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COVID-19 vaccination programme

Information for healthcare practitioners

COVID-19 immunisation
Protect yourself

Acknowledgement

The information in this document was adapted from a variety of COVID-19 resources produced by UK Health Security Agency (UKHSA). UKHSA granted permission to use their materials in Northern Ireland, this is gratefully acknowledged.

Document information

The information in this document was correct at time of publication. As COVID-19 is an evolving disease, a lot is still being learned about both the disease and the vaccines that have been developed to prevent it, and the knowledge base is still being developed. For this reason, some of the information may change. Updates will be made to this document as new information becomes available. Please use the online version to ensure you are accessing the latest version.

This document includes specific information about the COVID-19 vaccines Pfizer BioNTech (Comirnaty 30 micrograms/dose, Comirnaty 10 micrograms/dose, Comirnaty Original/ Omicron and Comirnaty 3 micrograms/dose), COVID-19 vaccines Moderna (Spikevax, Spikevax bivalent Original/Omicron), COVID-19 vaccine Novavax (Nuvaxovid) and COVID-19 Sanofi Pasteur vaccine (VidPrevtyn Beta).

The guidance will be updated as more information about these vaccines becomes available and will include other vaccines as they become available for use. **As each vaccine is presented, stored and prepared differently, immunisers must ensure they are familiar with the specific details of the vaccine that they are working with.**

COVID–19 disease

On 31 December 2019, the World Health Organization (WHO) was informed of a cluster of cases of pneumonia of unknown cause detected in Wuhan City, China.

On 12 January 2020, it was announced that a novel coronavirus was identified as the cause of the illnesses being detected. This virus is referred to as SARS-CoV-2, and the associated disease as COVID-19.

During late 2020 and 2021, a range of SAR-CoV-2 variants emerged, some of which have been associated with increased transmission. These more transmissible variants have become established globally and replaced the original Wuhan strain. They are associated with successive waves of infections in many countries.

What are the symptoms of COVID-19?

Whilst many individuals have asymptomatic infection, those who do develop symptoms report a range of symptoms, including fever, a new and continuous cough, anosmia (loss of smell) and ageusia (loss of taste), shortness of breath, fatigue and loss of appetite. Other symptoms include: myalgia, sore throat, headache, nasal congestion, diarrhoea, nausea and vomiting.

Around 40% of people who develop symptoms report mild symptoms and typically present without hypoxia or pneumonia. A further 40% present with moderate symptoms, which may include non-severe pneumonia, and 15% present with severe pneumonia and significant disease. Critical disease can lead to life threatening complications and is reported in around 5% of cases. Patients with critical disease may experience acute respiratory distress syndrome (ARDS), sepsis, septic shock, cardiac disease, thromboembolic events such as pulmonary embolism and multi-organ failure.

The long-term sequelae of COVID-19 infection, often referred to as ‘long COVID’ or Post-Acute Sequelae of SARS-CoV-2 (PASC) infection, are an area of ongoing research. In the UK, 4.5% of cases report long-term symptoms 12-16 weeks after the initial infection. Reported symptoms are varied, involving most organ systems and affecting both physical and mental health.

In general, children appear to experience asymptomatic or mild disease. Initial evidence suggested that children had a lower susceptibility to SARS-CoV-2 infection, and they were unlikely to be key drivers of transmission at a population level. However, a prospective study found higher secondary attack rates where the household index case was a child. A rare presentation of multisystem inflammatory syndrome temporally associated with COVID-19 in children and adolescents has been noted. The majority of children recover completely after acute SARS-CoV-2 infection and any persistent symptoms will improve with time. Serious long-term complications are rare in children.

How is COVID-19 spread?

SARS-CoV-2 virus is primarily transmitted between people through respiratory droplets and aerosols expelled from the nose and mouth through coughing, sneezing or speaking or when people touch their eyes, nose or mouth following contact with contaminated objects and surfaces or direct human contact.

Who is affected by COVID-19?

Increasing age and male gender have been shown to be significant risk factors for severe disease and infection fatality ratios are highest in the oldest age groups. In Europe and the UK, deaths attributed to SARS-CoV-2 were reported disproportionately from residential care homes. Comorbidities such as diabetes and severe asthma are associated with an increased risk of death and obesity and other

underlying health conditions can increase the risk for some people. Deprivation and being from a black, ethnic and minority group also results in an increased risk of death from COVID-19, although the contribution of each of the possible underlying factors to these differences is unclear. Additionally, health and social care workers are at increased risk of acquiring infection in their work setting and they may potentially transmit the virus to their families and to those in their care.

The risks to pregnant women and neonates following COVID-19 infection have changed over the course of the pandemic: the maternal mortality ratio as a result of COVID-19 significantly increased from 1.4 per 100,000 live births in the wildtype SARS-CoV-2 dominant period to 5.4 per 100,000 live births in the Delta dominant period. In contrast, pregnant women infected with SARS-CoV-2 were substantially less likely to have a preterm birth or maternal critical care admission during the Omicron period than during the Delta period; fewer stillbirths and no neonatal deaths were observed in the Omicron period.

COVID-19 vaccination programme

What is the aim of the vaccination programme?

The aim of the COVID-19 vaccination programme is to protect those who are at most risk from serious illness or death from COVID-19 and to protect the health and social care staff and system.

How was the vaccine developed?

Over 300 different COVID-19 vaccines are in various stages of development. Some have been made using existing vaccine technology, whilst others have been made using completely new approaches. While it normally takes several years to develop a vaccine, scientists across the world have worked collaboratively and rapidly to achieve the same amount of work in a few months in order to make a safe and effective vaccine available as soon as possible. Although clinical trials have been carried out more rapidly than they have for other vaccines, this has been achieved by conducting some of the steps in parallel rather than sequentially and vaccine safety has not been compromised. The vaccine trials have been subject to all of the usual strict trial and regulatory requirements.

There is more information about COVID-19 vaccines in development, at **https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/**

This document will discuss the COVID-19 vaccines authorised for supply in the UK. The guidance will be updated as more information about these vaccines becomes available and may include other vaccines as they are authorised for use in the UK.

As each vaccine will be presented and prepared differently, immunisers must ensure they are familiar with the specific details of the vaccine that they will be working with.

How long does the vaccine offer protection?

Israel was the first country to demonstrate waning protection from Pfizer BioNTech vaccine showing a decline in protection, even against severe disease, at around six months. In the USA, protection against hospitalisation for Pfizer BioNTech and Moderna vaccines remained high (around 84%) between three and six months.

Updated UK analysis to late August 2021 suggests that protection against symptomatic infection due to the Delta variant appears to decline after the second dose, although remains above 50% overall after five months. Levels of protection from AstraZeneca are lower than that seen after Pfizer BioNTech and remain around 20% lower after five months.

In contrast, protection against hospitalisation and death from Delta variant appears to be well sustained, remaining around 85% at six months after primary vaccination with both AstraZeneca and Pfizer BioNTech vaccines. The decline in protection appears to be mainly driven by older people (over 65 years) and those with clinical risk factors (including immunosuppression).

For the Omicron variant, protection against symptomatic infection from primary vaccination appears to decline to very low levels by six months after all the vaccines used in the UK programme.

COVID-19 vaccination eligibility

Vaccine priority groups

The objectives of the COVID-19 immunisation programme are to protect those who are at highest risk from serious illness or death. The Joint Committee on Vaccination and Immunisation (JCVI) therefore considered the available epidemiological, microbiological and clinical information on the impact of COVID-19 in the UK and provided the Government and Devolved Administrations with advice to support the development of a vaccine strategy.

Full details on vaccine eligibility, with detail on the at-risk conditions and the eligibility of health and social care and laboratory staff groups, are included in the Green Book Covid-19 chapter.

Can pregnant women receive the vaccine?

The risks to pregnant women and neonates following COVID-19 infection worsened over the early stages of the pandemic.

There is an increased risk of hospitalisation, admission to an intensive care unit, invasive ventilation and extracorporeal membrane oxygenation (ECMO) in comparison to non-pregnant women of reproductive age, as well as an increased risk of stillbirth and preterm birth.

Pregnant women are more likely to have severe COVID-19 infection if they are overweight or obese, are of black and Asian minority ethnic background, have co-morbidities such as diabetes, hypertension and asthma, or are 35 years old or older.

In December 2021, the JCVI announced that pregnant women should be considered a clinical risk group within the COVID-19 vaccination programme.

Studies following the use of the COVID-19 vaccines in pregnant women have shown the vaccines to be safe and highly effective in preventing serious complications. Analysis by the UKHSA looked at women who gave birth up to August 2021 and reassuringly found that there were similar rates of still birth, prematurity and low birth weight in vaccinated and unvaccinated women. It also found that pregnant women who are vaccinated are far more protected against serious COVID-19 than those who are unvaccinated.

There is no known risk associated with giving non-live vaccines during pregnancy. Since these vaccines cannot replicate, they cannot cause infection in either the woman or the unborn child. There is extensive post-marketing experience of the use of the Pfizer BioNTech and Moderna vaccines being given to pregnant women in the USA, with no safety signals being raised so far. Over 170,000 pregnant women have been vaccinated in England, Scotland and Wales. Because of more extensive experience with the Pfizer BioNTech (Comirnaty) and Moderna (Spikevax) vaccines in pregnancy, these

two vaccines are the preferred vaccines to offer to pregnant women aged 18 years and over. Pregnant women under 18 years of age should be offered the Pfizer BioNTech (Comirnaty) vaccine as that is the vaccine currently recommended for this age group.

Routine questioning about last menstrual period and/or pregnancy testing is not required before offering the vaccine. Women who are planning pregnancy or in the immediate postpartum can be vaccinated with a suitable product for their age and clinical risk group.

If a woman finds out she is pregnant after she has started a course of vaccine, she should complete vaccination during pregnancy at the recommended intervals.

The Royal College of Obstetricians and Gynaecologists (RCOG) and Royal College of Midwives (RCM) have a decision guide and other useful information on COVID-19 vaccines and pregnancy (**www.rcog.org.uk/en/guidelines-research-services/coronavirus-covid-19-pregnancy-and-womens-health/covid-19-vaccines-and-pregnancy/covid-19-vaccines-pregnancy-and-breastfeeding/**).

See also **www.gov.uk/government/news/pregnant-women-urged-to-come-forward-for-covid-19-vaccination**

Can breastfeeding women receive the vaccine?

There is no known risk associated with being given a non-live vaccine whilst breastfeeding. JCVI advises that breastfeeding women may be offered any suitable COVID-19 vaccine. Emerging safety data is reassuring: mRNA was not detected in the breastmilk of recently vaccinated women and protective antibodies have been detected in breastmilk.

The developmental and health benefits of breastfeeding are clear and should be discussed with the woman, along with her clinical need for immunisation against COVID-19.

Can children receive the vaccine?

Following careful consideration of the risks and benefits of vaccinating children and young people aged 6 months to 17 years, the JCVI has recommended vaccination of the following groups:

Children aged 6 months to 11 years in at risk groups

On 6th April 2023, the JCVI recommended that children aged 6 months to 4 years in a recognised clinical risk group who are at higher risk of severe COVID-19 (as defined in the Green Book COVID-19 chapter) should be offered two 3 microgram doses of the Pfizer BioNTech (Comirnaty) vaccine with an interval of eight weeks between the first and second doses.

On 22 December 2021, the JCVI recommended that children aged 5 to 11 years in the following two groups should be offered two 10 microgram doses of the Pfizer BioNTech (Comirnaty) vaccine with an interval of eight weeks between the first and second doses. The groups are:

- children in a recognised clinical risk group who are at higher risk of severe COVID-19 (as defined in Table 4 of the Green Book COVID-19 chapter) – this includes children who are about to commence immunosuppressive treatment.
- children who are a household contact of someone who is immunosuppressed (defined as those who expect to share living accommodation on most days (and therefore for whom continuing close contact is unavoidable) with individuals of any age who are immunosuppressed).

Children in at risk groups will continue to become eligible when they turn 5 years of age, as will those aged 5-11 years who become at risk. Those with severe immunosuppression will be eligible for a three dose primary course.

Children aged 5 to 11 years not in at risk groups

On 16 February 2022, the JCVI recommended a one-off, non-urgent programme to offer vaccination to all children aged 5 to 11 years of age who are not in a clinical risk group. This offer was intended to increase and broaden protection against severe COVID-19 in advance of a potential future wave of COVID-19.

Two doses of the Pfizer BioNTech (Comirnaty) 10 micrograms/dose vaccine was offered to children aged 5 to 11 years not in a risk group with an interval of at least twelve weeks between doses.

Children and young people aged 12 to 17 years not in an at-risk group

Aged 12 to 15 years

On 13 September 2021, the Chief Medical Officers recommended a first dose of Pfizer BioNTech (Comirnaty 30 micrograms/dose) COVID-19 vaccination for children aged 12-15 to reduce the chances of them catching COVID-19, reduce the number of outbreaks in schools, help avoid school absences and disruption to face-to-face education.

On 29 November 2021, the JCVI recommended that all young people in this age group be offered a second dose twelve weeks from the first dose.

Aged 16 to 17 years

On 4 August 2021, the JCVI recommended that all 16 to 17 year olds should be offered a first dose of the Pfizer BioNTech (Comirnaty 30 micrograms/dose) vaccine. This was followed by a further JCVI recommendation on 15 November 2021 that those in this age group who are not in an at-risk group should be offered a second dose after an interval of twelve weeks.

Young people aged 12 to 17 years at higher risk

Young people aged 12 to 17 years with underlying conditions that put them at increased risk of complications from COVID-19 (full details of the conditions included are listed in Table 4 in the Green Book COVID-19 chapter) are recommended to receive 2 doses of Pfizer BioNTech (Comirnaty 30 micrograms/dose) vaccine eight weeks apart, as are young people in this age group who are household contacts of immunosuppressed individuals, or who work in health and social care.

See summary table on page 9.

Can someone with immunosuppression or HIV receive the vaccine?

Individuals who have immunosuppression or HIV infection (regardless of CD4 count) should be given COVID-19 vaccine in accordance with the recommendations and contraindications stated in the PGD and the Green Book COVID-19 chapter. These individuals may not make a full antibody response and should therefore continue to follow advice to avoid exposure unless they are advised otherwise by their doctor.

The small number of patients who are about to receive planned immunosuppressive therapy should be considered for vaccination prior to commencing therapy (ideally at least two weeks before), when their immune system is better able to make a response. Where possible, it would also be preferable for the two-dose schedule to be completed prior to commencing immunosuppression. This would entail offering the second dose at the recommended minimum for that vaccine (three or four weeks from the first dose) to provide maximum benefit that may not be received if the second dose was given during the period of immunosuppression. Any decision to defer immunosuppressive therapy or to delay possible benefit from vaccination until after therapy should not be taken without due consideration of the risks from COVID-19 and from their underlying condition.

The JCVI advise that a third primary dose be offered to individuals aged 6 months and over who were severely immunosuppressed at the time of their first or second primary COVID-19 vaccine doses. If a third primary dose is required, ideally, it should be given at least eight weeks after the second dose with special attention paid to the timing of any planned or current immunosuppressive therapy as vaccines administered during periods of minimum immunosuppression are more likely to generate better immune responses. Where possible, the third dose should be delayed until 2 weeks after the period of immunosuppression, in addition to the time period for clearance of the therapeutic agent. If not possible, consideration should be given to vaccination during a treatment 'holiday' or when the degree of immunosuppression is at a minimum. The general principles for the administration of a third dose and the criteria for a third primary dose are described in the JCVI advice and the Green Book COVID-19 chapter.

Those aged 6 months and above in this group will also require booster doses to extend protection from their primary course. Further information regarding timing of booster doses can be found in the COVID-19 chapter of the Green Book.

From the end of the spring 2023 campaign, the primary course of COVID-19 vaccine becomes a targeted offer to those at higher risk and only during seasonal campaigns. The main exception to this would be unvaccinated individuals aged five years and above who are or have recently become severely immunosuppressed. These individuals should be considered for primary and booster vaccination, regardless of the time of year. Clinical judgment should be used to decide on the best timing to commence vaccination.

Individuals who have received a bone marrow transplant after vaccination should be considered for a re-immunisation programme for all routine vaccinations and for COVID-19. Specialist advice should be followed on which vaccines can be safely given and on the optimal timing for commencing revaccination.

Can someone with a history of COVID-19 disease receive the vaccine?

There are no safety concerns from vaccinating individuals with a past history of COVID-19 infection, or with detectable COVID-19 antibody. Vaccination of individuals who may be infected or incubating COVID-19 infection is unlikely to have a detrimental effect on the illness. As clinical deterioration can occur up to two weeks after infection, vaccination should ideally be deferred until clinical recovery. This is to avoid wrongly atrributing any new symptom or the progression of symptoms to the vaccine.

Summary table of COVID-19 vaccine recommendations for children and young people aged 6 months to 17 years

Age and risk group	Recommendations
Children aged 6 months to 4 years with specific underlying health conditions that put them at risk of severe COVID-19	• Offer two 3 microgram doses of the Pfizer BioNTech Comirnaty 3 micrograms/dose vaccine with an interval of 8 weeks between doses • Offer a third primary dose to those who had severe immunosuppression at or around the time of their first or second primary COVID-19 vaccine doses at least 8 weeks after second dose
Children aged 5 to 11 with specific underlying health conditions that put them at risk of severe COVID-19 or who are household contacts of an immunosuppressed person	• Offer two 10 microgram doses of the Pfizer BioNTech Comirnaty 10 micrograms/dose vaccine with an interval of 8 weeks between doses • Offer a third primary dose to those who had severe immunosuppression at or around the time of their first or second primary COVID-19 vaccine doses at least 8 weeks after second dose • Offer a booster dose at least 3 months after completion of primary course
Children aged 12 to 15 with specific underlying health conditions that put them at risk of severe COVID-19	• Offer two 30 microgram doses of the Pfizer BioNTech Comirnaty 30 micrograms/dose vaccine with an interval of 8 weeks between doses • Offer a booster dose at least 3 months after completion of primary course
Children and young people aged 12 years and over who are severely immunosuppressed	• Offer two 30 microgram doses of the Pfizer BioNTech Comirnaty 30 micrograms/dose vaccine with an interval of 8 weeks between doses • Offer a third primary dose at least 8 weeks after second dose to those who had severe immunosuppression at or around the time of their first or second primary COVID-19 vaccine doses • Offer a booster dose at least 3 months after completion of primary course
Young people aged 16 and 17 in a clinical risk group or who work in health and social care	• Offer two 30 microgram doses of the Pfizer BioNTech Comirnaty 30 micrograms/dose vaccine with an interval of 8 weeks between doses • Offer a booster dose at least 3 months after completion of primary course
All other young people aged 12 to 15 not in an at risk group	• Offer two 30 microgram doses of the Pfizer BioNTech Comirnaty 30 micrograms/dose vaccine with an interval of 12 weeks between doses

Age and risk group (continued)	Recommendations (continued)
All other young people aged 16 and 17 not in an at risk group	• Offer two 30 microgram doses of the Pfizer BioNTech Comirnaty 30 micrograms/dose vaccine with an interval of 12 weeks between doses
All other children	• Healthy children who turn 5 after 31 August 2022 are not eligible to receive COVID-19 vaccination

There is no need to defer immunisation in individuals after recovery from a recent episode with compatible symptoms, whether or not they are tested for COVID-19. During care home outbreaks, vaccination of residents with confirmed COVID-19 may go ahead, provided the residents are clinically stable. These populations are likely to be highly vulnerable and vaccination should be facilitated without the need for multiple visits, to maximise vaccination coverage in this vulnerable group. If antibodies have already been made to the disease following natural infection, receiving COVID-19 vaccine would be expected to boost any pre-existing antibodies.

For children aged 6 months to 4 years, the JVCI recommend the minimum interval between vaccination and recent SARS-CoV-2 infection should be four weeks.

Can someone experiencing prolonged COVID-19 symptoms ('Long COVID') receive the vaccine?

Having prolonged COVID-19 symptoms is not a contraindication to receiving COVID-19 vaccine but if there is evidence of current deterioration, deferral of vaccination may be considered to avoid incorrect attribution of any change in the person's underlying condition to the vaccine.

Is there a time interval between treatments for COVID-19 disease (for example dexamethasone, monoclonal antibody or antiviral medicines) and vaccine administration?

Dexamethasone is a steroid treatment given to patients experiencing severe COVID-19 symptoms to suppress the immune response and reduce inflammation. As the currently authorised COVID-19 vaccines are non-live vaccines, the response to these vaccines should not be affected by short-term steroid treatment. In addition, by the time a person who has received steroid treatment for COVID-19 infection is well enough to receive a COVID-19 vaccination, the suppressant effect of the steroid treatment should be gone.

Monoclonal antibody preparations containing specific man-made antibodies which bind to the surface of the SARS-CoV-2 virus and stop it from attaching to the body's cells and replicating further have recently been licensed for the treatment and prophylaxis of COVID-19 infection. Primate data suggests that administration of the AstraZeneca combination monoclonal antibody product did not interfere with the subsequent response to active vaccination. Based on this limited evidence, therefore, no specific interval is required between receipt of these products and COVID-19 vaccination, or vice versa. As the use of these products is likely to be prioritised to those who are less able to respond to vaccination, for example immunosuppressed individuals, additional doses of vaccine may be required.

Antivirals prevent the further replication of viruses. As none of the approved COVID-19 vaccines contain live virus, response to the vaccine will not be affected by prior or recent receipt of anti-viral medication.

Can individuals with a bleeding disorder receive the COVID-19 vaccine?

Individuals with bleeding disorders may be vaccinated intramuscularly if, in the opinion of a doctor familiar with the individual's bleeding risk, vaccines or similar small volume intramuscular injections can be administered with reasonable safety by this route. If the individual receives medication/treatment to reduce bleeding, for example treatment for haemophilia, intramuscular vaccination can be scheduled shortly after such medication/treatment is administered. A fine needle (23 or 25 gauge) should be used for the vaccination, followed by firm pressure applied to the site (without rubbing) for at least two minutes*. The individual/carer/parent should be informed about the risk of haematoma from the injection.

Can individuals taking anticoagulants receive the COVID-19 vaccine?

Individuals on stable anticoagulation therapy, including individuals on warfarin who are up-to-date with their scheduled INR testing and whose latest INR was below the upper threshold of their therapeutic range, can receive intramuscular vaccination. If in any doubt, consult with the clinician responsible for prescribing or monitoring the individual's anticoagulant therapy. The separate needles and syringes and the fixed-needle dose-sparing syringes being supplied for administration of the COVID-19 vaccines are suitable for use for vaccination of people with bleeding disorders or anticoagulation therapies.

COVID-19 vaccines

In the UK, the following COVID-19 vaccines are currently in use in the national COVID-19 vaccination programme:

1) COVID-19 vaccine Pfizer BioNTech (Comirnaty 30mcg/dose)

   Given authorisation for temporary supply by the Medicines and Healthcare products Regulatory Agency (MHRA) on 2 December 2020, and then granted Conditional Marketing Authorisation (CMA) on 9 July 2021. This vaccine is authorised for adults and adolescents from 12 years of age. The vaccine is also referred to as Comirnaty 30 concentrate.

2) COVID-19 vaccine Moderna (Spikevax)

   Given authorisation for temporary supply by the MHRA on 8 January 2021 and then granted CMA on 1 April 2021.

3) COVID-19 vaccine Pfizer BioNTech (Comirnaty 10mcg/dose)

   Granted CMA on 22 December 2021. This vaccine is authorised for children from 5 to 11 years of age.

4) COVID-19 Pfizer BioNTech bivalent vaccine (Comirnaty Original/Omicron BA.4-5)

   Granted CMA on 12 September 2022. Authorised for adults and adolescents from 12 years of age.

5) COVID-19 vaccine Moderna (Spikevax bivalent Original/Omicron BA.4-5)

   Granted CMA on 19 October 2022.

6) COVID-19 Sanofi Pasteur vaccine (VidPrevtyn Beta)

Granted CMA on 10 November 2022. Authorised for booster vaccination.

7) COVID-19 vaccine Novavax (Nuvaxvoid)

Granted CMA on 3 February 2022. This vaccine is authorised for adults and adolescents from 12 years of age, who are considered clinically unsuitable to receive an mRNA vaccine.

8) COVID-19 vaccine Pfizer BioNTech (Comirnaty 3mcg/dose)

Granted CMA on 19 October 2022. This vaccine is authorised for children from 6 months to 4 years of age.

All the currently authorised vaccines are presented in multi-dose vials. Using multi-dose vials can improve the efficiency of vaccine manufacture and distribution, enabling vaccine availability for those eligible at the earliest opportunity.

Pfizer BioNTech (Comirnaty) and Moderna (Spikevax) COVID-19 vaccines

The Pfizer BioNTech and Moderna COVID-19 vaccines are mRNA (messenger ribonucleic acid) vaccines. They contain the genetic sequence (mRNA) for the spike protein which is found on the surface of the SARS-CoV-2 virus, wrapped in a lipid envelope (referred to as a nanoparticle) to enable it to be transported into the cells in the body.

When injected, the mRNA is taken up by the host's cells which translate the genetic information and produce the spike proteins. These are then displayed on the surface of the cell. This stimulates the immune system to produce antibodies and activate T-cells which prepare the immune system to respond to any future exposure to the SARS-CoV-2 virus by binding to and disabling any virus encountered.

Comirnaty 30mcg/dose, Spikevax Original, and Comirnaty 10mcg/dose are all monovalent; they contain only the mRNA that encodes for the spike protein of the original (wildtype) virus. They are licensed for primary and booster dosing.

Spikevax bivalent Original/Omicron and Comirnaty Originial/Omicron are bivalent; they contain mRNA that encodes for the spike protein of the original (wildtype) virus and mRNA that encodes for the spike protein of the BA.1 or BA. 4-5 sub-lineages of the Omicron variant. As there is no whole or live virus involved, the vaccine cannot cause disease. The mRNA naturally degrades after a few days.

How do we know the COVID-19 Pfizer BioNTech vaccine is safe?

During clinical trials, local reactions at the injection site were found to be fairly common after vaccination with the Pfizer BioNTech COVID-19 vaccines. Over 80% of trial participants reported pain at the injection site. This occurred within seven days after the injection and resolved after a few days.

The safety of Pfizer BioNTech COVID-19 vaccine was evaluated in participants 16 years of age and older in two clinical studies conducted in the United States, Europe, Turkey, South Africa, and South America. The most frequent adverse reactions in participants 16 years of age and older were pain at the injection site (> 80%), fatigue (> 60%), headache (> 50%), myalgia (> 30%), chills (> 30%), arthralgia (> 20%) and pyrexia (> 10%) and were usually mild or moderate in intensity and resolved within a few days after vaccination. If required, symptomatic treatment with analgesic and/or anti-pyretic medicinal products (eg paracetamol-containing products) may be used.

Following a study in over 2,000 children aged 12-15 years, which generated additional safety and efficacy data, the approval of a 30 microgram dose was extended to those in this age group in June 2021. Trials have now been concluded in children aged 5-11 years, using a 10 microgram dose and children aged 6 months to 4 years, using a 3 microgram dose of the vaccine formulated for children.

Compared to adults and older children, children aged 5 to 11 years reported more injection-site redness (15-19% vs 5-7%) and local swelling (10-15% vs 5-8%), but less fever (3-7% vs 1-20%) and chills (5-10% vs 6-42%). The most frequent adverse reactions in children aged 6 months to 4 years of age that received any primary course dose included irritability (>60%), drowsiness (>40%), decreased appetite (>30%), tenderness at the injection site (>20%), injection site redness and fever (>10%). Safety data reported from other countries after routine use of the paediatric (10 microgram) dose of Pfizer BioNTech vaccine confirms the finding of lower rates of all reactions when compared to a full dose in older children and young people.

During clinical trials, all boosters led to short-term local and systemic reactions, similar to those seen after the primary course, including local pain at the injection site, fatigue, headache and muscle pain. Rates of reactions were higher with heterologous than homologous boosters and in those aged under 70 years when compared to older recipients.

How do we know the COVID-19 Pfizer BioNTech vaccine is effective?

The immunogenicity of the Pfizer BioNTech COVID-19 vaccine has been evaluated in clinical trials in six countries: US, Germany, Brazil, Argentina, South Africa and Turkey. Over 44,000 individuals aged 12 years and above have taken part in clinical trials of this vaccine. Half of the participants received the COVID-19 vaccine and the other half received a placebo vaccine.

Results from the phase three clinical trials suggested the vaccine can prevent 95% of vaccinated adults from getting COVID-19 disease and that the vaccine works equally well in people of all ages, races and ethnicities. The observed efficacy in adults over 65 years of age was over 94%.

The trials among 5-11 year olds, using a 10 microgram dose, have shown equivalent antibody response and slightly lower reactogenicity than the full adult/adolescent dose (30 micrograms) in those aged 16-25 years.

How do we know the COVID-19 Vaccine Moderna is safe?

The safety of COVID-19 Vaccine Moderna was evaluated in ongoing phase 3 clinical trials in the United States involving 30,351 participants 18 years of age and older.

The most frequently reported adverse reactions were injection site pain (92%), fatigue (70%), headache (65%), myalgia (62%), arthralgia (46%), chills (46%), nausea/vomiting (23%), auxillary swelling/tenderness (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.

There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers.

How do we know the COVID-19 Vaccine Moderna is effective?

The immunogenicity of the COVID-19 Vaccine Moderna has been evaluated in clinical trials in the United States with over 30,000 participants. In phase 1 testing of the Moderna mRNA-1273 vaccine, all patients seroconverted to IgG after the first dose of vaccine. Phase 3 placebo controlled testing in participants, showed a vaccine efficacy of 94.1%. Efficacy was similar in those over 65 years. Vaccine efficacy against severe COVID-19 was 100%. The cumulative case numbers in the phase 3 study showed a clear divergence between the vaccine and placebo groups from about 14 days days after the first dose.

Novavax COVID-19 vaccine (Nuvaxovid)

This vaccine uses a recombinant S protein (grown in baculovirus infected insect cells) as an antigen with the Matrix-MTM adjuvant. The latter adjuvant includes two saponins derived from tree bark.

When mRNA vaccines are not considered clinically suitable, Novavax COVID-19 vaccine (Nuvaxovid) may used for vaccination of those aged 12 years and over, including to complete a course or as a booster. As there are relatively few indications for this vaccine in the current programme, supplies of Nuvaxovid are currently only available at a limited number of sites.

How do we know the Novavax COVID-19 vaccine (Nuvaxovid) is safe?

Side effects after the vaccine are similar to other COVID-19 vaccines, with slightly lower rates of local reactions and systemic effects when compared to mRNA vaccines. Around 50% of dose 1 and 70% of dose 2 recipients reporting pain and/or tenderness at the injection site and around 40-50% report systemic symptoms including fatigue, malaise, headache and muscle pain, with rates of fever below 10%. Overall, there was a higher incidence of adverse reactions in younger age group (18-64 years).

How do we know the Novavax COVID-19 vaccine (Nuvaxovid) is effective?

Large vaccine efficacy studies in the UK and the USA showed an efficacy of 90% against symptomatic infection with 100% against severe disease.

Sanofi Pasteur COVID-19 vaccine (VidPrevtyn Beta)

This vaccine uses a recombinant protein (grown in baculovirus infected insect cells, derived from Sf9 cells of the fall armyworm, Spodoptera frugiperda) as an antigen with the AS03 adjuvant. The adjuvant is composed of squalene, DL-α-tocopherol and polysorbate 80.

Squalene is an essential ingredient in the adjuvant system. Squalene is a naturally occurring molecule found in plants and animals, and commercially extracted from fish oil. Combined with surfactants and other immunostimulants, emulsions of squalene have been shown to enhance the immune response when added to antigens. The squalene used in VidPrevtyn Beta is extracted from shark liver oil.

How do we know the Sanofi Pasteur COVID-19 vaccine (VidPrevtyn Beta) is safe?

When given as a first booster in individuals previously vaccinated with mRNA or adenovirus vector vaccines the most common side effects were injection site pain (76.2%), headache (41.4%), myalgia (37.8%), malaise (33.0%), arthralgia (28.7%), and chills (19.9%). Most side effects were short lived (less than 3 days) and of mild to moderate severity.

How do we know the Sanofi Pasteur COVID-19 vaccine (VidPrevtyn Beta) is effective?

VidPrevtyn Beta had shown efficacy as a primary vaccine and was then studied as a booster in adults who had received primary vaccination with either mRNA or adenovirus vaccines. Although targeted against the Beta variant, 91 days after vaccination, a booster dose of Sanofi Pasteur COVID-19 vaccine (VidPrevtyn Beta®) achieved similar levels of pseudo neutralising antibody against the original, Beta, Delta, BA.1 and BA.4/5 strains as those seen after the Moderna and Pfizer bivalent vaccines targeting the BA.1 strain (Spikevax® bivalent Original/Omicron and Comirnaty® Original/Omicron BA.1).

Variant vaccines

Following the recognition of the Omicron variant becoming the dominant global circulating strain during 2022, many vaccine manufacturers rapidly developed second generation vaccines that may have broader coverage against SARS-CoV-2 variants. Those approved or approaching licensure have been developed as boosters and have either replaced the spike protein from the original vaccine strain with an Omicron BA.1 or BA. 4-5 strain, or developed a bivalent formulation containing the spike protein sequences from both the ancestral strain and an Omicron variant.

So far, the emergence of new variants has been too rapid to enable incorporation of a new strain in time to respond to any increase in disease. Rates of infection in the summer of 2022 were largely driven by infection with Omicron BA.4 and BA.5.

Those that use a well established platform, such as mRNA vaccines, are licensed on the basis of immunobridging ie by showing non-inferiority of the neutralising antibody response to the ancestral strain, with potentially higher neutralising antibody response to the variant strain.

The JCVI now advise that the preference for primary vaccination is to use the bivalent mRNA vaccines with the latest variant. Pfizer BioNTech have made submissions to the MHRA and EMA to have Comirnaty Original/Omicron BA4.5 regulated as a primary course vaccine, however this may not be approved in time for the completion of the spring booster programme, therefore in line with JCVI advice the Comirnaty Original/Omicron BA 4.5 vaccine can be used 'off label' as a primary course during the spring programme. Further details can be found at **www.health-ni.gov.uk/sites/default/files/publications/health/doh-hss-md-15-23.pdf**

Vaccines for children and young people

Currently, the Pfizer BioNTech (Comirnaty) vaccines are the only vaccines recommended to be given to children and young people less than 18 years of age. Although the Moderna (Spikevax) vaccine is also approved in children from 12 years, the Pfizer BioNTech (Comirnaty) vaccines are currently preferred due to a lower reported rate of myocarditis (see page 22). The Pfizer BioNTech (Comirnaty) 30 micrograms/dose vaccine should be given to eligible children and young people from 12 years. The Pfizer BioNTech Comirnaty 10 micrograms/dose vaccine should be given to eligible children aged 5 to 11 years. The Pfizer BioNTech Comirnaty 3 micrograms/dose vaccine should be given to eligible children aged 6 months to 4 years.

It is not recommended that the Comirnaty 30 micrograms/dose vaccine licensed for adults and adolescents from 12 years of age is used for children under 12 years other than in exceptional circumstances – for example, where the Comirnaty 10 micrograms/dose vaccine is not available when protection is required rapidly. In this situation, 10 micrograms (0.1ml) of the Comirnaty 30 micrograms/dose vaccine may be used as an alternative. However, the use of a fractional dose of the Comirnaty 30 micrograms/dose vaccine would be off-label and healthcare providers need to have the necessary skills to deliver such fractional doses, with appropriate guidance, training and systems in place to support vaccine delivery.

Children aged 5 to 11 years who are given a fractional dose of the 30 micrograms/dose vaccine may complete their primary course with the 10 micrograms/dose vaccine formulation or vice versa.

Children aged 5 to 11 years who commence immunisation with the 10 microgram dose of the Pfizer BioNTech (Comirnaty) vaccine and then turn 12 years of age should complete vaccination with the 10 microgram dose. The 30 microgram adult or adolescent dose is an acceptable alternative if this is the only vaccine available.

A bivalent Pfizer BioNtech COVID-19 vaccine may become available later in 2023 for use in children aged 5 to 11 years. The Comirnaty® Original/Omicron BA.4/5 (5/5 micrograms), is a bivalent vaccine targeting some of the latest variants, and may be used to boost eligible children when available in the UK. Children aged 4 years who are given a 3 microgram dose and then turn 5 years of age between their doses in the vaccination course, should complete the course with a 3 microgram dose.

Can a different vaccine be used for the 2nd dose?

Evidence suggests that those who receive mixed schedules, including mRNA and adenovirus vectored vaccines, make a good immune response, although rates of side effects with a heterologous second dose are higher. Accumulating evidence now supports the use of heterologous schedules for primary immunisation, and these are now recognised by the European Medicines Agency (EMA).

Individuals who do receive a different vaccine for their second dose should be informed that they may experience more reactions to the second dose.

For individuals who started the schedule and who attend for vaccination at a site where the same vaccine is not available, for example, if the individual received their first dose abroad, or where the first product received is unknown, one dose of the locally available product should be given to complete the primary course if suitable for age and not contraindicated. For information relating to individuals who received their COVID-19 vaccination overseas, please refer to UKHSA COVID-19 vaccination programme: Information for healthcare practitioners **https://www.gov.uk/government/publications/covid-19-vaccination-programme-guidance-for-healthcare-practitioners**

Can the vaccine be administered with other inactivated or live vaccines?

Initially data on co-adminstration of COVID-19 with other vaccines was limited. In the absence of such data, first principles would suggest that interference between inactivated vaccines with different antigenic content is likely to be limited. Based on experience with other vaccines, any potential interference is most likely to result in a slightly attenuated (weaker) immune response to one of the vaccines. There is no evidence of any safety concerns, although it may make the attribution of any adverse events more difficult. Similar considerations apply to coadministration of COVID-19 vaccines with live vaccines such as MMR. In particular, live vaccines that replicate in the mucosa, such as live attenuated influenza vaccine (LAIV) are unlikely to be seriously affected by giving COVID-19 vaccine at the same appointment.

As the COVID-19 vaccines are considered inactivated, where individuals in an eligible cohort present having recently received another inactivated or live vaccine, COVID-19 vaccination should still be given. The same applies for other live and inactivated vaccines where COVID-19 vaccination has been received first or where a patient presents requiring 2 vaccines. It is generally better for vaccination to proceed to avoid any further delay in protection and to avoid the risk of the patient not returning for a later appointment.

A UK study of co-administration of AstraZeneca and Pfizer BioNTech COVID-19 vaccines with inactivated influenza vaccines confirmed acceptable immunogenicity and reactogenicity. Although a study of co-administration of Novavax (Nuvaxovid) COVID-19 vaccine with inactivated influenza, did show some attenuation of the antibody response to COVID-19, co-administration was still associated with high efficacy against COVID-19 in the phase 3 study. A recent study has also shown an acceptable safety profile when COVID-19 is co-administered with inactivated shingles vaccine. Where co-administration does occur, patients should be informed about the likely timing of potential adverse events relating to each vaccine. If the vaccines are not given together, they can be administered at any interval, although separating the vaccines by a day or two will avoid confusion over systemic side effects.

Booster programme

To maintain high levels of protection against severe COVID-19 disease and specifically, hospitalisation and death through the winter 2021, the JCVI initially advised that booster vaccines be offered to those most at risk from serious disease, and who were vaccinated during Phase 1 of the vaccine programme.

However, after extending the booster dose offer to all aged 40 to 49 years, on 29 November 2021, in response to the emergence of the Omicron variant, the JCVI advised accelerating the booster programme and offering a booster dose to all adults aged from 18 years.

On 27 January 2023, the JCVI announced that the 2021 booster offer for individuals aged 16 to 49 years who are not in a clinical risk group should no longer be offered following the close of the autumn 2022 vaccination campaign (31/03/2023).

The autumn booster campaign 2022

The JCVI has recommended a move to regular, planned and targeted boosting as the most important strategy to control COVID-19. For the 2022 autumn booster programme, the primary objective was to augment immunity in those at higher risk from COVID-19 and thereby optimise protection against severe COVID-19, specifically hospitalisation and death, over winter 2022/23.

The following groups were offered a COVID-19 booster vaccine in the autumn of 2022:

- residents in a care home for older adults and staff working in care homes for older adults
- frontline health and social care workers
- all adults aged 50 years and over persons aged 5 to 49 years in a clinical risk group, (as set out in Tables 3 and 4 of the Green Book chapter)
- persons aged 5 to 49 years who are household contacts of people with immunosuppression (as defined in Tables 3 and 4)
- persons aged 16 to 49 years who are carers (as defined in Table 3).

The spring booster campaign 2023

On 7 March 2023, recognising the small decline in observed vaccine effectiveness against hospitalisation for COVID-19 after the booster dose, the JCVI recommended a spring booster campaign for individuals at higher risk of severe COVID-19. In order to sustain protection, the JCVI recommended that a booster dose should be given around six months after the last vaccine dose to:

- adults aged 75 years and over
- residents in a care home for older adults, and
- individuals aged 5 years and over who are immunosuppressed (refer to Tables 3 & 4 in the Green Book COVID-19 chapter for definitions of immunosuppressed)

The vast majority of people aged over 75 years should be reaching an interval of around six months from their last dose between late March and June 2023. Operational flexibility is permitted to offer the booster to eligible individuals expected to reach the target age during the spring campaign. Boosters should be offered around six months from the previous dose, but can be given three months from the previous dose; this may be particularly important to facilitate delivery of the programme to residents in care homes and the housebound. For individuals who may have received a second or third primary dose more recently, a booster can be offered during the spring campaign provided there is at least three months from the previous dose - additional doses are not then generally required until they become eligible during the next seasonal campaign.

Further information about the booster programmes is available in the JCVI statements and also in the COVID-19 chapter of the Green Book.

Vaccine to be used for booster doses

The JCVI have advised that the following vaccines are suitable for boosting irrespective of the vaccine used for the primary course:

Eligible adults aged 75 years or over (including residents aged over 65 years in care homes for the elderly)

- A full 0.3ml dose of bivalent (15/15 micrograms) Pfizer BioNTech vaccine (Comirnaty® Original/ Omicron BA.4/5 or BA.1)
- A full 0.5ml booster dose of the bivalent (25/25 micrograms) of the bivalent Moderna COVID-19 vaccine (Spikevax® bivalent Original/Omicron BA.4/5 or BA.1)
- A full 0.5ml dose of the Sanofi Pasteur COVID-19 vaccine (VidPrevtyn Beta®)

Adults aged 18 to 74 (including pregnant women)

- A full 0.3ml dose of bivalent (15/15 micrograms) Pfizer BioNTech vaccine (Comirnaty® Original/ Omicron BA.4/5 or BA.1)
- A full 0.5ml booster dose of the bivalent (25/25 micrograms) of the bivalent Moderna COVID-19 vaccine (Spikevax® bivalent Original/Omicron BA.4/5 or BA.1)

As part of operational flexibility, eligible individuals aged 65 to 74 years may also receive Sanofi Pasteur COVID-19 vaccine (VidPrevtyn Beta®) where it would simplify delivery in that setting. This includes vaccination in domiciliary settings.

When mRNA vaccines are not considered clinically suitable, Novavax COVID-19 vaccine (Nuvaxovid®) may used for boosting across this age group. For those aged 65-74 years Sanofi Pasteur COVID-19 vaccine (VidPrevtyn Beta®) is also a suitable alternative.

Children and young adults aged 12 to 17 years (including during pregnancy)

- A full 0.3ml dose of bivalent (15/15 micrograms) Pfizer BioNTech vaccine (Comirnaty® Original/ Omicron BA.4/5 or BA.1)

When mRNA vaccines are not considered clinically suitable, Novavax COVID-19 vaccine (Nuvaxovid®) may used for boosting across this age group.

Children aged 5 to 11 years

- A full 0.2ml dose (10 micrograms) of paediatric Pfizer-BioNTech vaccine (Comirnaty 10 micrograms/ dose)
- A full 0.2ml dose (5+5 micrograms) of paediatric Pfizer-BioNTech vaccine Comirnaty® Original/Omicron BA.4/5 (if available)

Future COVID-19 vaccination programmes

The UK COVID-19 pandemic vaccine programme was initiated in December 2020 with the primary objective to prevent severe disease, hospitalisations, and deaths. Now that the vast majority of the UK adult population have been vaccinated and seroprevalence studies indicate that most of the adult and childhood population have been naturally infected, the UK COVID-19 vaccination programme is expected to transition during 2023 towards a longer-term more sustainable programme.

Evidence is becoming clear that all the current vaccines provide only modest and short-term protection against infection and therefore against transmission. Protection against mild symptomatic disease is moderate but also only sustained over the short-term. With the newly emerged variants lower levels of protection against mild disease have been seen, declining to negligible levels within four to six months of primary vaccination and three to four months after booster doses. Protection against more severe forms of disease and death appears to be higher and maintained over the medium term.

From the end of the spring 2023 campaign, primary course COVID-19 vaccination will become a targeted offer only to those at higher risk of severe COVID-19. After that, the offer is expected to be limited to adults over 50 years and those aged 5 to 49 years in a clinical risk group. The primary offer will only be available to eligible individuals during the planned seasonal booster campaigns.

Otherwise healthy persons aged 5 to 49 years who develop a new health condition that places them in a clinical risk group would normally become eligible for primary vaccination when they would also become eligible for booster vaccination during a subsequent seasonal campaign or any surge response.

Inadvertent vaccine administration errors

Does the vaccine dose need to be repeated if only the diluent is administered?

The diluent for the Pfizer BioNTech COVID-19 vaccines (Comirnaty 30 micrograms/dose and Comirnaty 10 micrograms/dose) is sodium chloride, which is purified water with a very small amount of salt in it. This diluent is commonly used to dilute other medicines and no adverse reactions would be expected if it was inadvertently administered alone. However, the diluent alone will not evoke an immune response so the person should be given a dose of properly reconstituted Pfizer BioNTech (Comirnaty) COVID-19 vaccine as soon as the error is realised.

What should you do if you inadvertently administer the whole multi-dose vial of vaccine instead of the recommended dose?

In a Phase I/II study of COVID-19 mRNA vaccines in adults, different strength doses of Pfizer BioNTech COVID-19 vaccine were given. The trial showed that a stronger dose (100 micrograms instead of the recommended 30 microgram dose) was not harmful but the recipients experienced more local reactions with very painful arms being reported. Participants who received 58 micrograms of COVID-19 mRNA vaccine in clinical trials did not report an increase in reactogenicity or adverse events. The Moderna vaccine has also been given at higher dose levels in clinical trials than the dose recommended in the UK vaccination programme.

If a person is given more than the recommended dose, they should be reassured that this is not harmful but that they may be more likely to experience pain in their injected arm. Any subsequent doses due should still be given as per the recommended schedule.

What should you do if you inadvertently administer an incomplete dose of vaccine or a dose that may have been affected by a storage or preparation error?

If less than the full dose of COVID-19 vaccine is inadvertently given, for example, if some vaccine leaks out as it is being administered or if the vaccine has been over-diluted, a risk assessment should be carried out to determine whether it is necessary to repeat the dose. Trial data for the Pfizer BioNTech and Moderna vaccines showed a good immune response was made to a lower dose of the vaccine than the recommended authorised dose, particularly in younger age groups and as a booster. This risk assessment is recommended because of the increased reactogenicity and the risk of myocarditis and pericarditis following mRNA re-vaccination, notably in younger age groups, which should be weighed against the risk of a lower immune response to the vaccine.

Where the risk of under-dosing is considered substantial, it is recommended that a full additional recommended dose should be given immediately. If the error is only realised after the individual leaves the vaccination clinic, it is recommended that the repeat dose should be offered from 48 hours after the possible partial dose was given. The 48 hour wait period is to allow for any reactions experienced following the incomplete dose to resolve before the repeat dose is given. It is recommended that the repeat dose should be given within 7 days of the incomplete dose to minimise the time the individual may be left susceptible to infection. If more than 7 days have elapsed, a further risk assessment will be required to decide on the optimal timing for a repeat dose, considering the individual risk and epidemiological context.

If the dose is repeated, the recipient should be advised of possible side effects and if this was the first primary dose, the 'second' dose of the 2 dose primary schedule (which will actually be the third dose in this case) should still be given at the recommended interval from the additional dose. If this was the second primary dose, the booster dose should still be given at the recommended interval (at least 3 months) from the additional dose.

If a dose of COVID-19 vaccine is given following an incident in which the potency may have been affected, for example by a storage or preparation error, seek expert advice from the local health protection team (Duty Room 0300 555 0119) and if recommended repeat the dose of vaccine. This should either be given on the same day as the potentially affected dose was given, or from 48 hours after the potentially affected dose was given.

What should you do if the second dose is given at less than the minimum recommended interval?

If the second dose of the Pfizer BioNTech (Comirnaty) vaccine is given less than 19 days after the first dose, the dose should be discounted and another dose (a third dose) should be given at least 21 days after the dose given too early. The 19 day interval is the minimum interval that was used in the clinical trials.

If the second dose of the Moderna (Spikevax) COVID-19 vaccine is given at less than the recommended 28 day interval, but at least 21 days after the first dose, it does not need to be repeated. If the second dose is given less than 21 days after the first, it should be discounted and another dose (a third dose) should be given at least 28 days after the dose given too early.

What should you do if longer than recommended interval is left between doses?

If an interval longer than the recommended interval is left between doses, the second dose should still be given (preferably using the same vaccine as was given for the first dose if possible). The course does not need to be restarted.

What if a different COVID-19 vaccine is given inadvertently for second dose than was given for first dose?

Evidence suggests that those who receive mixed schedules, including mRNA and adenovirus vectored vaccines, make a good immune response, although rates of side effects at the second dose are higher. Accumulating evidence now supports the use of heterologous schedules for primary immunisation, and these are now recognised by the European Medicines Agency (EMA). Reactogenicity and safety data from the Com-COV clinical trial showed that mixed schedule recipients were more likely to experience feverishness, chills, fatigue, headache, joint pain, malaise, and muscle ache. Therefore, if an individual is inadvertently given a different vaccine for their second dose than for their first dose, they should be informed that they may experience more side effects than they did following their first dose, but that a further dose is not required.

What if a different COVID-19 vaccine is inadvertently given at a short interval after the first dose?

If a dose of a different COVID-19 vaccine is inadvertently given a few days after the first dose was given, the person should be offered a third dose of vaccine at the currently recommended interval for second doses (8 weeks from when the second dose was given).

If different COVID-19 vaccines are given a minimum of 21 days apart, these doses should be counted as a completed course and no further doses are needed.

Inadvertent administration of 10 microgram dose of Pfizer BioNTech (Comirnaty) vaccine instead of the recommended 30 microgram dose to those 12 years and over

If a young person aged 12 to 15 years is inadvertently given a 10 microgram dose of the Pfizer BioNTech (Comirnaty) vaccine instead of the recommended 30 microgram dose, this dose can still be counted as a valid dose and does not need to be repeated.

If this was the first dose, children aged 12 years should complete their primary vaccination course with the 10 microgram dose (although the 30 microgram dose is an acceptable alternative if this is the only vaccine available). Those aged 13 to 15 years should be given the 30 microgram dose for their second dose.

Moderna (Spikevax) vaccine given in error to child or young person under 18 years

Although the Moderna (Spikevax) vaccine has been approved for use in children from 12 years of age, the Pfizer BioNTech (Comirnaty) vaccine is currently preferred due to a lower reported rate of myocarditis (see page 22).

If a child or young person under 18 years of age receives a dose of Moderna (Spikevax) vaccine in error, they should complete the course with the Pfizer BioNTech (Comirnaty) vaccine.

Half dose of Moderna vaccine given as third dose to an immunosuppressed individual in error

It is recommended that individuals who were immunosuppressed at or around the time they received their first or second primary dose should be offered a third primary dose of vaccine at least 8 weeks after their second dose and that, preferably, the Pfizer BioNTech (Comirnaty) vaccine or a full dose of the Moderna (Spikevax) vaccine should be given for this third dose.

However, if a half dose of Moderna (Spikevax) vaccine is inadvertently given to an immunosuppressed individual in error, the dose does not need to be repeated as it is expected that a half dose will still produce a good immune response and is expected to be equivalent to that of a full dose of Pfizer BioNTech (Comirnaty).

COVID-19 vaccine contraindications

COVID-19 vaccine should not be given to those who have had a previous systemic allergic reaction (including immediate-onset anaphylaxis) to:

- a previous dose of the same COVID-19 vaccine
- any components of the vaccine.

The COVID-19 chapter of the Green Book also provides full details about the contraindications to COVID-19 vaccine. Where there is any doubt as to whether the vaccine can be given, appropriate advice should be sought from the relevant specialist in the first instance.

A very small number of individuals have experienced anaphylaxis when vaccinated with the Pfizer-BioNTech (Comirnaty) vaccine and anaphylaxis events have also been reported after the Moderna (Spikevax) vaccine. Following close national surveillance, the MHRA is no longer advising that individuals with a history of anaphylaxis to any vaccine, medicine or food do not get the vaccine. Anyone with a previous history of allergic reactions to the ingredients of the vaccine should not receive it, but those with any other allergies (such as a food allergy) can now have the vaccine. Please refer to the Green Book COVID-19 vaccine chapter for management of individuals with a history of allergy.

Information for Healthcare Professionals on Pfizer/ BioNTech (Comirnaty) COVID-19 Vaccine for full list of excipients) **https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty#product-information-section**

Product information for COVID-19 Vaccine Novavax (Nuvaxovid) is in Information for Healthcare Professionals on **https://www.ema.europa.eu/en/medicines/human/EPAR/nuvaxovid**

Product information for the COVID-19 Vaccine Moderna (Spikevax) at **https://www.ema.europa.eu/en/medicines/human/EPAR/spikevax**

Product information for COVID-19 vaccine Sanofi Pasteur (VidPrevtyn) at **https://www.ema.europa.eu/en/documents/product-information/vidprevtyn-beta-epar-product-information_en.pdf**

Polyethylene glycol (PEG)

The Pfizer-BioNTech (Comirnaty) and Moderna (Spikevax) mRNA vaccines contain polyethylene glycol (PEG). PEGs (also known as macrogols) are a group of known allergens commonly found in medicines, many household products and cosmetics. Medicines containing PEG include some tablets, laxatives, depot steroid injections, and some bowel preparations used for colonoscopy. Evidence now shows that PEG allergy is implicated in only a minority of allergic reactions reported after COVID-19 vaccines. Furthermore, published data show that some individuals with prior allergic reaction to PEG-containing medicines (eg PEG-asparaginase) can tolerate the Pfizer BioNTech (Comirnaty) vaccine (although the historical reaction may have been due to a non-PEG component). Expert advice should be obtained and if a decision is made to administer an mRNA vaccine, then this should only be done in hospital under medical supervision.

Polysorbate 80

The COVID-19 vaccines Novavax (Nuvaxovid) and Sanofi Pasteur (VidPrevtyn) do not contain PEG but do contain a related compound called polysorbate 80. Some people with PEG allergy may also be allergic to polysorbate 80.

However, polysorbate 80 is widely used in medicines and foods, and is present in many medicines including monoclonal antibody preparations. Some injected influenza vaccines (including the main vaccine used in over 65 year olds) contain polysorbate 80. Individuals who have tolerated injections that contain polysorbate 80 (such as certain influenza vaccines) are likely to tolerate the Novavax (Nuvaxovid) and Sanofi Pasteur (VidPrevtyn) vaccines. The Sanofi Pasteur (VidPrevtyn Beta) vaccine contains polysorbate 80 at a higher level than influenza vaccines, as well as small amounts of polysorbate 20 (a similar compound). Despite very limited experience with this vaccine, it is unlikely that individuals with an allergy to PEG would react to the Sanofi Pasteur (VidPrevtyn Beta) vaccine, particularly if they have tolerated a previous influenza vaccine and/or an AstraZeneca or Novavax (Nuvaxovid) vaccine. Please see table 5 in the Green Book COVID-19 vaccine chapter.

Capillary Leak Syndrome

A small number of cases of capillary leak syndrome have been reported following vaccination with the Moderna (Spikevax) vaccine.

Capillary leak syndrome causes fluid and proteins to leak out of the capillaries into surrounding tissues. This may lead to very low blood pressure, low blood albumin levels and thickened blood due to a decrease in plasma volume. Initial symptoms may include tiredness, nausea, abdominal pain, extreme thirst and sudden increase in body weight. Complications can include general swelling, compartment syndrome, kidney failure and stroke.

Individuals with a history of capillary leak syndrome should be carefully counselled about the risks and benefits of vaccination and advice from a specialist should be sought.

Precautions to COVID-19 vaccines

Other precautions

It is recommended that individuals are observed for a minimum of 15 minutes following administration of COVID-19 vaccines. However, in recognition of the need to accelerate delivery of the programme in response to the emergence of the Omicron variant, the UK Chief Medical Officers have recommended suspension of this requirement. This suspension in individuals without a history of allergy, has also been agreed by the Commission on Human Medicines. **https://www.health-ni.gov.uk/sites/default/files/publications/health/doh-hss-md-21-2022.pdf**

As fainting can occur following vaccination, all those vaccinated with any of the COVID-19 vaccines should either be driven by someone else or should not drive for 15 minutes after vaccination.

Following COVID-19 vaccine administration, vaccinated individuals should be observed for any immediate reactions whilst they are receiving any verbal post vaccination information. Vaccinated individuals should be informed about how to access immediate healthcare advice if they require it following vaccination.

Patients with undiagnosed PEG allergy often have a history of immediate onset-unexplained anaphylaxis or anaphylaxis to multiple classes of drugs or an unexplained anaphylaxis. Such individuals should not be vaccinated with the Pfizer-BioNTech (Comirnaty) or Moderna (Spikevax) vaccine, except on the expert advice of an allergy specialist. A non-mRNA vaccine, such as Novavax (Nuvaxovid), can be used as an alternative (unless otherwise contraindicated), particularly if they previously tolerated an injected influenza vaccine. The vaccine should be administered in a setting with full resuscitation facilities (eg a hospital), and a 30 minute observation period is recommended.

The British Society for Allergy and Clinical Immunology (BSACI) has advised that individuals who have

a reaction to the first dose of a COVID-19 vaccine may be able to receive a 2nd dose of vaccine. Please see the flowchart for managing patients who have allergic reactions to the first dose of COVID-19 vaccine in the Green Book COVID-19 vaccine chapter for further information.

Individuals with non-allergic reactions (vasovagal episodes, non-urticarial skin reaction or non-specific symptoms) to the first dose of a COVID-19 vaccine can receive the second dose of vaccine in any vaccination setting. Observation for 15 minutes is recommended.

Further information can be found on the link to website, **https://www.resus.org.uk/** RCUK publishes, including hypersensitivity to the active substance or to any of the excipients, anaphylaxis guidance for vaccination settings.

Myocarditis and pericarditis

Cases of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the pericardium) have been reported in people who have received COVID-19 vaccine. The reported rate appears to be highest in those under 25 years of age and in males, and after the second dose. Onset is within a few days of vaccination and most cases are mild, recovering within a short time following standard treatment and rest without any sequalae.

Vaccinated individuals should be advised to seek immediate medical attention should they experience new onset of chest pain, shortness of breath, palpitations or arrhythmias. Those who develop myocarditis or pericarditis following the first COVID-19 vaccination should be assessed by an appropriate clinician to determine whether it is likely to be vaccine related. Subsequent doses should be deferred until further information becomes available.

Further detailed information for healthcare professionals on myocarditis and pericarditis following COVID-19 vaccination is also available: **https://www.gov.uk/government/publications/covid-19-vaccination-myocarditis-and-pericarditis-information-for-healthcare-professionals/information-for-healthcare-professionals-on-myocarditis-and-pericarditis-following-covid-19-vaccination**

Guillain-Barré syndrome (GBS)

Very rare reports have been received of Guillain-Barré syndrome (GBS) following COVID-19 vaccination, so healthcare professionals should be alert to the signs and symptoms of GBS to ensure correct diagnosis, in order to initiate adequate supportive care and treatment and to rule out other causes. Guillain-Barré syndrome is a very rare and serious condition that affects the nerves. It mainly affects the feet, hands and limbs, causing problems such as numbness, weakness and pain. In severe cases, GBS can cause difficulty moving, walking, breathing and or swallowing.

Individuals who have a history of GBS should be vaccinated as recommended for their age and underlying risk status.

In those who are diagnosed with GBS after the first dose of vaccine, the balance of risk benefit is in favour of completing a full COVID-19 vaccination schedule. Where GBS occurs following either of the mRNA vaccines (Pfizer BioNTech or Moderna), further vaccination can proceed as normal, once recovered. Further information can be found in the COVID-19 chapter of the Green Book.

Immune thrombocytopenia (ITP)

Immune thrombocytopenia (ITP) is a condition where the immune system does not function correctly and attacks and destroys platelets in the blood. Platelets help the blood to clot so this can lead to bruising and bleeding.

There is now emerging evidence of a small risk of ITP or ITP relapse following COVID-19 vaccination. To date, this has been reported extremely rarely and the MHRA Yellow card summary states that this is usually short-lived and of minor severity.

Previous ITP is not a contraindication for vaccination but guidance produced by the UK ITP Forum Working Party advises discussing the potential for a fall in platelet count in patients with a history of ITP receiving any COVID-19 vaccine and recommends a platelet count check 2 to 5 days after vaccination (British Society for Haematology COVID-19 updates: **https://b-s-h.org.uk/about-us/news/COVID-19-updates/**

Heavy menstrual bleeding

Since the widespread use of the Pfizer BioNTech (Comirnaty) and Moderna (Spikevax) COVID-19 vaccines post marketing, a number of conditions have been reported after vaccination and have been or are about to be added to the Summary of Product Characteristics (SmPC). This includes reports of heavy menstrual bleeding (in most cases temporary and non-serious). The MHRA and the independent experts of the Commission on Human Medicines (CHM) have conducted investigations, and the rigorous evaluation completed to date does not support a link between COVID-19 and other changes to menstrual periods.

There is no evidence to suggest that COVID-19 vaccines will affect fertility or the ability to have children.

Additional advice for recipients

Vaccine recipients should also be advised that it may take a few weeks for protection from their COVID-19 vaccination to develop and that they should continue to follow advice current at the time regarding reducing the risk of infection.

As no vaccine is completely effective, some people may still become infected with coronavirus despite having been vaccinated (although this should be less severe). The vaccine cannot cause COVID-19 infection.

Postponing immunisation

Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation. If an individual is acutely unwell, immunisation may be postponed until they have fully recovered. This is to avoid confusing the differential diagnosis of any acute illness (including COVID-19) by wrongly attributing any signs or symptoms of the illness as being possible reactions to the vaccine.

Useful links

Northern Ireland COVID-19 Vaccination Programme:
https://www.publichealth.hscni.net/covid-19-coronavirus/northern-ireland-covid-19-vaccination-programme

Green Book COVID-19 chapter:
www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a

UK Health Security Agency Coronavirus resources:
https://www.gov.uk/government/collections/covid-19-vaccination-programme

GOV.UK Coronavirus (COVID-19) in the UK: **https://coronavirus.data.gov.uk/**

WHO COVID-19 Worldwide Dashboard:
https://covid19.who.int/?gclid=EAIaIQobChMInr6P36Dc7AIVBWHmCh3IswIXEAAYASAAEgIPT_D_BwE

LSHTM COVID-19 vaccine tracker: **https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/**

Royal College of Nursing - COVID-19 vaccination page:
www.rcn.org.uk/clinical-topics/public-health/immunisation/covid-19-vaccination

Product information for the COVID-19 Vaccine Pfizer BioNTech (Comirnaty):
https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf

Liu, X, Shaw, RH, Stuart, ASV and others. Safety and Immunogenicity Report from the Com-COV Study – a Single-Blind Randomised Non-Inferiority Trial Comparing Heterologous And Homologous Prime-Boost Schedules with An Adenoviral Vectored and mRNA COVID-19 Vaccine. Available at SSRN:
https://ssrn.com/abstract=3874014 or **http://dx.doi.org/10.2139/ssrn.3874014**

Shaw, RH and others. Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data. Lancet 2021 May 12: **https://doi.org/10.1016/S0140-6736(21)01115-6**

Product information for the COVID-19 Vaccine AstraZeneca (Vaxzevria):
https://www.ema.europa.eu/en/documents/product-information/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-product-information_en.pdf

Product information for the COVID-19 Vaccine Moderna (Spikevax):
https://www.ema.europa.eu/en/documents/product-information/spikevax-previously-covid-19-vaccine-moderna-epar-product-information_en.pdf

Product information for the COVID-19 Vaccine Novavax (Nuvaxovid):
https://www.ema.europa.eu/en/documents/product-information/nuvaxovid-epar-product-information_en.pdf

Product information for the COVID-19 Vaccine Sanofi Pasteur (VidPrevtyn):
https://www.ema.europa.eu/en/documents/product-information/vidprevtyn-beta-epar-product-information_en.pdf

British Society of Immunology, A guide for COVID-19 vaccinations:
https://www.immunology.org/public-information/guide-vaccinations-for-covid-19

MHRA weekly summary of Yellow Card reports:
https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions

Vaccination, helping to protect those most vulnerable.

If you need more information on the COVID-19 vaccination please visit: www.nidirect.gov.uk/covid-vaccine

HSC Public Health Agency

Public Health Agency
12-22 Linenhall Street, Belfast BT2 8BS.
Tel: 0300 555 0114 (local rate).
www.publichealth.hscni.net

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