Public Health England

Protecting and improving the nation's health

COVID-19 vaccination programme

Information for healthcare practitioners

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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 involved in the COVID-19 national vaccination programme before it began in December 2020.

Following authorisation for temporary supply by the UK Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency being given to the COVID-19 Vaccine Pfizer BioNTech on 2 December 2020, the COVID-19 Vaccine AstraZeneca on 30 December 2020 and the COVID-19 Vaccine Moderna on 8 January 2021, this document has been updated to provide specific information about the storage and preparation of these vaccines. 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-19 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

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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	1. Additional section added on timing of administration of COVID-19 vaccine to individuals who are immunosuppressed 2. New anaphylaxis guidance added for the COVID-19 mRNA Vaccine BNT162b2 3. 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
3.0	1. Vaccine specific information about the COVID-19 Vaccine AstraZeneca added 2. Advice about obtaining 6th dose from COVID-19 mRNA Vaccine BNT162b2 vial added 3. Pregnancy and breastfeeding sections updated 4. Revision of specific precautions to the COVID-19 mRNA Vaccine BNT162b2	31 December 2020
3.1	1. Advice about additional dose from COVID-19 Vaccine AstraZeneca vial added 2. Section about best interest decision added 3. Section on advice following immunisation added	11 January 2021
3.2	1. Timing of offer of vaccine to those who are about to receive immunosuppressive therapy and allergy advice sections updated to reflect updated advice in Green Book COVID-19 chapter 2. Section on surveillance of COVID-19 cases in vaccinated individuals added 3. Revised advice for action to take following inadvertent administration of incomplete dose of vaccine and new advice following administration of vaccine whose	3 February 2021

	potency may have been adversely affected by an inadvertent storage or preparation error added 4. Change from 5 doses in a vial of Pfizer BioNTech vaccine to 6 doses as per updated Regulation 174 Information for UK healthcare professionals on Pfizer/BioNTech COVID-19 vaccine	
3.3	Advice added regarding inadvertent administration of a different COVID-19 vaccine at a short interval after the first dose	11 February 2021
3.4	1. Updated advice in contraindications and precautions section to include updated advice on allergy and vaccinating those with a history of reaction to the first dose of a COVID-19 vaccine in line with updates to the Green Book COVID-19 chapter 2. Pregnancy section updated 3. Vaccine specific information about the COVID-19 Vaccine Moderna added	26 February 2021
3.5	1. Pregnancy section updated 2. New contraindications for COVID-19 vaccine AstraZeneca added 3. Advice about which vaccines to give those vaccinated abroad added	28 April 2021
3.6	Added information about the exceptional circumstances in which a different second vaccine to the first can be given	11 May 2021
3.7	Updated vaccine schedule section and added section about administering second dose beyond recommended interval	20 May 2021
3.8	Pfizer BioNTech vaccine storage conditions updated from 5 days to 31 days to reflect change in the Information for Healthcare Professionals on Pfizer BioNTech Vaccine document.	9 June 2021
3.9	1. Updated the following sections in line with revisions made to the Green Book COVID-19 Chapter: -duration of protection and booster doses -interchangeability of different COVID-19 vaccines -COVID-19 vaccines schedule -advice to vaccine recipients following immunisation -COVID-19 vaccine contraindications and precautions	6 July 2021

	-co-administration of COVID-19 vaccine with other inactivated or live vaccines 2. Appendix 1 Vaccine interchangeability guidance updated	
3.10	1. Updated to include - revisions to the Green Book COVID-19 Chapter - GBS and Capillary Leak syndrome - vaccination of 12 to 17 year olds - consent for children and young people 2. Appendix 2 revised to detail transition from use of the Pfizer BioNTech vaccine under Reg 174 to use under Conditional Marketing Authorisation	6 August 2021

Contents

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.

On 8 December 2020, a COVID-19 vaccination programme began in the UK.

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. It also shows the number of people vaccinated (both daily and cumulative) and the numbers of people who have received their first dose and those who have received their second dose.

Information on the effectiveness of COVID-19 vaccination being monitored by PHE can be found on the GOV.UK website.

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 COVID-19 chapter and the PHE COVID-19 PGDs and Protocols.

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.

Whilst many people may have asymptomatic infection, 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. The long-term effects of coronavirus (‘long COVID’) are described on the NHS UK website.

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 have been shown 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, asian or minority ethnic 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.

COVID-19 vaccination programme

Aim of the programme

The aim of the COVID-19 vaccination programme is to protect those who are at highest risk from serious illness or death from COVID-19 or at risk of transmitting infection to multiple vulnerable persons or other staff in a health or social care environment.

Vaccine development

Over 300 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. Whilst 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 safe and effective vaccines 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.

[1] Williamson EJ and others. 'Factors associated with COVID-19-related death using OpenSAFELY'. Nature 2020 July 8. 584:430–436

This document will discuss the first 3 COVID-19 vaccines to be authorised for supply in the UK. 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.

Duration of protection and booster doses

It is not yet known how long protection will last, whether regular booster doses will be needed and to what extent the vaccine stops people from catching and spreading the virus or just prevents them from becoming ill.

On 30 June 2021, the JCVI issued interim advice which stated that any potential COVID-19 booster programme should be offered in 2 stages from September 2021, starting with those most at risk from serious disease. This includes care home residents, people aged over 70, frontline health and social care workers, clinically extremely vulnerable adults and those who are immunosuppressed.

The JCVI will continue to review emerging scientific data over the next few months, including data relating to the duration of immunity from the current vaccines. Final advice on booster vaccination may change as a result of this.

COVID-19 vaccination eligibility

Vaccine priority groups

The Joint Committee on Vaccination and Immunisation (JCVI) 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 the COVID-19 vaccine strategy. See Joint Committee on Vaccination and Immunisation: advice on priority groups for COVID-19 vaccination 30 December 2020 statement for information about the first phase of the vaccine programme and the JCVI final statement on phase 2 of the COVID-19 vaccination programme: 13 April 2021.

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.

COVID-19 vaccines

In the UK, 3 COVID-19 vaccines are currently in use in the UK national COVID-19 vaccination programme. These are:

1. **COVID-19 Vaccine Pfizer BioNTech**
   given authorisation for temporary supply by the MHRA on 2 December 2020 and then granted Conditional Marketing Authorisation (CMA) on 9 July 2021.

2. **COVID-19 Vaccine AstraZeneca**
   given authorisation for temporary supply by the MHRA on 30 December 2020 and then granted Conditional Marketing Authorisation (CMA) on 24 June 2021.

3. **COVID-19 Vaccine Moderna**
   given authorisation for temporary supply by the MHRA on 8 January 2021 and then granted Conditional Marketing Authorisation (CMA) on 1 April 2021.

Any other COVID-19 vaccines which are given regulatory approval will be added to this document when this occurs.

The Pfizer BioNTech and Moderna COVID-19 vaccines use an mRNA platform and the COVID-19 Vaccine AstraZeneca is an adenovirus vector vaccine.

All the currently UK-authorised vaccines are supplied in multi-dose vials and require completion of a 2-dose course. Using multi-dose vials can improve the efficiency of

vaccine manufacture and distribution, enabling vaccine availability at the earliest opportunity.

COVID-19 Vaccine Pfizer BioNTech and COVID-19 Vaccine Moderna

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.

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

COVID-19 Vaccine AstraZeneca

COVID-19 Vaccine AstraZeneca is a viral vector vaccine which uses a weakened adenovirus as a carrier to deliver the genetic sequence for the SARS-CoV-2 spike protein. The adenovirus has been modified so that it cannot replicate in human cells and therefore cannot cause any disease. Once it has delivered the SARS-CoV-2 spike protein genetic code, the adenovirus is destroyed by the body.

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, the modified adenovirus binds to the surface of human cells and delivers the genetic code for the spike protein. The cells then process this genetic code to 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. If the SARS-CoV-2 virus is later encountered, the immune system should be able to respond rapidly.

Interchangeability of different COVID-19 vaccines

Evidence from trials suggest that those who receive mixed schedules, including mRNA and adenovirus vectored vaccines make a good immune response[2], although rates of side effects following the second dose are higher compared to those who received the

[2] Lui X, Shaw RS, 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

same vaccine for both doses[3]. Initial reactogenicity and safety data from the Com-COV clinical trial[3], showed that mixed schedule recipients were more likely to experience feverishness, chills, fatigue, headache, joint pain, malaise, and muscle ache. However, there were no hospitalisations due to these symptoms, and most of the increase in reactogenicity was observed in the 48 hours after immunisation.

Because of this increased risk of side effects, every effort should be made to determine which vaccine the individual received for their first dose and to complete the 2-dose course with the same vaccine (unless contraindicated). Individuals who do receive a different vaccine for their second dose (see below) 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, it is reasonable, in these circumstances, to offer 1 dose of the locally available product to complete the schedule if suitable for age and not contraindicated (see Appendix 1 and Individuals who received COVID vaccination overseas section below). This option is preferred if that individual is likely to be at immediate high risk or is considered unlikely to attend again. Further doses of vaccine would not then be required.

Individuals who received COVID vaccination overseas

If a person has received a first dose of a COVID-19 vaccine overseas that is also available in the UK, they should receive the same vaccine for their second dose. If the vaccine they received for their first dose is not available in the UK, the most similar alternative should be offered (see table in Appendix 1). If the vaccine received overseas is not listed in the table, a full course of the appropriate vaccine recommended for the individual in the UK (which may depend on their age) should be given. The recommendations in this table will be reviewed regularly as more vaccines and information about the efficacy of these vaccines becomes available.

The various groups of vaccines are:

- Adenovirus (ChAdOx) vector: AstraZeneca, Covishield
- mRNA: Pfizer, Moderna
- whole inactivated Coronavirus: Sinopharm, Sinovac, Covaxin

The other adenovirus-based vaccines (Janssen, Sputnik, CanSinoBio) use different vectors and so are not immunologically the same as either the AstraZeneca or Covishield adenovirus vector vaccines. However, as they, and the Novavax vaccine, are

[3] 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

all based on spike protein, the vaccine course can be completed with any of the locally available vaccines as appropriate for the individual's age.

Exceptional circumstances in which a different second vaccine to the first can be given

In addition to giving a different second vaccine where the first vaccine is unknown or was a vaccine given abroad that is not available in the UK, there are certain other situations in which it may be appropriate to give a different second vaccine to the first, providing there are no contraindications. These are:

Housebound patients or care home residents

Housebound patients or care home residents who received the Pfizer BioNTech or Moderna vaccine for their first vaccination in a hospital setting but are resident in a nursing home or are newly housebound when the second dose is due: as these individuals would have to travel to a vaccination centre to receive a second dose of the same vaccine which may not be suitable or possible, they should be vaccinated at home or in the care home with the AstraZeneca vaccine (which is easier to transport) if over 40 years of age and appropriate after clinical assessment. Individuals under 40 years of age should preferably be offered a second dose of Pfizer BioNTech vaccine.

Individuals who experience severe adverse reactions after the first dose, including:

- people with severe allergies or anaphylaxis to the vaccine or its components (for example, polyethylene glycol (PEG))
- after discussion with, and on the advice of, an allergy specialist, people with idiopathic anaphylaxis or a history of anaphylaxis to multiple other medicines
- individuals who experience a clotting episode with concomitant thrombocytopenia following the first dose of AstraZeneca vaccine

If an individual experienced a severe adverse reaction to their first dose of COVID-19 vaccine, advice in the Green Book COVID-19 chapter regarding second doses should be followed and expert clinical opinion from a specialist should be sought if further advice is required.

Vaccine supply not available locally

It is not recommended to give a different second vaccine simply because the same vaccine is not available that day. If all efforts to enable an individual to receive the same vaccine at another time and/or location have been exhausted, it may be necessary to use a different vaccine where the risk of not vaccinating is greater than the risk of

further delay. However, age specific recommendations on vaccine type as set out in the Green Book COVID-19 chapter should be followed.

COVID-19 vaccines schedule

Although the 2 recommended doses of Pfizer BioNTech vaccine can be given a minimum of 21 days apart and the AstraZeneca and Moderna vaccine doses can be given a minimum of 28 days apart, JCVI is currently recommending an interval of 8 weeks between doses of all the available COVID-19 vaccines where a two-dose primary schedule is used. Operationally, this consistent interval should be used for all vaccines with a two-dose primary schedule to avoid confusion and simplify booking and will help to ensure a good balance between achieving rapid and long-lasting protection.

The main exception to the 8 week lower interval would be those about to commence immunosuppressive treatment. In these individuals, the minimal intervals (21 days for Pfizer BioNTech vaccine or 28 days for Moderna and AstraZeneca vaccines) may be followed to ensure that the vaccine is given whilst their immune system is better able to respond.

Administering the second dose beyond the recommended interval

Whilst it is strongly advised that the second dose is given at the recommended interval, if it is inadvertently or unavoidably delayed beyond this interval, for example because an individual is unable to attend their vaccination appointment, it is unlikely that their response to this second dose and their longer term protection will be adversely affected.

Evidence shows that delaying the second dose to 12 weeks after the first improves the boosting effect. Data from clinical trials shows that the efficacy of the AstraZeneca vaccine was higher when the second dose was given at, or after 12 weeks[4], and a study of people aged over 80 years found that extending the second dose interval to 12 weeks for the Pfizer BioNTech vaccine markedly increased the peak spike-specific antibody response by three and a half times compared to those who had their second vaccine at 3 weeks[5].

If an interval longer than that recommended is left between doses, there is no need to restart the course and the second dose should be given as soon as it can be arranged (preferably using the same vaccine to complete the course). Although good protection is provided by the first dose, and this is likely to last beyond 12 weeks, individuals should be encouraged to receive their second dose on time as this will significantly boost their protection and prevent further hospitalisations and deaths. Timely administration of the

[4] Regulation 174 Information for UK healthcare professionals on COVID-19 Vaccine AstraZeneca
[5] Parry H and others. 'Extended interval BNT162b2 vaccination enhances peak antibody generation in older people' (pre-print) May 2021. Available at: www.medrxiv.org/content/10.1101/2021.05.15.21257017v1

second dose is especially important when COVID-19 community infection rates are high or increasing.

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 infection and hands should be cleaned with alcohol-based gel or soap and water before vaccine preparation, between patients, and so on. 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, preferably 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 or 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.

The separate needles and syringes and the fixed-needle dose-sparing syringes being supplied by PHE for administration of the COVID-19 vaccines are suitable for use for vaccination of people with bleeding disorders or anticoagulation therapies.

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

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 COVID-19 vaccine PGDs and Protocols and Green Book COVID-19 chapter.

Individuals with immunosuppression may not make a full immune response to vaccination. As there is limited evidence on response in immunosuppressed individuals there is also very little evidence upon which to base advice on the optimal timing of delivery. However, 1 study[6] suggested immune responses were better in patients with cancer who received their chemotherapy at least 2 weeks earlier. 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-19 and the patient's likelihood of exposure.

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 2 weeks before), when their immune system is better able to make a response. Where possible, it would also be preferable for the 2-dose schedule to be completed prior to commencing immunosuppression. This would entail offering the second dose at the recommended minimum for that vaccine (3 or 4 weeks from the first dose) to provide maximum benefit that may not be received if the second dose was given during

[6] Monin-Aldama L and others. Interim results of the safety and immune-efficacy of 1 versus 2 doses of COVID-19 vaccine BNT162b2 for cancer patients in the context of the UK vaccine priority guidelines 2021 March 17

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.

Individuals aged 12 years or over who are household contacts of immunosuppressed patients of any age should be offered vaccine to reduce the risks of exposure.

Information about post-vaccination antibody testing of individuals with severe immunosuppression is provided in the Green Book COVID-19 chapter.

Period of observation following immunisation with COVID-19 vaccine

Following COVID-19 vaccine administration, individuals should be observed for any immediate reactions whilst they are receiving any verbal post vaccination information (such as possible reactions and what, if anything, to do about these). They, or their carers, should also be informed where they can obtain further advice if they require it following vaccination.

It is recommended that individuals are observed for a minimum of 15 minutes following administration of the Pfizer BioNTech and Moderna vaccines. There is no requirement for 15 minutes observation following the AstraZeneca vaccine. However, 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.

Advice to vaccine recipients following immunisation with COVID-19 vaccine

Following COVID-19 vaccine administration, vaccine recipients should be given information about possible reactions to the vaccine (see adverse reactions section below), how to treat these, and when and from whom to seek further advice if required. Vaccinators should ensure they are familiar with the content of the latest version of the What to expect after your COVID-19 vaccination leaflet given to vaccine recipients.

Thrombosis with thrombocytopenia syndrome

A rare condition involving serious thromboembolic events accompanied by thrombocytopaenia, has been reported after AstraZeneca vaccination. Vaccinated individuals should be advised to seek immediate medical attention if they develop new symptoms from around 4 days to 4 weeks after vaccination such as:

- new onset of severe headache, which is getting worse and does not respond to simple painkillers
- an unusual headache which seems worse when lying down or bending over, or may be accompanied by blurred vision, nausea and vomiting, difficulty with speech, weakness, drowsiness, confusion or seizures

- new onset of unexplained pinprick bruising or bleeding
- shortness of breath, chest pain, leg swelling or persistent abdominal pain

Myocarditis and pericarditis

A number of cases of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the pericardium) have been reported in people who have received the Pfizer BioNTech and Moderna COVID-19 vaccines. 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 if they experience new onset of chest pain, shortness of breath, palpitations or arrhythmias.

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 and to rule out other causes, in order to initiate adequate supportive care and treatment.

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. Cases of GBS that occur following vaccination may occur by chance (the rate of GBS is 2 per 100000 per year in the population); no causal link with vaccination has been proven. As there is no evidence to suggest that having had a prior diagnosis of GBS predisposes an individual to further episodes, 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. Based on an understanding of the natural history of GBS, the same vaccine product may be used to complete the course as using an alternative product may increase the chance of experiencing known side effects.

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 social distancing, wearing a face mask and washing their hands thoroughly and frequently.

Vaccinees should also be advised to follow the current advice on testing and self-isolation if they develop any coronavirus symptoms or undergo regular testing as a health or social care worker. Vaccination will not affect testing. The lateral flow device (LFD) test detects a different protein of the virus than the one encoded in the vaccine, and the polymerase chain reaction (PCR) test detects different genes of the virus than the one included in the vaccine.

It is not yet known whether vaccination will stop people from catching and passing on the virus and as no vaccine is completely effective, some people may still become infected with COVID-19 despite having been vaccinated (although this should be less severe). The vaccine cannot cause COVID-19 infection.

COVID-19 vaccine and clinical trial participants

Individuals who are participating in a clinical trial of COVID-19 vaccines who present for vaccination should be referred back to the trial investigators. Eligible individuals who are enrolled in vaccine trials should then be provided with written advice on whether and when they can be safely vaccinated in the routine programme. Many of these individuals in the trials will have received the appropriate number of doses of a vaccine which has since received MHRA authorisation and will require no further doses unless a booster dose is subsequently recommended by the JCVI.

Further advice for residents in England who have taken part in COVID-19 vaccine clinical trials is available on the GOV.UK website.

Surveillance of COVID-19 cases in vaccinated individuals.

The PHE Immunisation Department is conducting enhanced surveillance of cases of infection in vaccinated individuals in England, in order to confirm infection, identify risk factors and outcomes, and monitor phenotypic and genetic characteristics of SARS-CoV-2 isolates and to compare these cases to those in unvaccinated individuals. Individuals will mainly be identified by active follow up of a sample of cases identified by linkage between community testing and vaccination data.

Clinicians who are seeing patients face to face are also encouraged to report any confirmed cases in partially or fully vaccinated individuals if they tested positive within the preceding 7 days. This provides the best opportunity to get early and complete sampling from these cases. Further information, criteria for reporting and the reporting form.

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 Pfizer BioNTech vaccine 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 (reported by more than 60% of participants), 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[7].

The types of reactions reported in adolescents aged 12 to 15 years who received the Pfizer BioNTech vaccine in clinical trials were the same as those reported in older individuals but they were reported slightly more frequently: injection site pain (> 90%), fatigue and headache (> 70%), muscle aches and chills (> 40%), joint pain and raised temperature (> 20%).

More than 60% of COVID-19 Vaccine AstraZeneca trial participants reported tenderness at the injection site with redness, swelling, itching, warmth and pain at the injection site also being reported. The most frequently reported systemic reactions were headache and tiredness (by more than 50% of participants); muscle aches and feeling generally unwell (>40%); raised temperature (pyrexia) and chills (>30%) and joint pain and nausea (>20%). The majority of adverse events reported during the clinical trials of the COVID-19 Vaccine AstraZeneca were mild to moderate and short-lasting, usually resolving within a few days of vaccination. When compared with the first dose, adverse reactions reported after the second dose were milder and reported less frequently[3]. Prophylactic use of paracetamol was found not to affect the immune response to this vaccine[8].

The most frequently reported adverse reactions to the COVID-19 Vaccine Moderna were injection site pain (92%), fatigue (70%), headache (65%), myalgia (62%), arthralgia (46%) chills (46%), nausea/vomiting (23%), axillary 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. Older vaccinees experienced a slightly lower frequency of reactions.

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[7] Regulation 174 Information for UK Healthcare professionals on COVID-19 mRNA Vaccine BNT162b2

[8] Folegatti, P and others. ‘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

Overall, there was a higher incidence of some adverse reactions in younger age groups: the incidence of axillary swelling/tenderness, fatigue, headache, myalgia, arthralgia, chills, nausea or vomiting and fever was higher in adults aged 18 to < 65 years than in those aged 65 years and above. Local and systemic adverse reactions were more frequently reported after the second dose than after the first dose. If required, symptomatic treatment with analgesic and/or anti-pyretic medicinal products (for example, paracetamol-containing products) may be used[9].

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 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.

The MHRA publish a weekly report covering adverse reactions to approved COVID-19 vaccines: weekly summaries of Yellow Card reports.

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 there are epidemiological or other clinical reasons to suspect SARS-CoV-2 infection.

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 1 to 2 days without treatment but analgesics and/or anti-pyretics 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, or any other symptoms that make them think they might have COVID-19, they should get tested. The COVID-19 vaccine will not interfere with testing for COVID-19 infection.

[9] Summary of Product Characteristics for COVID-19 Vaccine Moderna.

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 previous systemic allergic reaction (including immediate-onset anaphylaxis) to:

- a previous dose of the same COVID-19 vaccine
- any components (excipient) of the vaccine, for example polyethylene glycol (PEG)

The COVID-19 chapter of the Green Book provides full details about the contraindications and precautions to COVID-19 vaccine. Everyone involved in the COVID-19 vaccination programme should ensure they have read the latest online version of this Green Book chapter so that they are familiar with all the contraindications and precautions to the COVID-19 vaccines. 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 immunisation team or health protection team.

Thrombosis and thrombocytopenia

Following widespread use of the AstraZeneca vaccine, a rare condition involving serious thromboembolic events accompanied by thrombocytopaenia, has been reported after AstraZeneca vaccination. The condition presents with unusual venous thrombosis, including cerebral venous sinus thrombosis, portal vein thrombosis, and sometimes arterial thrombosis, with low platelet count and high D-dimer measurements. The condition has similarities to heparin-induced thrombocytopenia and thrombosis (HITT or HIT type 2) and patients usually have positive antibody to platelet factor 4. The majority of the events have occurred between 5 and 16 days following vaccination[10].

The current reported rate of this event in the UK is around 15 cases per million after the first dose, although a higher incidence appears to be seen in younger individuals. After the second dose the reported rate is much lower, particularly in younger individuals.

[10] Greinacher A, Thiele T, Warkentin TE and others. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. NEJM, 2021. DOI: 10.1056/NEJMoa2104840

Individuals who experience a clotting episode with concomitant thrombocytopaenia following the first dose of AstraZeneca vaccine should be properly assessed. **If they are considered to have the reported condition, further vaccination should be deferred until their clotting has completely stabilised, and they should then be considered for a second dose of an alternative product**.

Individuals who have received the first dose of AstraZeneca vaccine without developing this rare condition are advised to receive the second dose of the same vaccine at the currently recommended interval. To date, there is no signal of an increased risk of this condition after the second dose and the rate of other reactions is lower at the second dose than after the first dose of this vaccine. Using an alternative product for the second dose is more likely to lead to common side effects.

Caution should also be used when vaccinating individuals who have a history of a previous episode of heparin induced thrombocytopenia and thrombosis (HITT or HIT type 2). The Information for Healthcare Professionals on COVID-19 Vaccine AstraZeneca advises that, as a precautionary measure, administration of the AstraZeneca vaccine in patients with a history of HITT or HIT type 2 should only be considered when the benefit outweighs any potential risks.

Extremely rare reports of capillary leak syndrome have been reported after AstraZeneca vaccine in individuals with a prior history of this condition. These individuals may be offered vaccination with an alternative COVID-19 vaccine.

The revised contraindications and precautions to the AstraZeneca vaccine, including changes to age group recommendations for this vaccine, are detailed in the COVID-19 chapter of the Green Book. Further detailed information is also available in the Information for healthcare professionals on blood clotting following COVID-19 vaccination document and a COVID-19 vaccination and blood clotting leaflet is available for patients. A JCVI statement on the use of the AstraZeneca COVID-19 vaccine has also been published.

Capillary Leak Syndrome

A small number of cases of capillary leak syndrome have been reported across Europe within 4 days of AstraZeneca vaccination. Around half of those affected had a history of capillary leak syndrome.

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 prior history of this condition may be offered vaccination with an alternative COVID-19 vaccine.

Minor illness at time vaccination due

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.

Vaccination of individuals with a 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 (and to prevent infecting anyone else in the vaccination centre). Vaccination of individuals who may be infected or asymptomatic or incubating COVID-19 infection is unlikely to have a detrimental effect on the illness. Vaccination should be deferred in those with confirmed infection to avoid confusing the differential diagnosis. As deterioration in some people with COVID-19 can occur up to 2 weeks after infection, ideally vaccination should be deferred until they have recovered to around 4 weeks after onset of symptoms or 4 weeks from the first confirmed positive test in those who are asymptomatic.

There is no evidence 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.

Children or adults who have tested positive for COVID-19 infection in the previous 28 days and who require other vaccines (such as DTaP/IPV/Hib/HepB-containing vaccines) can receive these vaccines once they have recovered and have completed the required isolation period for COVID-19. If they fulfil these 2 conditions, they do not have to wait 28 days but the parent/carer who brings them for vaccination would need to ensure they are following current COVID-19 guidance and not attend if they are symptomatic or self-isolating.

Recent vaccination with other vaccines such as MMR and Td/IPV-containing vaccines will not affect testing for COVID-19 infection. The lateral flow device (LFD) test looks to detect a protein of the SARS-CoV-2 virus and the polymerase chain reaction (PCR) test looks for genes from the SARS-CoV-2 virus.

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 the patient is seriously debilitated, still under active investigation, or has evidence of recent 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 2 specific man-made antibodies.

As the currently authorised 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 none of the currently authorised COVID-19 vaccines contain live replicating 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 1 of the vaccines. There is no evidence of any safety concerns, although it may make the attribution of any adverse events more difficult.

As the Pfizer BioNTech, AstraZeneca and Moderna 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 most 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. An exception to this is the live attenuated shingles vaccination, where a 7 day interval should ideally be observed given the potential for an inflammatory response to COVID-19 vaccine to reduce the response to the live virus.

Studies are on-going to support co-administration of COVID-19 vaccines with influenza in the 2021 to 2022 season.

Where co-administration does occur, patients should be informed about the likely timing of potential adverse events relating to each vaccine.

Pregnant women

Although clinical trials on the use of COVID-19 vaccines during pregnancy are not advanced, the available data do not indicate any harm to pregnancy. JCVI has therefore advised that women who are pregnant should be offered vaccination at the same time as non-pregnant women, based on their age and clinical risk group.

There is now extensive post-marketing experience of the use of the Pfizer BioNTech and Moderna vaccines in the USA, with no safety signals being raised so far. Over 50,000 women now report having been vaccinated whilst pregnant or when they might be pregnant in England. Because of wider experience with the Pfizer BioNTech and Moderna vaccines, these 2 vaccines are the preferred vaccines to offer to pregnant women. Clinicians should discuss the risks and benefits of vaccination with the woman, who should be told about the limited evidence of safety for the vaccine in pregnancy.

Routine questioning about last menstrual period and/or pregnancy testing is not required before offering COVID-19 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 COVID-19 vaccine, she may complete vaccination during pregnancy using the same vaccine product (unless contraindicated).

Termination of pregnancy following inadvertent immunisation should not be recommended. Surveillance of inadvertent administration of COVID-19 vaccines in pregnancy (where the woman did not know she was pregnant at the time of vaccination) is being conducted for the UK by the PHE Immunisation Department. If a pregnant woman is inadvertently given COVID-19 vaccine from the first day of her last menstrual

period to any time in pregnancy, this should be reported to PHE. Women who are inadvertently vaccinated in early pregnancy should be offered the second dose of the same product.

Further information about the safety of COVID-19 vaccines when given in pregnancy is available on the PHE website.

Breastfeeding

There is no known risk associated with giving non-live vaccines whilst breastfeeding. JCVI advises that breastfeeding women may be offered vaccination with any suitable COVID-19 vaccine.

The developmental and health benefits of breastfeeding should be considered along with the woman's clinical need for immunisation against COVID-19, and at the same time, the woman should be informed about the absence of full safety data for the vaccine in breastfeeding women.

Children and young people

Following careful consideration of the risks and benefits of vaccinating children and young people aged 12 to 17 years, the JCVI have recommended vaccination of the following:

1) **Children and young people aged 12 years and over with specific underlying health conditions that put them at risk of serious COVID-19**

These conditions are:

- severe neuro-disabilities and/or neuromuscular conditions that compromise respiratory function. This includes conditions (such as cerebral palsy, autism and muscular dystrophy) that may affect swallowing and protection of the upper airways, leading to aspiration, and reduce the ability to cough and resulting overall in increased susceptibility to respiratory infections
- a learning disability including those with Down's syndrome, profound and multiple learning disabilities (PMLD) or severe learning disabilities and those who are on the learning disability register
- immunosuppression due to disease or treatment. Further detail about this group is provided in the Green Book COVID-19 chapter

2) **Children and young people aged 12 years and over who are household contacts of immunosuppressed individuals**

Those aged 12 years and above 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.

JCVI have also recommended that **all 16 to 17 year olds should be offered a first dose of the Pfizer BioNTech vaccine**. This is in addition to the existing offer of 2 doses of vaccine to 16 to 17 year-olds who are in 'at-risk' groups. Pending further evidence on effectiveness and safety in this age group, a second vaccine dose is anticipated to be offered later to increase the level of protection and contribute towards longer term protection. Further information about second doses will be given before these are due. This does not include those turning 18 years of age in the next three months who should be offered two doses 8 weeks apart in accordance with recommendations for those aged 18 to 29 years.

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 'Patient group directions: who can use them'). Registered doctors are appropriate prescribers so have their own prescribing rights and do not need to work under a PGD.

PHE are developing and publishing PGDs for the COVID-19 vaccines as they are authorised. See 'Protocols and patient group directions (PGDs)'.

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. The national protocols 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 specifies: the characteristics of and training required for 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 also includes 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 vaccine, a description of the vaccine, route of administration, dose, frequency, reporting of adverse reactions, recording, storage and disposal.

The protocol 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 or contractor must ensure that all elements of the protocol are complied with in the provision of vaccination to each individual. The service provider/contractor is responsible for ensuring that health care workers are trained and competent to safely deliver the activity they are employed to provide under the 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.

Consent

Before giving a COVID-19 vaccine, vaccinators must ensure that they have obtained Informed consent from the individual or a person legally able to act on the person's behalf, and that this has been recorded appropriately. Where a person lacks the capacity to consent at the time of vaccination and there is no Lasting Power of Attorney (LPA), Welfare Attorney or appointed deputy, in accordance with the Mental Capacity Act 2005, a decision to vaccinate may be made in the individual's best interests. Obtaining consent is discussed in Chapter 2 of 'Immunisation against infection disease' (the Green Book). Best interest decisions are discussed below.

Administering COVID-19 vaccine to individuals without the mental capacity to consent

If offering a COVID-19 vaccine to someone who may lack the mental capacity to consent, in the first instance, all practicable steps should be taken to support the person to make the decision for themselves.

Where it has been established that the person lacks capacity to consent, a best interests decision should be taken in line with the best interest checklist in Section 4 of the Mental Capacity Act. This means that the decision-maker must consider all the relevant circumstances, including the person's wishes, beliefs and values, the views of their family and what the person would have wanted if they had the capacity to make the decision themselves. The decision maker should make a record of their best interests decision. Best interests decisions should be made on an individual basis.

Where appropriate, the person's advocates or those with power of attorney should be consulted, and if there is a deputy or attorney with relevant authority then consent must be sought from them to be able to make a decision on the person's behalf to receive the vaccination.

If there are any issues or uncertainties when making a best interests decision, ask for advice from an experienced colleague.

For further information on caring for, or treating, a person who lacks the relevant mental capacity during the COVID-19 pandemic see The Mental Capacity Act (2005) (MCA) and deprivation of liberty safeguards (DoLS) during the coronavirus (COVID-19) pandemic: additional guidance.

Consent for children and young people

At 16 years of age, a young person is presumed in law to have the capacity to consent, so young people aged 16 or 17 years should consent to their own medical treatment and a parent cannot override that consent.

Children under 16 can consent for themselves if they have the capacity and maturity to understand what they are consenting to and fully understand what is involved in the proposed procedure (this is referred to as ‘Gillick competence’). Although they can give their own consent, it is advised that ideally, the parents of those under 16 are involved in the consent process. However, if a Gillick-competent child consents to vaccination, a parent cannot override that consent and if a Gillick-competent child refuses vaccination, that refusal should be accepted.

If a healthcare professional considers that the child is not Gillick competent or the child is not able to give or withhold consent, the consent of someone with parental responsibility should be sought, provided that person is capable of consenting to the immunisation and is able to communicate their decision.

Consent for the course of vaccination can be given, although checking that consent is still valid needs to be confirmed on the day each time and consent can be withdrawn at any time during the course of the vaccination.

If there is any new information between the time consent was given and when the immunisation is offered, it may be necessary to inform the young person or their parent(s) and for them to re-confirm their consent (for example when there is new evidence about the vaccine’s risks and benefits, or if there is a significant change in the individual’s condition).

Inadvertent vaccine administration errors

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

The diluent for the Pfizer BioNTech vaccine 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 properly reconstituted dose 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 (Pfizer BioNTech) 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 (100 micrograms instead of the recommended 30 microgram dose) was not harmful, 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[2].

If a person is given more than the recommended dose, they should be monitored and treated for any symptoms as required. 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 (or from 48 hours later if not repeated on the same day).

Inadvertent administration of incomplete dose of vaccine

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, a full dose should be drawn up and given as soon as possible after the error is realised. If a full dose is not given on the same day as the partial dose, for example if the error is realised after the individual has left the vaccination centre, or if it is suspected but not known for certain whether an individual received a partial dose, a full 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, seek expert advice.

If this was the first dose, the ‘second’ dose of the 2 dose schedule (which will actually be the third dose in this case) should still be given at the recommended interval from the additional dose.

Administration of a dose of vaccine whose potency may have been adversely affected by an inadvertent storage or preparation error

If a dose of COVID-19 vaccine is given following an incident in which the potency may have been affected, for example, a storage or preparation error, and expert advice has recommended that the dose of vaccine should be repeated, 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. The 48 hour wait period is to allow for any reactions experienced following the potentially affected dose to resolve before the replacement dose is given. It is recommended that the replacement dose should be given within 7 days of the potentially affected dose to minimise the time the individual may be left susceptible to infection. If more than 7 days have elapsed, seek expert advice.

If this was the first dose, the 'second' dose of the 2 dose schedule (which will actually be the third dose in this case) should still be given at the recommended interval from the additional dose.

Second dose given at less than the minimum recommended interval

If the second dose of the Pfizer BioNTech 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 AstraZeneca or Moderna 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. See also Administering the second dose beyond the recommended interval section above

Different COVID-19 vaccine inadvertently given for second dose than was given for first dose at correct interval

Evidence from trials suggest that those who receive mixed schedules, including mRNA and adenovirus vectored vaccines, make a good immune response[2], although rates of side effects at the second dose are higher[3]. Reactogenicity and safety data from the

Com-COV clinical trial[3], 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.

Inadvertent administration of a different COVID-19 vaccine 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). As clinical trials showed that compared with the first dose, adverse reactions reported after the second dose of the AstraZeneca vaccine were milder and reported less frequently[4], it is recommended that the AstraZeneca vaccine is given for this third dose where possible and only if suitable for age as it is likely to be less reactogenic as an additional dose.

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.

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.

Useful links

British Society of Immunology. 'A guide to vaccinations for COVID-19' and other useful coronavirus resources www.immunology.org/coronavirus

COVID-19 Vaccine Pfizer BioNTech Manufacturers information for healthcare practitioners

COVID-19 Vaccine AstraZeneca Manufacturers information for healthcare practitioners

COVID-19 Vaccine Moderna Manufacturers information for healthcare practitioners

GOV.UK Coronavirus (COVID-19) in the UK The official UK government website for data and insights on coronavirus (COVID-19).

Green Book COVID-19 chapter

Health Publications website – to order leaflets, posters, record cards, stickers and also download BSL videos to support people who are deaf. You can also order braille, large print, translated resources in 19 languages and Easy read versions

LSHTM COVID-19 vaccine tracker

MHRA weekly summary of Yellow Card reports

Product information for the COVID-19 mRNA Vaccine BNT162b2

Product information for the COVID-19 Vaccine AstraZeneca

Product information for the COVID-19 Vaccine Moderna

Public Health England. Coronavirus resources

Royal College of Nursing. COVID-19 vaccination page

Specialist Pharmacy Services. COVID-19 Vaccines

Vaccine update: issue 315, December 2020, COVID-19 special edition and Vaccine update: issue 322, June 2021, COVID-19 phase 2 special edition

WHO COVID-19 Worldwide Dashboard

Appendix 1. Vaccine interchangeability guidance

Vaccine manufacturer	Vaccine names (if applicable)	Type	Efficacy (whole course)*	Approval	Comments	Manufacturer's authorised schedule	PHE advice	UK alternative
AstraZeneca	Vaxzevria AZD1222	Recombinant adenovirus vector (ChAdOx) vs spike	80% [1]	MHRA, EMA, WHO	RCTs and robust observational data	18yrs+, 2 doses, 4 to 12 weeks apart	If partial vaccination: • complete course with same vaccine if possible (or closest alternate) with at least 8 week interval from previous dose • if more than 8 weeks since first dose, complete course as soon as possible If complete course given: • no further immediate vaccine needed • enrol for booster in UK if introduced	Locally available
Pfizer BioNTech	Comirnaty BNT162b2	mRNA vs spike	95% [2]	MHRA EMA, FDA, WHO		12yrs+, 2 doses, at least 21 days apart		Moderna
Institute of India	Covishield	Identical to AstraZeneca	80%	WHO		18yrs+, 2 doses, 4 to 12 weeks apart		AstraZeneca
Moderna	Moderna COVID-19 Vaccine mRNA-1273	mRNA vs spike	94.1% [3]	MHRA EMA, FDA, WHO	RCTs	18yrs+, 2 doses, 4 weeks apart		Pfizer
Novavax	NVX-CoV2373 Covovax	Recombinant spike protein with novel adjuvant	89.7% [4]	-	RCTs	18yrs+, 2 doses, 3 weeks apart		Locally available

Vaccine manufacturer	Vaccine names (if applicable)	Type	Efficacy (whole course)*	Approval	Comments	Manufacturer's authorised schedule	PHE advice	UK alternative
Janssen/ Johnson & Johnson	COVID-19 Vaccine Janssen JNJ-78436735 Ad26.COV 2.S	Recombinant adenovirus (Ad26) vector vs spike	66.9% [5]	MHRA EMA, FDA, WHO	RCTs	18yrs+, single dose	As above	Not required as single dose schedule
Gamaleya National Centre of Epidemiology and Microbiology	Sputnik V Gam-COVID-Vac	Recombinant adenovirus (Ad26 and Ad5) vector vs spike	91.6% [6]	-	RCT (interim results)	18yrs+, 2 doses, 3 weeks apart		Locally available
Gamaleya National Centre of Epidemiology and Microbiology	Sputnik Light	Recombinant adenovirus (Ad26) vector vs spike	79.4% [7]	-	RCT (interim results)	18yrs+, single dose	If vaccinated with 1 or 2 doses: • provide 1 dose of UK approved vaccine 8 weeks after previous dose • enrol for booster in UK if introduced If vaccinated with 3 doses:	Locally available
Sinopharm	COVID-19 vaccine BIBP	Whole inactivated coronavirus	78.1% [8]	WHO	RCTs. Limited testing in people over 60	18yrs+, 2 doses (3 in some		Locally available

Vaccine manufacturer	Vaccine names (if applicable)	Type	Efficacy (whole course)*	Approval	Comments	Manufacturer's authorised schedule	PHE advice	UK alternative
	BBIBP-CorV				years of age. Low efficacy in some observational studies	cases), 3 to 4 weeks apart	• no further immediate vaccine needed • enrol for booster in UK if introduced	
Sinovac Biotech	CoronaVac	Whole inactivated coronavirus	50 to 83.5% [9]	WHO		18yrs+, 2 doses, 2 to 4 weeks apart		Locally available
CanSino Biologics	Ad5-nCoV Convidecia	Recombinant adenovirus vector (Ad5) vs spike	65.7%	-	RCTs	single dose	If vaccinated with 1 or 2 doses • provide 1 dose of UK approved vaccine 8 weeks after previous dose • enrol for booster in UK if introduced	Locally available
Bharat Biotech	Covaxin	Whole inactivated coronavirus	77.8% [10]	-	RCT (interim results based on 43 cases)	2 doses, 4 weeks apart		Locally available

*All trials use different criteria for what counts as an infection which can lead to variations in results for effectiveness so trials should not be compared. However, all vaccines will reduce hospitalisations and deaths. Effectiveness will also vary by country depending on virus strain circulating at the time.

If the vaccine received overseas is not listed in the table, a full course of the appropriate vaccine recommended for the individual in the UK (which may depend on their age) should be given.

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Appendix 2. Storage and preparation of the COVID-19 Pfizer BioNTech Vaccine

The Pfizer BioNTech COVID-19 vaccine received temporary authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA) for supply under Regulation 174 of The Human Medicines Regulations 2012 on 1st December 2020. In response to certain public health threats, such as the current pandemic, the MHRA can temporarily authorise the supply of an unlicensed medicine or vaccine for use, under Regulation 174, when it is satisfied that there is robust evidence to show the safety, quality and effectiveness of the medicine/vaccine.

However, supply of this vaccine under the Reg174 authorisation was always intended to be a temporary arrangement until there was sufficient information about the vaccine for it to be given marketing authorisation (also known as a license).

On 9th July 2021, the Pfizer BioNTech vaccine was given a conditional marketing authorisation (CMA) by the MHRA. CMA is the fast-track approval of a medicine or vaccine that fulfils an unmet medical need. During the COVID-19 pandemic, CMA is being used to expedite the approval of safe and effective COVID-19 treatments and vaccines once they have met rigorous standards for safety, efficacy and quality.

To date, the Pfizer BioNTech COVID-19 vaccine that has been used in the UK has been the vaccine approved for supply on a temporary basis under Regulation 174. This vaccine is known as “COVID-19 mRNA Vaccine BNT162b2”. Now that it has CMA, the Pfizer BioNTech vaccine expected to be supplied from mid-August will be known by its brand name of “Comirnaty”.

Changes to labels, packaging and wording

It is important to note there are no changes to the vaccine itself. It is exactly the same vaccine that has been supplied from December 2020. Manufacture of the vaccine remains unchanged, as do the clinical, pharmacological and pharmaceutical properties of the vaccine.

However, there will be changes to the vaccine vial labels, packaging and wording within the information leaflets. As these vaccines are being supplied under two different regulatory frameworks (Reg174 and CMA), separate PGDs and Protocols will be available for the vaccine supplied under Reg174 and the vaccine supplied under CMA (Comirnaty).

Although Comirnaty will be delivered to vaccine centres and clinics from mid-August, there is likely to be a short period of time when both the Reg174 'COVID-19 mRNA Vaccine BNT162b2' vaccine and the CMA 'Comirnaty' vaccine are available concurrently. It is important that vaccinators know which PGD or Protocol they should be working to and which information leaflet they should give to patients depending on which of the two differently labelled vaccines they are giving.

As stated, there are no differences in the vaccine itself. However, there are a few minor differences in the storage and handling information provided for the Reg174 authorised product and that given in the SPC for Comirnaty. The following pages will describe how the Pfizer BioNTech vaccine should be stored and prepared for use. Where there are any differences between the vaccine supplied under Reg174 and the vaccine supplied under CMA (Comirnaty), these will be indicated.

Vaccine composition

In addition to the highly purified messenger RNA, the Pfizer BioNTech COVID-19 vaccine 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

Vaccine presentation

The Pfizer BioNTech COVID-19 vaccine packs contain 195 vials of vaccine.

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 6 doses of 0.3 ml.

If the dose-sparing needles and syringes being supplied with the vaccine are used, it should be possible to obtain 6 full 0.3ml doses from the vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Care should be taken to ensure a full 0.3 ml dose will be administered to the patient from the same vial. If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 ml, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

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.

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.

Ordering

Pre-authorised NHS Trusts should order the Pfizer BioNTech COVID-19 vaccine via PHE's ImmForm platform. PCN designated sites need to use the Foundry system to order vaccines. Ordering is only available 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 combined 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 -80ºC and -60ºC (Reg174) or -90°C to -60°C (Comirnaty)
- the vaccine should be kept upright, in its original packaging and away from prolonged light exposure
- shelf-life is 6 months at -80°C to -60°C (Reg174) or 6 months at -90°C to -60°C (Comirnaty)

Thawing

- when required, frozen vials should be transferred to 2°C to 8°C to thaw; a 195 vial pack may take 3 hours to thaw at this temperature
- alternatively, the vaccine supplied under Reg174 can be defrosted and kept for up to 2 hours at up to 25ºC before being diluted for use
- frozen vials of Comirnaty may be thawed at temperatures up to 30°C for 30 minutes for immediate use. It must not be kept at room temperature (up to 30°C) for any longer than 2 hours prior to dilution
- once thawed, the vaccine should not be re-frozen

Delivery in a thawed state

The Pfizer BioNTech COVID-19 vaccine may be delivered to where it is going to be administered thawed but refrigerated between +2 and +8°C:

- refrigerated vaccine must be transferred immediately to a vaccine fridge on arrival and stored in a carefully monitored temperature range of +2 and +8°C
- when removed from the freezer, the thawed, unopened, undiluted vaccine has a maximum shelf life of up to 1 month at +2 and +8ºC

- the Reg 174 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 one month later if it has not been used
- the Comirnaty pack has a space on the label on the front which should state the expiry date on it
- 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 Pfizer BioNTech COVID-19 vaccine 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 Pfizer BioNTech COVID-19 vaccine 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
- an alcohol swab, a green hubbed needle and a 2 ml syringe to reconstitute - needles and syringes will be supplied together in boxes of 100 units

Reconstituting the vaccine

- clean hands with alcohol-based gel or soap and water
- assemble 1 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 1 vial of vaccine
- if removing the multidose vaccine vial directly from a ULT freezer, allow the vaccine to thaw as described above
- if removing the multidose vaccine vial from cold storage between +2 and +8°C, check that it has not been stored there for longer than 1 month
- allow the vaccine to come to room temperature, then gently invert the vial 10 times prior to dilution. One inversion means turning the vial upside down and back again. **Do not shake** – this could affect the potency of the vaccine
- check the expiry date and the appearance of the vaccine. Prior to dilution, the thawed vaccine may contain white to off-white opaque amorphous particles. Return the vial to the manufacturer if the appearance of the vaccine does not match this description
- clean the vial stopper with the single use antiseptic swab and allow to air dry fully
- connect the needle with a green hub to the 2 ml syringe
- invert the ampoule containing the Sodium Chloride 0.9% Solution for Injection diluent and withdraw 1.8ml slowly to avoid formation of bubbles. 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 time and date of dilution for the Reg174 vaccine. For Comirnaty, the date and time of discard should be recorded on the vial label

After dilution the vaccine should be used as soon as is practically possible. Reconstituted vaccine can be stored between 2°C and 25°C (Reg174) or 2°C and 30°C (Comirnaty) but **must be used within 6 hours following dilution.**

You can watch a video showing how to reconstitute and prepare the vaccine for use under Reg174 and use under CMA (Comirnaty)

Vaccine dose preparation

- if the vaccine has previously been reconstituted, check that it is still within the 6 hour allowed time period from when it was reconstituted
- clean top of vial with a single use antiseptic swab and allow to air dry fully
- unwrap 1 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.

2 doses of Pfizer BioNTech COVID-19 vaccine are required with a minimum 21 day interval between doses (but see COVID-19 vaccines schedule above).

Appendix 3. Storage and preparation of the COVID-19 Vaccine AstraZeneca

Vaccine composition

The COVID-19 Vaccine AstraZeneca contains recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein.

It also contains:

- L-Histidine
- L-Histidine hydrochloride monohydrate
- magnesium chloride hexahydrate
- polysorbate 80
- ethanol
- sucrose
- sodium chloride
- disodium edetate dihydrate
- water for injections

The vaccine does not contain preservative and it does not contain any components of animal origin.

Presentation

COVID-19 Vaccine AstraZeneca vaccine is presented in a multidose vial containing a solution which should be colourless to slightly brown, clear to slightly opaque and free of particles. **It does not require reconstitution**. The vial has a halobutyl rubber stopper and is sealed with an aluminium overseal. There is no latex in the vial stopper (bung).

COVID-19 Vaccine AstraZeneca will be delivered in packs that contain 10 vials.

2 different presentations of the AstraZeneca vaccine will be provided:

- 80 dose packs (Ten 4 ml vials with at least 8 doses per vial)

- 100 dose packs (Ten 5 ml vials with at least 10 doses per vial)

Only 1 product presentation will be available to order at 1 time. The majority of the vaccine provided will be the 8 doses per vial presentation but the 10 doses per vial presentation may be provided initially. **Vaccinators must check how many doses the vial they are using contains so that vaccine is not wasted.**

Each vial contains at least the number of doses stated. After withdrawing 8 or 10 full 0.5ml doses from the vial (depending on vial size), it may be possible to withdraw an additional full dose if the dose-sparing needles and syringes being provided with the vaccine are being used. Care should be taken to ensure a full 0.5 ml dose will be administered to the patient from the same vial. Where a full 0.5 ml dose cannot be extracted, the remaining contents should be discarded.

Ordering

NHS Trusts should order the COVID-19 Vaccine AstraZeneca via PHE's ImmForm platform. PCN designated sites need to use the Foundry system to order vaccines. Ordering is only available for pre-authorised sites.

Combined 1 ml fixed-needle (23g or 25g, 25mm length) dose-sparing syringes for administration will be available to order separately on ImmForm, as will syringes and longer-length (38mm) needles for administration to those who are morbidly obese.

Each carton of vaccine vials will include 1 Healthcare Professional Information sheet and 1 pad of the corresponding number of Patient Information Leaflets. Patient vaccination record cards will also be supplied with vaccine ordered.

Vaccinators are advised to read the latest administration instructions in the product information.

Storage

Upon delivery, COVID-19 Vaccine AstraZeneca should be transferred to a fridge immediately and stored between +2°C and +8°C. Vials should be kept upright in their box (mulberry colour panel is the bottom) and away from direct sunlight to prevent prolonged light exposure.

Once the vial bung is punctured, the vaccine must be used as soon as possible and within 6 hours of first puncture (during which time it can be stored between at +2°C to +25°C).

As the vaccine does not contain preservative, any unused vaccine must be discarded if not used within this 6 hour time period.

Vaccine dose preparation

COVID-19 Vaccine AstraZeneca does not require reconstitution.

- before drawing up a dose of vaccine from the multidose vial, clean hands with alcohol-based gel or soap and water
- each multi-dose vial should be clearly labelled with the date and time of expiry (which should be 6 hours from when it was first punctured)
- do not use the vaccine if the time of first puncture was more than 6 hours previously
- check the appearance of the vaccine. It should be colourless to slightly brown, clear to slightly opaque and free of any particles. Discard the vaccine if particulates or discolouration are present
- do not shake the vaccine vial
- the vial bung should be wiped with an alcohol swab and allowed to air-dry fully
- a 1 ml dose-sparing syringe with a 23g or 25g, 25mm fixed-needle should be used to draw up and administer the AstraZeneca vaccine
- separate 38mm length needles and syringes should be used for morbidly obese patients to ensure the vaccine can be injected into the muscle
- withdraw a dose of 0.5 ml 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

Dose and schedule

A single dose is 0.5ml.

2 doses of AstraZeneca vaccine are required with a minimum 28 day interval between doses (but see COVID-19 vaccines schedule above).

Appendix 4. Storage and preparation of the COVID-19 Vaccine Moderna

Vaccine composition

The COVID-19 Vaccine Moderna contains single-stranded RNA embedded in lipid nanoparticles.

It also contains:

- Lipid SM-102
- cholesterol
- 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
- 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)
- Trometamol (Tris)
- Trometamol hydrochloride (Tris HCl)
- Acetic acid
- sodium acetate trihydrate
- sucrose
- water for injections

The vaccine does not contain preservative and it does not contain any animal products.

Presentation

COVID-19 Vaccine Moderna vaccine is presented in a multidose vial containing a solution which should be white to off-white and may contain white or translucent product-related particulates. **It does not require reconstitution**. The vial has a chlorobutyl rubber stopper and is sealed with an aluminium overseal. There is no latex in the vial stopper (bung).

COVID-19 Vaccine Moderna will be delivered in cartons which each containing 10 multidose vials.

Ordering

NHS Trusts should order the COVID-19 Vaccine Moderna via PHE's ImmForm platform. PCN designated sites need to use the Foundry system to order vaccines. Ordering is only available for pre-authorised sites.

Combined 1 ml fixed-needle (23 gauge, 25mm length) dose-sparing syringes for administration will be available to order separately on ImmForm, as will syringes and longer-length (38mm) needles for administration to those who are morbidly obese.

Vaccination record cards and the Patient Information leaflets will also be provided with each vaccine pack.

Delivery in frozen state

The COVID-19 Vaccine Moderna vaccine will be delivered frozen **to healthcare facilities with the appropriate freezers to store the vaccine vials between -25 °C to -15 °C until ready for use**.

- thaw in refrigerated conditions between +2°C to +8°C for 2½ hours. Let each vial stand at room temperature for 15 minutes before administering. To note: whilst this is the thawing advice stated in the Moderna vaccine's Summary of Product Characteristics, in practice it has been found to take significantly longer than this to thaw. The Specialist Pharmacy Service Standard Operating Procedure "**Unpacking of frozen Moderna COVID-19 Vaccine and transfer to fridges to thaw**" states that the vials may take up to 24 hours to thaw in a fridge
- alternatively, thaw at room temperature between +15°C to +25°C for 1 hour
- once thawed, the vaccine cannot be re-frozen and may be stored refrigerated at +2°C to +8°C, protected from light, for up to 30 days if not used (if it has not been opened and the bung has not been punctured by a needle)
- shelf-life is 7 months at -25°C to -15°C

Delivery in thawed state

The COVID-19 Vaccine Moderna may be delivered to where it is going to be administered thawed but refrigerated between +2°C and +8°C:

- refrigerated vaccine must be transferred immediately to a vaccine fridge on arrival and stored in a carefully monitored temperature range of +2°C and +8°C
- once thawed, the unopened vaccine may be stored refrigerated at +2°C to +8°C, protected from light, for up to a maximum of 30 days

- the vaccine pack should have a label on the front stating the time it was removed from the freezer into storage at +2°C to +8°C and the date and time by which it must be discarded 30 days later if it has not been used
- The unopened vaccine may be stored at +8°C to +25°C for up to 12 hours after removal from refrigerated conditions.

Use of the vaccine once bung punctured

Once the vial bung is punctured, the vaccine must be used as soon as possible and within 6 hours of first puncture (during which time it can be stored between +2°C to +25°C).

As the vaccine does not contain preservative, any unused vaccine must be discarded if not used within this 6 hour time period.

Vaccine dose preparation

COVID-19 Vaccine Moderna does not require reconstitution.

- before drawing up a dose of vaccine from the multidose vial, clean hands with alcohol-based gel or soap and water
- each multi-dose vial should be clearly labelled with the date and time of expiry (which should be 6 hours from when it was first punctured)
- do not use the vaccine if the time of first puncture was more than 6 hours previously
- check the appearance of the vaccine. It should be white to off-white and may contain white or translucent product-related particulates. If other particulate matter or discolouration are present, the vaccine should not be administered.
- swirl the vial gently after thawing and between each withdrawal. **Do not shake the vaccine vial**
- the vial bung should be wiped with an alcohol swab and allowed to air-dry fully
- a 1 ml dose-sparing syringe with a 23g, 25mm fixed-needle should be used to draw up and administer the Moderna vaccine (these will be provided with the vaccine).
- separate 38mm length needles and syringes should be used for morbidly obese patients to ensure the vaccine can be injected into the muscle
- withdraw a dose of 0.5 ml 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

Dose and schedule

A single dose is 0.5ml.

2 doses of Moderna vaccine are required with a minimum 28 day interval between doses (but see: COVID-19 vaccines schedule above).

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