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Comirnaty (*COVID-19 mRNA Vaccine (nucleoside modified)*)

An overview of Comirnaty, including its adapted vaccine, and why it is authorised in the EU

What is Comirnaty and what is it used for?

Comirnaty is a vaccine for preventing coronavirus disease 2019 (COVID-19) in people aged 5 years and older.

Comirnaty contains tozinameran, a messenger RNA (mRNA) molecule with instructions for producing a protein from the original strain of SARS-CoV-2, the virus that causes COVID-19.

Comirnaty is also available as two adapted vaccines:

- Comirnaty Original/Omicron BA.1 contains tozinameran and riltozinameran, another mRNA molecule with instructions for producing a protein from the Omicron BA.1 subvariant of SARS-CoV-2.
- Comirnaty Original/Omicron BA.4-5 contains tozinameran and famtozinameran, another mRNA molecule with instructions for producing a protein from the Omicron BA.4 and BA.5 subvariants of SARS-CoV-2.

The adapted vaccines are only used in people aged 12 years and older who have received at least a primary vaccination course against COVID-19.

Comirnaty and its adapted vaccines do not contain the virus itself and cannot cause COVID-19.

How is Comirnaty used?

Primary vaccination

Comirnaty is given as two injections, usually into the muscle of the upper arm, 3 weeks apart. Adults and adolescents from the age of 12 are given 30 micrograms per dose; children aged 5 to 11 years are given 10 micrograms per dose.

An additional dose of Comirnaty may be given to people aged 5 years and older with a severely weakened immune system, at least 28 days after their second dose.

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Booster vaccination

A booster dose of Comirnaty may be given to people aged 12 years and older at least 3 months after primary vaccination with Comirnaty. In adults a booster dose of Comirnaty can also be given after primary vaccination with another mRNA vaccine or an adenoviral vector vaccine.

A booster dose of Comirnaty Original/Omicron BA.1 or Comirnaty Original/Omicron BA.4-5 (30 micrograms per dose) may be given to people aged 12 years and older at least 3 months after the last dose of a COVID-19 vaccine.

The vaccines should be used according to official recommendations issued at national level by public health bodies.

For more information about using Comirnaty or its adapted vaccines, see the package leaflet or consult a healthcare professional.

How does Comirnaty work?

Comirnaty works by preparing the body to defend itself against COVID-19. It contains a molecule called mRNA which has instructions for making the spike protein. This is a protein on the surface of the SARS-CoV-2 virus which the virus needs to enter the body's cells and can differ between variants of the virus. Adapted vaccines work in the same way as Comirnaty and are expected to broaden protection against the virus as they also contain mRNA matching other variants of the virus.

When a person is given the vaccine, some of their cells will read the mRNA instructions and temporarily produce the spike protein. The person's immune system will then recognise the protein as foreign and produce antibodies and activate T cells (white blood cells) to attack it.

If, later on, the person comes into contact with SARS-CoV-2, their immune system will recognise it and be ready to defend the body against it.

The mRNA from the vaccine does not stay in the body but is broken down shortly after vaccination.

What benefits of Comirnaty have been shown in studies?

Primary vaccination

A very large clinical trial showed that Comirnaty, given as a two-dose regimen, was effective at preventing COVID-19 in people from 12 years of age.

The trial involved around 44,000 people aged 16 and above in total. Half received the vaccine and half were given a dummy injection. People did not know whether they received the vaccine or the dummy injection.

Efficacy in people aged 16 and above was calculated in over 36,000 participants (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 got COVID-19 symptoms) compared with people who received a dummy injection (162 cases out of 18,325 got COVID-19 symptoms). This means that the vaccine demonstrated a 95% efficacy in the trial.

The trial in people aged 16 years and older also showed around 95% efficacy in the participants at risk of severe COVID-19, including those with asthma, chronic lung disease, diabetes, high blood pressure or obesity.

The trial was extended to include 2,260 children aged 12 to 15. It showed that the immune response to Comirnaty in this group was comparable to the immune response in the 16 to 25 age group (as measured by the level of antibodies against SARS-CoV-2). The efficacy of Comirnaty was calculated in close to 2,000 children from 12 to 15 who had no sign of previous infection. These received either the vaccine or a placebo (a dummy injection), without knowing which one they were given. Of the 1,005 children receiving the vaccine, none developed COVID-19 compared with 16 children out of the 978 who received the dummy injection. This means that, in this study, the vaccine was 100% effective at preventing COVID-19 (although the true rate could be between 75% and 100%).

Another study showed that an additional dose of Comirnaty increased the ability to produce antibodies against SARS-CoV-2 in organ transplant adult patients with severely weakened immune systems.

A study in children aged 5 to 11 showed that the immune response to Comirnaty given at a lower dose (10 micrograms) was comparable to that seen with the higher dose (30 micrograms) in 16- to 25-year-olds (as measured by the level of antibodies against SARS-CoV-2). The efficacy of Comirnaty was calculated in almost 2,000 children from 5 to 11 years of age who had no sign of previous infection. These children received either the vaccine or a placebo. Of the 1,305 children receiving the vaccine, three developed COVID-19 compared with 16 out of the 663 children who received placebo. This means that, in this study, the vaccine was 90.7% effective at preventing symptomatic COVID-19 (although the true rate could be between 67.7% and 98.3%).

Booster vaccination

Comirnaty

A booster dose of Comirnaty, given after primary vaccination with the vaccine, led to a rise in antibody levels in people from 18 to 55 years old with a normal immune system.

The company also presented supporting evidence from a study of a booster dose of Comirnaty in adolescents aged 16 and over, together with published literature and post-authorisation data plus real-world evidence from the use of booster doses in young people in Israel. Taking all available knowledge into account, it was concluded that the immune response to a booster dose of Comirnaty in adolescents would be at least equal to that in adults.

Comirnaty Original/Omicron BA.1

Another study in adults over 55 years old who had previously received 3 doses of Comirnaty (primary vaccination and a booster) found that the immune response to the Omicron BA.1 subvariant was higher after a second booster dose of Comirnaty Original/Omicron BA.1 than after a second booster with the original Comirnaty vaccine (as measured by the level of antibodies against Omicron BA.1). In addition, the immune response to the original SARS-CoV-2 strain was comparable for both vaccines. The study involved more than 1,800 people, of whom about 300 received Comirnaty Original/Omicron BA.1 in its final composition.

Further data from a study involving over 600 people aged between 18 and 55 years who had previously received 3 doses of Comirnaty showed that the immune response to Omicron BA.1 was higher in people who received a booster with a vaccine containing only the Omicron BA.1 component (riltozinameran) than in those given a booster with the original Comirnaty vaccine.

Based on these data, it was concluded that the immune response to Omicron BA.1 following a booster with Comirnaty Original/Omicron BA.1 in people aged 18 to 55 years would be at least equal to that in people aged over 55. Further, based on previous data in younger people, it was also concluded that the immune response to a booster dose with Comirnaty Original/Omicron BA.1 in adolescents would be at least equal to that in adults.

Comirnaty Original/Omicron BA.4-5

Apart from containing mRNA matching different, but closely related, Omicron subvariants, Comirnaty Original/BA.1 and Comirnaty Original/Omicron BA.4-5 have the same composition. Therefore, based on clinical studies showing that Comirnaty Original/Omicron BA.1 triggers an immune response to the original strain and Omicron BA.1, Comirnaty Original/Omicron BA.4-5 is expected to generate an immune response against both the original strain and the subvariants BA.4 and BA.5. In particular, Comirnaty Original/Omicron BA.4-5 is expected to be more effective than Comirnaty at triggering an immune response against the BA.4 and BA.5 subvariants. These data are further supported by non-clinical laboratory data on the ability of Comirnaty Original/Omicron BA.4-5 to trigger an adequate immune response.

Can children be vaccinated with Comirnaty?

Comirnaty is not currently authorised for children below 5 years of age.

The adapted vaccines are currently not authorised for children below 12 years of age.

Can immunocompromised people be vaccinated with Comirnaty?

There are limited data on immunocompromised people. Although immunocompromised people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can still be vaccinated as they may be at higher risk from COVID-19.

Severely immunocompromised people may be given an additional dose of Comirnaty as part of their primary vaccination.

Can pregnant or breast-feeding women be vaccinated with Comirnaty?

Comirnaty can be used during pregnancy. A large amount of data from pregnant women vaccinated with Comirnaty during the second or third trimester of their pregnancy has been analysed and showed no increase in pregnancy complications. Although data in the first trimester of pregnancy are more limited, no increased risk of miscarriage was seen.

Comirnaty can also be used during breast-feeding. Data from women who were breast-feeding after vaccination have not shown a risk of adverse effects in breast-fed babies.

No data are currently available regarding the use of the adapted vaccines in pregnant or breastfeeding women. However, based on similarity with the vaccine targeting the original strain, including a comparable safety profile, Comirnaty Original/Omicron BA.1 can be used during pregnancy and breast-feeding. In addition, based on the data available for Comirnaty and Comirnaty Original/Omicron BA.1, Comirnaty Original/Omicron BA.4-5 can also be used during pregnancy and breast-feeding.

Can people with allergies be vaccinated with Comirnaty?

People who already know they have an allergy to one of the components of the vaccine listed in section 6 of the package leaflet should not receive the vaccine.

Allergic reactions (hypersensitivity) have been seen in people receiving the vaccine. A very small number of cases of anaphylaxis (severe allergic reaction) have occurred since the vaccine started being used in vaccination campaigns. Therefore, as for all vaccines, Comirnaty and its adapted vaccines should be given under close medical supervision, with the appropriate medical treatment available. People who have a severe allergic reaction when they are given a dose of Comirnaty or its adapted vaccines should not receive subsequent doses.

How well does Comirnaty work for people of different ethnicities and genders?

The main Comirnaty trial included people of different ethnicities and genders. Efficacy of around 95% was maintained across genders and ethnic groups.

What are the risks associated with Comirnaty?

The most common side effects with Comirnaty are usually mild or moderate and get better within a few days after vaccination. These include pain and swelling at the injection site, tiredness, headache, muscle and joint pain, chills, fever and diarrhoea. They may affect more than 1 in 10 people.

Redness at the injection site, nausea and vomiting may occur in up to 1 in 10 people. Itching at the injection site, pain in the arm where the vaccine was injected, enlarged lymph nodes, difficulty sleeping, feeling unwell, decreased appetite, lethargy (lack of energy), hyperhidrosis (excessive sweating), night sweats, asthenia (weakness), and allergic reactions (such as rash, itching, itchy rash, and rapid swelling under the skin) are uncommon side effects (affecting less than 1 in 100 people). Weakness in muscles on one side of the face (acute peripheral facial paralysis or palsy) occurs in less than 1 in 1,000 people.

Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the membrane around the heart) may occur in up to 1 in 10,000 people.

Very few cases of extensive swelling of the vaccinated arm, swelling of the face in people with a history of injections with dermal fillers (soft, gel-like substances injected under the skin), erythema multiforme (red patches on the skin with a dark red centre and paler red rings) paraesthesia (unusual feeling in the skin, such as tingling or a crawling feeling) and hypoesthesia (decreased feeling or sensitivity in the skin) have occurred. Allergic reactions have also occurred with Comirnaty, including a very small number of cases of severe allergic reactions (anaphylaxis). As for all vaccines, Comirnaty and its adapted vaccine should be given under close supervision with appropriate medical treatment available.

Comirnaty Original/Omicron BA.1 has comparable side effects to Comirnaty.

Based on the safety data for Comirnaty and for Comirnaty Original/Omicron BA.1, the safety profile for Comirnaty Original/Omicron BA.4-5 is expected to be comparable to those of these vaccines.

Why is Comirnaty authorised in the EU?

Comirnaty offers a high level of protection against COVID-19 which is a critical need in the current pandemic. The main trials showed that the vaccine has a high efficacy in all age groups. Most side effects are mild to moderate in severity and are gone within a few days.

Comirnaty Original/Omicron BA.1 was found to trigger high levels of antibodies against the original strain of SARS-CoV-2 and the Omicron BA.1 subvariant. Its safety profile was comparable to that of Comirnaty. In addition, Comirnaty Original/Omicron BA.4-5 is expected to trigger immunity against both the original strain of SARS-CoV-2 and the subvariants BA.4 and BA.5, and its safety profile is expected to be comparable to that of Comirnaty and Comirnaty Original/Omicron BA.1.

The Agency therefore decided that the benefits of Comirnaty, including its adapted vaccines, are greater than its risks and that it can be authorised for use in the EU.

Comirnaty has been granted a conditional marketing authorisation. This means that there is more evidence to come about the vaccine (see below), which the company is required to provide. The

Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Comirnaty?

As Comirnaty received a conditional marketing authorisation, the company that markets Comirnaty will continue to provide results from the main trial in adults, which is ongoing for 2 years, as well as from the trials in children. These trials and additional studies, including independent studies of COVID-19 vaccines coordinated by EU authorities, will provide more information on the vaccine's long-term safety and its benefit.

What measures are being taken to ensure the safe and effective use of Comirnaty?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Comirnaty and its adapted vaccines have been included in the summary of product characteristics and the package leaflet.

A risk management plan (RMP) is also in place and contains important information about the vaccine's safety, how to collect further information and how to minimise any potential risks.

Safety measures for Comirnaty and its adapted vaccines are implemented in line with the EU safety monitoring plan for COVID-19 vaccines to ensure that new safety information is rapidly collected and analysed. The company that markets Comirnaty will provide regular safety reports.

As for all medicines, data on the use of Comirnaty and its adapted vaccines are continuously monitored. Suspected side effects are carefully evaluated and any necessary action taken to protect patients.

Other information about Comirnaty

Comirnaty received a conditional marketing authorisation valid throughout the EU on 21 December 2020.

More information about the COVID-19 vaccines, such as the use of adapted vaccines and boosters, is available on the COVID-19 vaccines key facts page.

Further information on Comirnaty, including its adapted vaccines, can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/comirnaty

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