vitro which will release the genetic material useful for the production of the spike protein. The latter will then be extracted, purified and compacted to obtain viral nanoparticles that can contain up to 14 spikes.
These particles, added with an adjuvant molecule used to further stimulate the immune system, are thus ready to be injected into the human body to obtain the production of antibodies against the SARS-CoV-2 spike protein.

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Nuvaxovid (Novavax)

1. What is it and what is it used for?

Nuvaxovid is a vaccine used for active immunisation for the prevention of COVID-19, a disease caused by the SARS-CoV-2 virus, in people aged 18 years or older. The vaccine causes the immune system (the body's natural defenses) to produce antibodies and specialised white blood cells to fight the virus, in order to provide protection against COVID-19. None of the components of this vaccine is capable of causing SARS-CoV-2 or COVID-19 infection.

2. How is it administered?

Nuvaxovid is administered as an injection into the upper arm as a course of 2 doses of 0.5 mL each. During and after each injection of the vaccine, the doctor, pharmacist or nurse will keep the patient under observation for about 15 minutes to monitor for any signs of an allergic reaction.

In the event that the appointment for the second injection of Nuvaxovid is not respected, it is necessary to ask the doctor or nurse for advice because with a single dose of Nuvaxovid the protection from COVID-19 could be incomplete.

3. What does it contain?

One dose (0.5 mL) contains 5 micrograms of purified SARS-CoV-2 spike protein* produced by recombinant DNA technology with adjuvant Matrix-M. Adjuvants are substances added to some vaccines to increase an immune response and thus allow to accelerate, improve and/or prolong the protective effects of the vaccine.

The other ingredients (excipients) contained in Nuvaxovid are:

- disodium hydrogen phosphate heptahydrate
- sodium dihydrogen phosphate monohydrate
- disodium hydrogen phosphate dihydrate
- sodium chloride
- polysorbate 80
- cholesterol
- phosphatidylcholine (including all racemic α-tocopherol)
- potassium dihydrogen phosphate
- potassium chloride
- sodium hydroxide (for pH adjustment)
- hydrochloric acid (for pH adjustment)
- water for injections.

4. What interval is expected between the administration of the first and second dose?

The second dose of Nuvaxovid should be administered three weeks after the first dose to complete the primary vaccination course. Importantly, the second dose is needed to achieve an optimal immune response.

5. Who should Nuvaxovid not be administered?

Nuvaxovid should not be used in people who are allergic to the active substance or to any of the other ingredients of this medicine.

Also, it is necessary to report to the doctor if the person has already had a severe allergic reaction after receiving any other vaccine by injection or after Nuvaxovid has been administered in the past.

6. How were the clinical studies conducted?

The clinical efficacy, safety, and immunogenicity of Nuvaxovid were evaluated in two pivotal phase III placebo-controlled studies, Study 1 (2019nCoV-301) conducted in North America and Study 2 (2019nCoV-302) conducted in the UK, as well as in a Phase IIa / b study, Study 3 (2019nCoV-501) conducted in South Africa.

7. How effective is it?

In Study 1, the efficacy of the Nuvaxovid vaccine for the prevention of the onset of COVID-19 starting seven days after Dose 2 was 90.4% (95% CI, 82.9-94.6). No severe COVID-19 cases were reported among 17,312 participants who received Nuvaxovid, compared with 4 severe COVID-19 cases reported among 8,140 placebo recipients.

In Study 2, the efficacy of the Nuvaxovid vaccine for the prevention of the onset of COVID-19 starting seven days after Dose 2 was 89.7% (95% CI, 80.2-94.6). No cases of severe COVID-19 were reported among the 7,020 participants who received Nuvaxovid, compared with 4 cases of severe COVID-19 reported among the 7,019 participants who received placebo.

In Study 3, conducted in South Africa where variant B.1.351 (Beta) was in circulation at the time of the study, the primary efficacy analysis was conducted on 2,770 participants who received two doses of Nuvaxovid (n = 1,408) or placebo (n = 1,362) and vaccination efficacy was 48.6% (95% CI: 28.4, 63.1). In total, 147 mild, moderate or severe symptomatic cases of COVID-19 were recorded among all adult participants, seronegative (to SARS-CoV-2) at baseline.

8. Is the protection effective immediately after the injection?

Protection may not be complete until 7 days after the second dose is administered. As with all vaccines, vaccination with Nuvaxovid may not protect everyone who is vaccinated.

9. How long does the vaccine induced protection last?

The duration of protection offered by Nuvaxovid is unknown as it is still being determined in ongoing clinical trials.

10. What adverse reactions were observed in the experimental studies?

Like all medicines, Nuvaxovid can cause side effects, although not everybody gets them. In particular, the following symptoms and signs have been reported:

Very common (may affect more than 1 in 10 people)

- headache
- nausea or vomiting
- muscle pain
- joint pain
- pain or tenderness at the point where the injection is performed
- feeling of extreme tiredness (fatigue)
- general malaise

Common (may affect up to 1 person in 10 people)

- redness where the injection is performed

- swelling where the injection is performed
- fever (>38 °C)
- chills
- pain or discomfort in the arm, hand, leg and/or foot (pain in the limbs)

Most of the symptoms and signs disappear within a few days of onset. If symptoms persist, you should contact your doctor, pharmacist or nurse.

11. Is it possible to drive and use machines after vaccination?

Nuvaxovid may temporarily reduce the ability to drive and use machines due to feeling faint or dizzy, or feeling extremely tired. If you feel unwell after vaccination it is advisable to wait until any effects of the vaccine have passed before driving or using machines.

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