Public Health England

Protecting and improving the nation's health

COVID-19 vaccination programme

Information for healthcare practitioners

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About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-leading science, research, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health and Social Care, and a distinct delivery organisation with operational autonomy. We provide government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

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Document information

This document was originally published provisionally, ahead of authorisation of any COVID-19 vaccine in the UK, to provide information to those who will be involved in the COVID-19 national vaccination programme expected to start in December 2020.

Following authorisation for temporary supply by the UK Department of Health and Social Care and the Medicines & Healthcare products Regulatory Agency being given to the COVID-19 mRNA Vaccine BNT162b2 (Pfizer-BioNTech) on 2 December 2020, this document has been updated to provide specific information about the storage and preparation of this vaccine**.**

Information about any other COVID-19 vaccines which are given regulatory approval will be added when this occurs.

The information in this document was correct at time of publication. As COVID is an evolving disease, much is still being learned about both the disease and the vaccines which have been developed to prevent it. For this reason, **some 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.

Document revision information

Version number	Details	Date
1.0	Document created	27 November 2020
2.0	Vaccine specific information about the COVID-19 mRNA Vaccine BNT162b2 (Pfizer-BioNTech) added	4 December 2020
2.1	Additional section added on timing of administration of COVID-19 vaccine to individuals who are immunosuppressed New guidance added on not giving COVID-19 mRNA Vaccine BNT162b2 to those with a history of anaphylaxis to a vaccine, medicine or food Some amendments to the COVID-19 mRNA Vaccine BNT162b2 storage and reconstitution section following republication of updated Information for Healthcare Professionals on Pfizer/BioNTech COVID-19 vaccine document	11 December 2020

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Background

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.

On 30 January 2020, the WHO Emergency Committee agreed that the outbreak met the criteria for a Public Health Emergency of International Concern and on 11 March 2020, the WHO declared COVID-19 as a pandemic.

The Coronavirus (COVID-19) in the UK dashboard shows the UK summary of the daily number of cases and deaths from COVID-19. The dashboard also shows the number of virus tests processed daily and healthcare figures including the daily number of patients admitted to hospital, patients in hospital and patients in ventilator beds.

Further information on COVID-19 disease, epidemiology, the vaccination programme and vaccine efficacy can be found in the Green Book COVID-19 chapter.

Further information on vaccine eligibility is described in the JCVI advice, Green Book chapter and will be included in the PHE COVID-19 PGD and Protocol once available.

Patient information leaflets and resources can be ordered from the Health Publications website

COVID-19 disease

Clinical symptoms

COVID-19 is an emerging disease and complications can be severe and fatal, particularly for those in risk groups.

Asymptomatic infection has been reported but those who do develop symptoms report a range of symptoms which include fever, a new and continuous cough, shortness of breath, fatigue, loss of appetite, anosmia (loss of smell) and ageusia (loss of taste). 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.

Evidence is growing that the longer-term consequences of more severe complications associated with the inflammatory response may be considerable in those who experience critical and life-threatening illness. Rare neurological and psychiatric complications, which can also occur in patients without respiratory symptoms, include stroke, meningo-encephalitis, delirium, encephalopathy, anxiety, depression and sleep disturbances.

Fewer than 5% of SARS-CoV-2 infection cases are amongst children and in general they appear to experience milder symptoms than adults. Further evidence is needed about the association between underlying conditions and risk of COVID-19 disease in children. A rare presentation of multisystem inflammatory syndrome temporarily associated with COVID-19 in children and adolescents has been noted.

Transmission

SARS-CoV-2 virus is primarily transmitted between people through respiratory droplets 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.

Groups affected by COVID-19

Increasing age and male gender are thought to be significant risk factors for severe disease and infection fatality ratios are highest in the oldest age groups. Co-morbidities 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[1]. Further information on high risk groups (those who are clinically extremely vulnerable) and moderate risk groups (those who are clinically vulnerable) can be found on the NHS.UK webpage: Who's at higher risk from coronavirus (COVID-19). Deprivation and being from a black, ethnic and minority group also results in an increased risk of death from COVID-19. 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.

[1] Williamson EJ, Walker AJ et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature 2020 July 8. 584:430–436 https://doi.org/10.1038/s41586-020-2521-4

COVID-19 vaccination programme

Aim of the 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.

Vaccine history and development

Over 270 different COVID-19 vaccines are in various stages of development. Some have been made using currently used 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.

For more information about COVID-19 vaccines in development, see the LSHTM COVID-19 vaccine tracker.

This document will discuss the first COVID-19 vaccine to be authorised for supply in the UK and another vaccine which is has been submitted to the MHRA for review for authorisation. The guidance will be updated as more information about these vaccines become available and will include other vaccines as they become available for use. **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.**

Duration of protection

As COVID-19 vaccines have only been given in clinical trials in recent months, there is currently no data available to describe how long protection from vaccination will last. Post-authorisation surveillance and continued follow-up of trial participants may indicate the need for booster doses but they are not currently recommended.

COVID-19 vaccination eligibility

Vaccine priority groups – provisional list

The objectives of the COVID immunisation programme is 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 with advice to support the development of a vaccine strategy. See **Joint Committee on Vaccination and Immunisation: advice on priority groups for COVID-19 vaccination 2 December 2020.**

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.

Pregnant women

Although the currently available data do not indicate any safety concerns or harm to pregnancy, there is currently insufficient evidence to recommend the use of COVID-19 vaccines during pregnancy. Given the lack of evidence, it is recommended that COVID-19 vaccine is not given in pregnancy and women should be advised not to attend for vaccination if they are, or may be pregnant, or are planning a pregnancy within three months of the first dose.

Vaccinated women who are not pregnant should be advised to avoid becoming pregnant for two months after the second dose of vaccine.

If a woman finds out she is pregnant after she has started a course of vaccine, she should complete her pregnancy before finishing the recommended schedule. Termination of pregnancy following inadvertent immunisation should **not** be recommended. Surveillance of inadvertent administration in pregnancy is being conducted by the PHE Immunisation Department, to whom such cases should be reported (www.gov.uk/guidance/vaccination-in-pregnancy-vip).

Until more information is available, it is also recommended that women who are breastfeeding should not be vaccinated until they have finished breastfeeding.

Children

SARS-CoV-2 vaccine trials have only just begun in children and therefore, there are, very limited data on safety and immunogenicity in this group. Children and young people have a very low risk of COVID-19, severe disease or death due to SARS-CoV-2 compared to adults and so COVID-19 vaccines are not routinely recommended for children and young people under 16 years of age.

There are currently very limited data on clinical risk factors in childhood, but children with neurological comorbidities are over-represented in those who develop severe COVID-19 requiring intensive care and those who die of COVID-19. Given the increased risk of exposure to infection and outbreaks in institutional settings, vaccination may be considered for children with serious neuro-disabilities (including cerebral palsy, severe autism and Down's syndrome) who spend regular time in institutional settings. As there are limited data on the use of COVID-19 vaccines in children, vaccination should be mainly restricted to older children (for example, those aged 12 years and older), who have higher risk of acquiring and becoming sick from infection.

Recommendations on vaccinating children with other underlying conditions will be reviewed after the initial roll-out phase by which time additional data on use of the vaccines in adults should allow a better assessment of risks and benefits.

Immunosuppression and HIV

Individuals who have immunosuppression and HIV infection (regardless of CD4 count) should be given COVID vaccine in accordance with the recommendations and contraindications stated in the PGD or Protocol and 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.

COVID-19 vaccines

In the UK, two COVID-19 vaccines are expected to be used first following regulatory approval for supply within the UK national vaccination programme. One vaccine, the COVID-19 mRNA Vaccine BNT162b2 (manufactured by Pfizer-BioNTech) was given authorisation for temporary supply by the MHRA on 2 December 2020. The other vaccine, manufactured by AstraZeneca is currently under review for authorisation by the MHRA. Information about any other COVID-19 vaccines which are given regulatory approval will be added when this occurs.

The COVID-19 mRNA Vaccine BNT162b2 uses an mRNA platform and the AstraZeneca COVID-19 vaccine is an adenovirus vector vaccine.

Both vaccines are presented in multi-dose vials and require completion of a two-dose course. Using multi-dose vials can improve the efficiency of vaccine manufacture and distribution, enabling vaccine availability for those eligible at the earliest opportunity.

COVID-19 mRNA Vaccine BNT162b2 (Pfizer-BioNTech)

The COVID-19 mRNA Vaccine BNT162b2 is an mRNA (messenger ribonucleic acid) vaccine. It contains 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.

As there is no whole or live virus involved, the vaccine cannot cause disease. The mRNA naturally degrades after a few days.

Clinical trials

The safety and immunogenicity of the COVID-19 mRNA Vaccine BNT162b2 has been evaluated in clinical trials in six countries: US, Germany, Brazil, Argentina, South Africa and Turkey.

Over 44 000 participants have taken part in the 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 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%.

AstraZeneca COVID-19 vaccine

AstraZeneca COVID-19 vaccine is a viral vector vaccine which uses a weakened adenovirus as a carrier to deliver the SARS-CoV-2 antigen. The adenovirus has been modified so that it cannot replicate (grow and multiply by making copies of itself) in human cells and therefore cause any disease.

The genes that encode for the spike protein on the SARS-CoV-2 virus have been inserted into the adenovirus's genetic code to make the vaccine. When the vaccine is injected, it enters the host's cells which then manufacture the spike protein. This then stimulates the immune system which reacts by producing antibodies and memory cells to the SARS-CoV-2 virus without causing disease.

Clinical trials

Trials of the AstraZeneca COVID-19 vaccine showed that it produced neutralising antibodies in Rhesus macaques as well as a reducing the amount of detectable virus in the lower respiratory tract following challenge with SARS-CoV-2[2]. In human trials, the vaccine was compared with a placebo vaccine in healthy adults aged between 18-55 years. Preliminary findings show that neutralising antibodies were induced after the first vaccination and that levels of these increased after a second dose. Specific T cell responses were also induced after a single immunisation and were maintained after the second dose. Data showed that spike antibody responses and neutralising antibody 28 days after the second dose were similar across the three age cohorts (18–55 years, 56–69 years, and ≥70 years). More than 99% of the participants had neutralising antibody responses two weeks after the booster dose. Peak T-cell responses were seen 14 days after the first dose and were broadly equivalent in the three age groups[3].

Further clinical trial data for both of these vaccines will be added when this becomes available.

Interchangeability of different COVID-19 vaccines

There is no evidence as to the interchangeability of the different COVID-19 vaccines although studies are underway. Therefore, every effort should be made to determine which vaccine the individual received and to complete with the same vaccine.

For individuals who started the schedule and who attend for vaccination at a site where the same vaccine is not available, or where the first product received is unknown, it is reasonable to offer a single dose of the locally available product. This option is preferred

[2] Van Doremalen, N et al. ChAdOx1 nCoV-19 vaccination prevents SARS-CoV-2 pneumonia in rhesus macaques. Nature 2020 July 30. 586: 578–582 https://doi.org/10.1038/s41586-020-2608-y
[3] Ramasamy M et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. Lancet 2020 Nov18. https://doi.org/10.1016/S0140-6736(20)32466-1

if that individual is likely to be at immediate high risk or is considered unlikely to attend again. In these circumstances, as both the Pfizer-BioNTech and AstraZeneca vaccines are based on the spike protein of the virus, it is likely that the second dose will help to boost the response to the first dose. Further doses of vaccine are not required unless additional information becomes available.

Administration of COVID-19 vaccine

Infection prevention and control

All those attending for vaccination and those delivering vaccination should wear appropriate personal protective equipment (PPE) as described in the infection prevention and control (IPC) advice current at the time of administering the vaccine.

Hand hygiene is critical to prevent the spread of disease and hands should be cleaned with alcohol-based gel or soap and water before vaccine preparation, between patients, etc. Those preparing and administering the vaccine should maintain good hand hygiene throughout and should take care not to touch the vial bung with their fingers.

Injection technique

COVID-19 vaccines should be administered by intramuscular (IM) injection into the deltoid muscle of the upper arm.

Individuals who have minimal muscle mass in the deltoid area of the upper arm, or a particular reason to avoid immunisation in the deltoid muscle, can be given their vaccine in the vastus lateralis muscle in the thigh if necessary.

The area for injection should be clearly visible and accessible. Garments with long or tight sleeves may need to be removed. The injection site does not need to be cleaned unless visibly dirty. If cleaning is required, water should be used and the area dried with a gauze swab. It is not necessary to disinfect the skin.

Insert the needle into the injection site far enough to ensure it will deliver the vaccine into the muscle and depress the plunger. There is no need to pull back on the plunger (aspirate) before the plunger is depressed to release the vaccine into the muscle because there are no large blood vessels at the recommended injection sites.

Ensure the full dose is administered as a partial dose will not evoke a full immune response. Remove the needle and if there is any visible blood at the injection site, the patient can apply pressure to the site with a piece of gauze/cotton wool.

Administering COVID-19 vaccine to individuals with a bleeding disorder

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 2 minutes (ACIP, 2019). The individual/carer should be informed about the risk of haematoma from the injection.

Administering COVID-19 vaccine to individuals taking anticoagulants

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.

Timing of administration of COVID-19 vaccine to individuals who are immunosuppressed

Individuals with immunosuppression may not make a full immune response to vaccination. As there is no evidence on response in immunosuppressed individuals there is also no evidence upon which to base advice on the optimal timing of delivery. Specialists may advise their patients based on their knowledge and understanding of their immune status and likely immune response to vaccination but should also consider the risk from COVID and the patient’s likelihood of exposure.

As two doses are required to make a full response in healthy individuals, a decision to defer any possible benefit from vaccination or to suspend therapy should not be taken without due consideration of the risks from COVID and from their underlying condition. Although the immune correlates of protection are currently unknown, post-vaccination testing may be considered. Until further information becomes available vaccinated patients with immunosuppression should continue to follow advice to reduce the chance of exposure.

Period of observation following immunisation with COVID-19 vaccine

Recipients of COVID-19 vaccine should be observed for a minimum of 15 minutes following vaccination for any immediate reactions during the period they are receiving

any post-immunisation information and making a subsequent appointment if required. The MHRA have advised that they should be observed for longer than 15 minutes when indicated after a clinical assessment.

Adverse reactions following vaccination

Possible adverse reactions following vaccination

Local reactions at the injection site were found to be fairly common after vaccination with the COVID-19 mRNA Vaccine BNT162b2 during clinical trials. Over 80% of trial participants reported pain at the injection site. This occurred within 7 days after the injection and resolved after a few days

In clinical trials, the most frequently reported systemic reactions in participants were tiredness (> 60%), headache (> 50%), muscle aches (> 30%), chills (> 30%), joint pain (> 20%) and a raised temperature (pyrexia) (> 10%). These symptoms 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[4].

Mild pain and tenderness at the injection site was also common with AstraZeneca COVID-19 vaccine, occurring in 88% of 18-55 year olds, 73% of 56-69 year olds and 61% of people aged 70 years or over; similar levels were reported after each dose. Short lived systemic symptoms including fatigue and headache were also common but decreased with age. These reactions were unusual after the second dose[3]. Mild fever (>38°C) was recorded in the first 48 hours for around a quarter of younger participants and but was not reported in those over 55 years of age or in any age group after the second dose[3]. Prophylactic use of paracetamol was found not to affect the immune response to this vaccine[5].

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[4] COVID-19 mRNA Vaccine BNT162b2 .REG 174 Information for UK Healthcare professionals. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/940565/Information_for_Healthcare_Professionals_on_Pfizer_BioNTech_COVID-19_vaccine.pdf

[5] Folegatti, P et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2 single-blind, randomised controlled trial. Lancet 2020 August 15, 396(10249): 467-478

Reporting adverse reactions

Suspected adverse reactions following administration of COVID-19 vaccine should be reported to the MHRA using the specially established Coronavirus Yellow Card reporting scheme (coronavirus-yellowcard.mhra.gov.uk/ or call 0800 731 6789). Both patients and healthcare providers can and should report any possible adverse reactions observed with these vaccines using the Yellow Card scheme. As a new vaccine product, MHRA have a specific interest in the reporting of adverse drug reactions for the new COVID-19 vaccines.

Any adverse reaction to a vaccine should be documented in the individual's record and the individual's GP should be informed.

Differentiating between a reaction to the vaccine and symptoms of COVID-19 disease

Vaccinated individuals should be advised that the COVID-19 vaccine may cause a mild fever which usually resolves within 48 hours. This is a common, expected reaction and isolation is not required unless COVID-19 is suspected.

Feeling generally unwell, shivery, achy and tired were also symptoms commonly reported by vaccine recipients in the clinical trials. Generally these symptoms were found to resolve within one to two days without treatment but paracetamol can be given if necessary to relieve any of these symptoms.

The most commonly reported COVID-19 symptoms are: a high temperature, a new, continuous cough, or a loss or change to sense of smell or taste. If someone experiences any of these symptoms they should get tested. The COVID-19 vaccine will not interfere with testing for COVID-19 infection.

As has always been recommended, any fever after vaccination should be monitored and if individuals are concerned about their health at any time, they should seek advice from their GP or NHS 111.

COVID-19 vaccine contraindications and precautions

COVID-19 vaccine contraindications

COVID-19 vaccine should not be given to those who have had:

- a confirmed anaphylactic reaction to a previous dose of COVID-19 vaccine
- a confirmed anaphylactic reaction to any components of the vaccine

There are **some additional specific contraindications for the COVID-19 mRNA Vaccine BNT162b2 Pfizer-BioNTech vaccine** which were published on 9 December 2020 following anaphylactic reactions to the vaccine. It is extremely important that vaccinators are aware of, and check for, the contraindications to this vaccine which are described in Appendix A below and also in the Information for Healthcare Professionals on Pfizer/BioNTech COVID-19 vaccine on the MHRA website.

The COVID-19 chapter of the Green Book also provides full detail 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, or from the local screening and immunisation team or health protection team.

COVID-19 vaccine precautions

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.

Current or previous history of COVID-19 disease

People currently unwell and experiencing COVID-19 symptoms should not receive COVID-19 vaccine until they have recovered. This is to avoid wrongly attributing any new symptom or the progression of symptoms to the vaccine. As deterioration in some people with COVID-19 can occur up to two weeks after infection, ideally vaccination should be deferred until they have recovered and at least four weeks after onset of

symptoms or four weeks from the first PCR positive specimen in those who are asymptomatic.

There is no evidence from clinical trials of any safety concerns from vaccinating individuals with a past history of COVID-19 infection, or with detectable COVID-19 antibody so people who have had COVID-19 disease (whether confirmed or suspected) can still receive COVID-19 vaccine. This is because it is not known how long antibodies made in response to natural infection persist and whether immunisation could offer more protection. 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.

Vaccination of people experiencing prolonged COVID-19 symptoms ('Long COVID')

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.

Time interval between treatments for COVID-19 disease (for example dexamethasone, convalescent plasma, 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.

Convalescent plasma is a preparation of pooled antibodies taken from people who have recently recovered from COVID-19. The antibodies bind to the surface of the SARS-CoV-2 virus and stop it from attaching to the body's cells and replicating further.

Monoclonal antibody treatment works in the same way as convalescent plasma but is a specific preparation containing two specific man-made antibodies.

As the COVID-19 mRNA Vaccine BNT162b2 Pfizer-BioNTech and AstraZeneca COVID-19 vaccines are non-live vaccines, it is not anticipated that these treatments would contraindicate the vaccine. Although theoretically, high levels of antibodies in the convalescent plasma could interfere with the immune response to the vaccine, passively acquired antibodies from the plasma treatment are not thought to persist for long so by the time a person who has received this is well enough to receive a COVID-19 vaccination, these antibodies are likely to have gone.

Antivirals prevent the further replication of viruses. As neither of the above mentioned COVID-19 vaccines contain live virus, response to the vaccine will not be affected by prior or recent receipt of anti-viral medication.

Co-administration of COVID-19 vaccine with other inactivated or live vaccines

Although no data for co-administration of COVID-19 vaccine with other vaccines exists, 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.

Because of the absence of data on co-administration with COVID-19 vaccines, COVID-19 vaccine should not be routinely offered at the same time as other vaccines. Based on current information about the first COVID-19 vaccines which may be used, scheduling of COVID-19 vaccine and other vaccines should ideally be separated by an interval of at least 7 days to avoid incorrect attribution of potential adverse events.

As both the Pfizer-BioNTech and AstraZeneca COVID-19 vaccines are considered inactivated, where individuals in an eligible cohort present having received another inactivated or live vaccine, COVID-19 vaccination should still be considered. The same applies for other live and inactivated vaccines where COVID-19 vaccination has been received first. In many cases, vaccination should proceed to avoid any further delay in protection and to avoid the risk of the patient not returning for a later appointment. In such circumstances, patients should be informed about the likely timing of potential adverse events relating to each vaccine.

Legal aspects of vaccine administration

All vaccines are classified as prescription only medicines (POMS). This means that they are subject to legal restrictions and in order to give them, there needs to be an appropriate legal framework in place before they can be supplied and/or administered to eligible people. Additionally, any person who supplies and administers a vaccine must have a legal authority to do so. This legal authority may be in the form of a written patient specific prescription, a Patient Specific Direction (PSD), a Patient Group Direction (PGD) or another process such as a Written Instruction or a Protocol.

Using a Patient Group Direction (PGD) to give COVID-19 vaccine authorised under regulation 174

In response to certain public health threats, such as the current pandemic, the UK Medicines and Healthcare products Regulatory Agency (MHRA) can temporarily authorise the supply of an unlicensed medicine or vaccine for use, under regulation 174 of The Human Medicines Regulations 2012, when it is satisfied that there is robust evidence to show the safety, quality and effectiveness of the medicine/vaccine.

In October 2020, new legislation amending The Human Medicines Regulations 2012 was passed. Prior to this, PGDs could only be used for licensed medicines. The change to legislation allows medicines which have been temporarily authorised for supply in the UK under regulation 174 to be administered in accordance with a PGD. So registered healthcare professionals who are allowed to work to a PGD may supply and administer COVID-19 vaccines, temporarily authorised under Regulation 174, using a PGD. The workforce that can administer under PGDs has not changed (see www.gov.uk/government/publications/patient-group-directions-pgds/patient-group-directions-who-can-use-them).

PHE will develop and publish PGDs for COVID-19 vaccines.

Protocols for the supply and/or administration of COVID-19 vaccine

In order to ensure that the UK has a sufficiently sized workforce to deliver a COVID-19 vaccine programme, the changes to the Human Medicines Regulations (The Human Medicines (Coronavirus and Influenza) (Amendment) Regulations 2020), also brought about a new regulation (247A). While a disease is pandemic, regulation 247A permits the supply or administration of a medicinal product used for vaccination or immunisation against coronavirus in accordance with a protocol that is approved by ministers. Such a national protocol may allow specified classes of people, which need not be limited to registered healthcare professionals, to administer COVID-19 vaccine

In accordance with regulation 247A, the protocol will specify: the classes (that is characteristics and training required) of health care workers permitted to administer vaccine under the protocol, the requirement for individuals to be designated and authorised to administer medicines under the protocol by an appropriate manager (in the employing organisation), record keeping requirements (including the requirement to record the name of the person who administers the vaccine) and requirements for the supervision, where appropriate, of the people administering the vaccine.

The protocol will also include information similar to that commonly found in PGDs, for example, who is eligible for vaccination under the protocol and who is not, actions to be taken if the patient is excluded or declines the medicine, a description of the vaccine(s), route of administration, dose, frequency, reporting of adverse reactions, recording, storage and disposal.

It is expected that the protocol will allow flexibility for different delivery models. It may be followed wholly from patient assessment through to post-vaccination by a single person. Alternatively, multiple health care workers may undertake stages in the patient vaccination pathway in accordance with the protocol. Where multiple person models are used, the service provider must ensure that all elements of the protocol are complied with in the provision of vaccination to each patient. The service provider is responsible for ensuring that health care workers are trained and competent to safely deliver the activity they are employed to provide under this protocol.

Accountability

When working to some or all of the protocol, registered healthcare workers are responsible and accountable for their practice. They are accountable to their regulatory body and to their employer.

When administering vaccines under the protocol, non-registered healthcare workers are accountable to their employer. Their employer is responsible for ensuring they are suitably trained, have completed the necessary competency assessment and are provided with an appropriate level of supervision when carrying out their duties under the protocol.

Inadvertent vaccine administration errors

Inadvertent administration of the diluent only (for COVID-19 vaccines that require dilution)

The diluent for the COVID-19 mRNA Vaccine BNT162b2 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 COVID-19 mRNA Vaccine BNT162b2 as soon as the error is realised.

Inadvertent administration of 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 COVID-19 mRNA Vaccine BNT162b2 were given. This means that some people in the trials have already received higher doses of a similar vaccine (BNT162b1) than the currently recommended dose. The trial showed that although a stronger dose was not harmful, the recipients experienced more local reactions with very painful arms being reported. 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. The second dose of vaccine should still be given as per the recommended schedule.

Inadvertent administration of over-diluted vaccine

As the amount of active content in a dose of over-diluted vaccine will be less, the vaccine dose should be repeated as soon as the error is realised using a correctly reconstituted vaccine.

Second dose given at less than the minimum recommended interval

If the second dose of the COVID-19 mRNA Vaccine BNT162b2 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 AstraZeneca 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.

Longer than recommended interval 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.

Different COVID-19 vaccine given for second dose than was given for first dose

There is no evidence on the interchangeability of the COVID-19 vaccines although studies are underway. Therefore, every effort should be made to determine which vaccine the individual received and to complete the course with the same vaccine. However, as both of the vaccines discussed in this document are based on the spike protein, it is likely that even if the vaccine given for the second dose is different to the first, it will help to boost the response to the first dose. For this reason, until additional information becomes available, further doses are not required.

COVID-19 vaccine administered to a person not in an eligible cohort

If COVID-19 vaccine is inadvertently administered to a person not in an eligible cohort and the person is aged 50 or over, they should be offered a second dose as per the recommended schedule. If the person is under 50 years of age, they should be advised to wait for their second dose until their age group is invited to attend for vaccination. They can be reassured that the longer interval between doses should not affect vaccine efficacy.

Reporting vaccine errors

Errors or incidents in vaccine storage, preparation or administration should be reported to the vaccination session team leader or the local Screening and Immunisation team. As some errors will require immediate action, they should be reported as soon as possible after they are realised.

They should also be reported to the MHRA, CQC or HSE as appropriate and recorded on STEIS, the NRLA or any locally-established or specially-established COVID-19 vaccine reporting systems.

COVID-19 vaccine inadvertently administered to a pregnant woman should be reported to the PHE Immunisation Department (Tel: 020 8200 4400).

Useful links

Green Book COVID-19 chapter www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book

Public Health England Coronavirus resources
www.gov.uk/government/collections/immunisation

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://vaclshtm.shinyapps.io/ncov_vaccine_landscape/

Royal College of Nursing. Immunisation services and large-scale vaccination delivery during COVID-19. www.rcn.org.uk/clinical-topics/public-health/immunisation/immunisation-services-and-large-scale-vaccination-delivery-during-covid-19#planningandriskassessmentprocess

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 mRNA Vaccine BNT162b2 is available at www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19 and https://coronavirus-yellowcard.mhra.gov.uk/productinformation

Appendix One Storage and preparation of the COVID-19 mRNA Vaccine BNT162b2 (Pfizer BioNTech)

Vaccine contraindications

COVID-19 mRNA Vaccine BNT162b2 should not be given to people who have hypersensitivity to any of the components in the vaccine (see Vaccine composition section below).

Special warnings and precautions for use

On 9 December 2020, the MHRA published guidance to vaccination centres on managing allergic reactions following COVID-19 vaccination with the Pfizer/BioNTech vaccine.

The MHRA's updated advice (also included in the vaccine Reg174 Information for UK Healthcare Professionals document) is:

- any person with a history of immediate-onset anaphylaxis to a vaccine, medicine or food should not receive the COVID-19 mRNA Vaccine BNT162b2
- a second dose of the COVID-19 mRNA Vaccine BNT162b2. should not be given to those who have experienced anaphylaxis to the first dose of COVID-19 mRNA Vaccine BNT162b2
- vaccine recipients should be monitored for 15 minutes after vaccination, with a longer observation period when indicated after clinical assessment
- a protocol for the management of anaphylaxis and an anaphylaxis pack must always be available whenever the COVID-19 mRNA Vaccine BNT162b2 vaccine is given. Immediate treatment should include early treatment with 0.5mg intramuscular adrenaline (0.5ml of 1:1000 or 1mg/ml adrenaline), with an early call for help and further IM adrenaline every 5 minutes. The health professionals overseeing the immunisation service must be trained to recognise an anaphylactic reaction and be familiar with techniques for resuscitation of a patient with anaphylaxis

Vaccine composition

In addition to the highly purified BNT162b2 messenger RNA, the COVID-19 mRNA Vaccine BNT162b2 also contains:

ALC-0315 = (4-hydroxybutyl) azanediyl)bis (hexane-6,1-diyl)bis(2-hexyldecanoate)

ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide

1,2-Distearoyl-sn-glycero-3-phosphocholine

cholesterol

potassium chloride

potassium dihydrogen phosphate

sodium chloride

disodium hydrogen phosphate dihydrate

sucrose

water for injections

COVID-19 mRNA Vaccine BNT162b2 does not contain any preservative and no animal products are used in the manufacture of this vaccine.

Polyethylene glycol (PEG) is an allergen commonly found in medicines and also in household goods and cosmetics. Known allergy to PEG is extremely rare but would contraindicate receipt of this vaccine.

Full product information about the COVID-19 mRNA Vaccine BNT162b2 is available at https://coronavirus-yellowcard.mhra.gov.uk/productinformation

Vaccine presentation

The COVID-19 mRNA Vaccine BNT162b2 packs contain 195 vials of vaccine (975 doses per pack as each vial contains 5 doses).

The vaccine is contained in a multidose clear glass vial. The vial has a rubber (bromobutyl) stopper, aluminium seal and a flip-off plastic cap. Bromobutyl is a synthetic rubber – the vial stopper does not contain latex.

Each vial contains 0.45 ml of vaccine and should be diluted with 1.8 ml of Sodium Chloride 0.9% Solution for Injection (also referred to as normal saline). Once diluted, each reconstituted vaccine will supply 5 doses of 0.3 ml (30 mcg). There will be a small amount of vaccine left in the vial after withdrawing 5 doses. This is to ensure that 5 complete doses can be withdrawn. Any vaccine remaining in the vial after this should be discarded.

Diluent for reconstitution

A separate ampoule containing a minimum of 2 ml of Sodium Chloride 0.9% Solution for Injection is required for vaccine reconstitution. Each ampoule of diluent is single use and any remaining diluent must be discarded after 1.8 ml has been withdrawn, regardless of the ampoule volume.

Ordering

COVID-19 mRNA Vaccine BNT162b2 should be ordered via PHE's ImmForm platform. The vaccine is currently only available to order by the pre-agreed providers for pre-authorised sites.

Each pack of vaccine ordered should automatically generate an order for the required number of packs of diluent, dilution syringes and needles and syringes and needles for vaccine administration for that vaccine pack. Vaccination record cards and information leaflets for vaccine recipients will also be provided with each vaccine pack.

Longer length (38mm) needles are recommended for morbidly obese individuals to ensure the vaccine is injected into muscle. These can be ordered from ImmForm when ordering vaccine if required in addition to the 25mm needles and syringes that will be supplied.

Storage

The Pfizer BioNTech COVID-19 vaccine will be **delivered frozen to healthcare facilities with ultra low temperature (ULT) freezers**. The following is provided for information only as those handling vaccines at ultra low temperatures should have received specific additional training for this and should be working to detailed standard operating procedures.

- vaccine packs will be shipped inside isothermic boxes (validated boxes which will maintain a constant temperature for a specified period of time) inside a cardboard box
- the isothermic box will also contain dry ice which should be disposed of carefully following local protocols
- upon delivery, the vaccine packs should be removed from the isothermic boxes and transferred to a suitable ULT freezer to ensure ongoing storage between -75ºC and +/-15ºC
- the vaccine should be kept upright, in its original packaging and away from prolonged light exposure
- the vaccine packs must not be opened until the vaccine is going to be thawed
- once removed from the freezer, the undiluted vaccine can be stored for up to 5 days at 2°C to 8°C, and up to 2 hours at temperatures up to 25°C, prior to use
- once thawed, the vaccine cannot be re-frozen
- shelf-life is 6 months at -80°C to -60°C

There are no special storage requirements for the diluent and this can be stored with other ambient products (needles and syringes) in a dry environment away from direct sunlight.

Delivery in a thawed state

The COVID-19 mRNA Vaccine BNT162b2 may then be delivered to where it is going to be administered thawed but refrigerated between +2 and +8ºC:

- refrigerated vaccine must be transferred immediately to a vaccine fridge on arrival and stored in a carefully monitored temperature range of +2 and +8ºC
- when removed from the freezer, the undiluted vaccine has a maximum shelf life of up to 5 days (120 hours) at +2 and +8ºC and an additional 2 hours at temperatures up to 25°C in preparation for dilution
- the vaccine pack will have a yellow label on the front stating the time it was removed from the freezer into storage at +2 to +8°C and the date and time by which it must be discarded 5 days (120 hours) later if it has not been used

- vaccine should be stored in the original package to protect it from light. Exposure to room light should be minimised and exposure to direct sunlight and ultraviolet light should be avoided.

Storage and use of the vaccine

The COVID-19 mRNA Vaccine BNT162b2 has very specific storage, reconstitution and 'use within' requirements.

All those involved in the delivery of the COVID-19 vaccination programme must be aware of the recommended storage requirements.

The vaccine must not be given if you are not confident that it has been stored or reconstituted as recommended by the manufacturer or as advised by a vaccine expert.

If the vaccine is stored incorrectly:

- label and isolate affected vaccines in the fridge and do not use until further notice
- seek advice from the manufacturer or a source of expert advice

Equipment required to reconstitute the vaccine

The following equipment is required for reconstitution:

- one COVID-19 mRNA Vaccine BNT162b2 multidose vial
- one plastic ampoule of Sodium Chloride 0.9% Solution for Injection - this will be supplied in multiple presentations (different manufacturers and different sized ampoules). It does not need to be kept in the fridge
- a green hubbed needle and a 2 ml syringe to reconstitute - needles and syringes will be supplied together in 2 boxes of 100 units

Reconstituting the vaccine

- clean hands with alcohol-based gel or soap and water
- assemble one ampoule of Sodium Chloride 0.9% Solution for Injection, a single use alcohol swab, a needle with a green hub and a 2ml syringe
- from cold storage, remove one vial of vaccine
- if removing the multidose vaccine vial directly from a ULT freezer, allow the vaccine to thaw for 30 minutes at temperatures up to 25°C and reconstitute within 2 hours

- if removing the multidose vaccine vial from cold storage between +2 and +8ºC, check that it has not been stored there for longer than 5 days (120 hours)
- when the thawed vaccine is at room temperature, gently invert the vial 10 times prior to dilution. **Do not shake**
- check the expiry date and the appearance of the vaccine. Prior to dilution, the vaccine should be an off-white solution with no particulates visible. Discard the vaccine if particulates or discolouration are present
- connect the needle with a green hub to the 2 ml syringe
- clean the vial stopper with the single use antiseptic swab and allow to air dry fully
- draw up 1.8 ml of Sodium Chloride 0.9% Solution for Injection, then discard the diluent ampoule and any remaining diluent in it. Do not use any other type of diluent
- add diluent to the vaccine vial. You may feel some pressure in the vial as you add the diluent. Equalise the vial pressure by withdrawing 1.8 ml of air into the empty diluent syringe before removing the needle from the vial
- gently invert the diluted solution 10 times. Do not shake
- the diluted vaccine should be an off-white solution with no particulates visible. Discard the diluted vaccine if particulates or discolouration are present
- dispose of green hub needle and syringe into yellow sharps bin
- the diluted vial should be clearly labelled with the dilution time and date

After dilution the vaccine should be used as soon as is practically possible. Reconstituted vaccine can be stored between 2ºC and 25°C but **must be used within 6 hours following dilution.**

Vaccine dose preparation

- if the vaccine has previously been reconstituted, check that the time of reconstitution was within the last 6 hours.
- clean top of vial with a single use antiseptic swab and allow to air dry fully.
- unwrap one of the 1 ml combined 23g/25mm blue hub needle and syringes provided (recommended needle length depends on body mass of patient. Longer length (38mm) needles are recommended for morbidly obese individuals to ensure the vaccine is injected into muscle. These can be ordered from ImmForm when ordering

vaccine if required in addition to the 25mm length needles and syringes that will be supplied)

- withdraw a dose of 0.3 ml of diluted product for each vaccination. Take particular care to ensure the correct dose is drawn up as a partial dose may not provide protection
- any air bubbles should be removed before removing the needle from the vial in order to avoid losing any of the vaccine dose
- the same needle and syringe should be used to draw up and administer the dose of vaccine to prevent under dosing of the vaccine to the person
- the needle should only be changed between the vial and the patient if it is contaminated or damaged

Dose and schedule

A single dose is 0.3 ml (30 mcgs). Two doses of COVID-19 mRNA Vaccine BNT162b2 are required with a minimum 21-day interval between doses.

For operational purposes, scheduling the second dose of COVID-19 vaccine from 28 days is recommended since using a consistent interval between all two-dose COVID-19 vaccines simplifies the messaging to the public and arrangements within clinic settings where alternative vaccines may be supplied at short notice. COVID-19 mRNA Vaccine BNT162b2 can be scheduled from 21 days after the first dose where rapid protection is required however.