

5a

COVID-19

SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2, SARS-COV-2

NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the Summary of Product Characteristics (SmPC) of the vaccines. When this occurs, the recommendations in these guidelines, which are based on current expert advice from NIAC, should be followed.

NOTE:

This chapter will be updated as new evidence becomes available.

Acronyms used in this document

AEFI	Adverse event following immunisation
BMI	Body mass index
BTS/SIGN	British Thoracic Society/Scottish Intercollegiate Guidelines Network
COPD	Chronic Obstructive Pulmonary Disease
COVID-19	Coronavirus disease 2019
EC	European Commission
EMA	European Medicines Agency
HCW	Healthcare worker
HPRA	Health Products Regulatory Authority
HPV	Human Papillomavirus
IM	Intramuscular
MERS	Middle East Respiratory Syndrome
mRNA	Messenger RNA
NIAC	National Immunisation Advisory Committee
NIO	National Immunisation Office
NA	Neutralising antibody
PCR	Polymerase Chain Reaction
PEG	Polyethylene glycol
S antigen	Spike glycoprotein
SARS	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SmPC	Summary of Product Characteristics
VLP	Virus-Like Particle
WHO	World Health Organization

Key Updates

- COVID-19 Vaccine AstraZeneca®
 - pregnancy

5a.1 Introduction

Prior to the 2020 pandemic, six coronaviruses were known to be capable of causing disease in humans. Four of these (229E, NL63, OC43, HKU1) generally cause minor respiratory illnesses such as the common cold. More rarely, they can cause more serious lower respiratory tract disease in those with underlying pulmonary disorder or immunocompromise. Two coronaviruses – Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV, identified 2002) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV, identified 2012) - cause more severe disease, with mortality rates of 10% and 35% respectively.

In December 2019, an outbreak of severe pneumonia was reported in Wuhan, China. The causative organism was a coronavirus, since named **Severe Acute Respiratory Syndrome CoronaVirus** type 2 (SARS-CoV-2). The disease it causes is called **Coronavirus disease 2019** (COVID-19). On March 11th 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic.

5a.2 Epidemiology

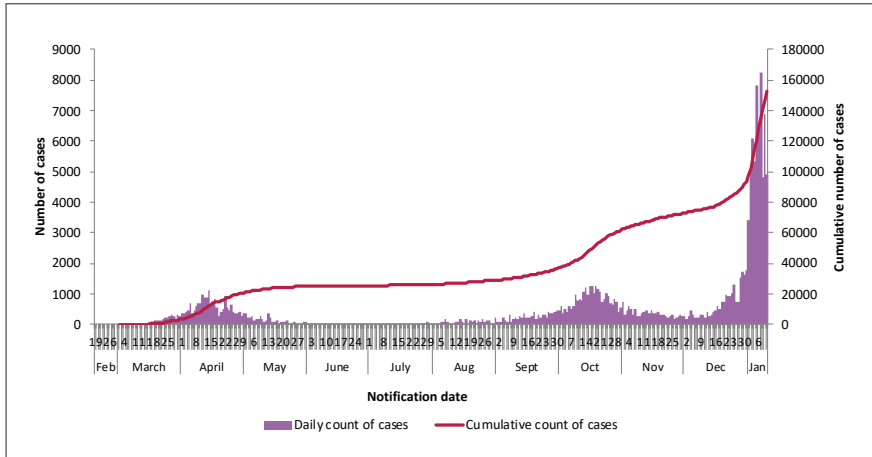
Note: Refer to www.hpsc.ie for the most up-to-date information on COVID-19 epidemiology.

As of 6 January 2021, the WHO has reported over 86.5 million cases and 1.87 million deaths from COVID-19.

The first laboratory confirmed case of COVID-19 in Ireland was on 29 February 2020. As of 10 January 2021, 152,539 confirmed COVID-19 cases and 2352 deaths (2092 confirmed) have been reported with a case fatality rate of 1.5%. The cumulative number of COVID-19 cases rose sharply until the end of April 2020. Following a period of significant public health restrictions, case numbers were low in the summer months. A second wave occurred between August and November 2020. A third larger wave began in November, 2020 and is ongoing.

Figure 5a.1 Number and cumulative number of confirmed COVID-19 cases notified in Ireland by notification date to midnight 10/01/2021

Source: HPSC



COVID-19
12 February 2021

The highest proportion of hospitalisations and deaths are in those aged 65 and older. Of those hospitalised with COVID-19, 63% had an underlying medical condition. Of those admitted to an intensive care unit, 89% had an underlying medical condition.

The main underlying medical conditions associated with increased risk of hospitalisation are chronic respiratory disease, chronic heart disease, hypertension, Type I and Type II diabetes mellitus, chronic neurological disease, cancer, obesity (Body mass index (BMI) ≥ 40), and chronic kidney disease.

Healthcare workers account for 17% of COVID-19 cases; 32% of these cases occurred in those working in long-stay care facilities (nursing homes, residential institutions, community hospitals).

Outbreaks have occurred among patients and staff in hospitals, and among people living or working in crowded situations where self-isolation and physical distancing may be difficult to maintain (e.g. meat processing plants, the Irish Traveller community and direct provision centres).

The lowest proportion of hospitalisations and deaths is in those under 15 years of age.

In Ireland, during the first wave, 56% of deaths occurred among residents of nursing homes and long-term care facilities.

Transmission occurs mainly through close contact (within 2 metres for more than 15 minutes cumulative exposure) via respiratory droplets. Transmission can also occur by aerosol spread or contact with contaminated fomites. Airborne transmission is not believed to be a major driver of the pandemic. The virus has been detected in stools, but this has not been proven to be an important route of transmission.

Most transmission occurs indoors, particularly in settings with poor ventilation. People living or working in crowded settings are at increased risk of acquiring infection because of an increased likelihood of close contact.

The incubation period is on average 5 – 6 days (range 2 to 14 days) following exposure. The reproductive number (R_0) of SARS-CoV-2 in an unmitigated setting is estimated to be between 4-6.

Infectivity is highest at the time of symptom onset and for a limited time (up to 3 days) before symptoms develop. The risk of transmission decreases significantly after the first week of illness. Whether individuals who remain asymptomatic throughout the course of their infection commonly transmit infection is not clear. While there are conflicting data, young children appear less likely to transmit infection than adolescents or adults.

5a.3 Effects of Covid-19

COVID-19 affects people in different ways. Overall, 80% of infections are asymptomatic or mild, 15% moderate and 5% severe. These figures are estimates and vary across different countries, age cohorts and ethnic groups.

The most common symptoms are fever, dry cough, dyspnoea, fatigue, anorexia and loss or change of taste (ageusia/dysgeusia) or smell (anosmia/parosmia). Less common symptoms include myalgia, sore throat, diarrhoea, conjunctivitis, headache, rash, and chest pain or pressure.

Symptoms among those aged 65 years and older and those with underlying medical conditions may be atypical, and they may present without fever or respiratory symptoms. While severe illness and death have been reported at all ages, the risk of severe outcome increases with age and for those with chronic medical conditions.

Morbidity and mortality are higher in those:

- Age 65 and older
- Age 18-64 with:
 - Cancer
 - Cardiovascular disease (e.g., cardiomyopathy, chronic heart failure, congenital heart disease, coronary artery disease)
 - Chronic kidney disease (receiving dialysis, or eGFR <15 ml/min)
 - Chronic liver disease
 - Chronic neurological disease compromising clearance of respiratory secretions
 - Chronic respiratory disease e.g., chronic obstructive pulmonary disease (COPD), cystic fibrosis, severe asthma (BTS/SIGN≥4)
 - Diabetes mellitus, Types 1 and 2
 - Down syndrome
 - Hypertension
 - Immunocompromise due to disease or treatment
 - Obesity (BMI >40)
 - Organ transplant history
 - Sickle cell disease
- From Black, Asian and minority ethnic backgrounds

Pregnant women: Pregnant women are at a similar risk to non-pregnant women of contracting COVID-19 disease. Most pregnant women who are infected with COVID-19 will only experience mild to moderate symptoms, and the risk of passing COVID-19 virus to the baby is low.

However, pregnant women who become ill from COVID-19 may be more likely to be admitted to hospital, to need care in an ICU, and to die when compared with non-pregnant women patients. Women from Black, Asian and minority ethnic backgrounds may be more likely than other pregnant women to be admitted to hospital with COVID-19 disease.

The following factors may increase the risks of severe illness in pregnant women:

- Those with the listed risk factors in the bullets above
- Age >35 years
- Infection in the third trimester (28 weeks or more)
- BMI ≥30

Children: In addition to the above conditions, the risks of severe disease and death may be increased in children and adolescents with medical complexity and some severe genetic disorders. Consideration may be given to offering vaccination to those aged >12 years of age.

5a.4. Vaccines

All vaccines seek to introduce key antigens into the cell to stimulate protective immune responses. For SARS-CoV-2 the key antigen of interest is the spike protein, as it is the main target for neutralising antibodies. Neutralising antibodies (NA) act to block virus entry into the host's cell by interfering with attachment of the receptor binding domain of the spike protein to the angiotensin-converting enzyme 2 cellular receptor. Immunity to SARS-CoV-2 is likely to be enhanced if an appropriate cellular as well as humoral response can be elicited.

There are several SARS-CoV-2 vaccines in Phase 3 trials using existing and novel technologies. The European Commission (EC) has authorised two messenger RNA (mRNA) vaccines and one virus vector vaccine.

mRNA vaccines

Messenger RNA vaccines consist of genetic material (mRNA) that instructs the recipient's antigen-presenting cells to make the identified antigen, thus stimulating an immune response against the virus.

For SARS-CoV-2, mRNA vaccines encode the spike protein that, when expressed on the cell surface, provokes generation of NAs and activation of T-cells. When exposed to SARS-CoV-2, the NAs prevent infection by blocking virus fusion with the host cell. To facilitate entry into a host cell, the mRNA is encapsulated in a lipid nanoparticle. Rapid degradation of mRNA within cells contributes to the safety profile of these vaccines.

Advantages of mRNA vaccines include their high potency, ability for rapid development, and cost-efficient production. They allow the potential to combine multiple mRNAs into a single vaccine. As no viral vector is required, mRNA vaccines evade pre-existing immunity, which can limit effectiveness of vector-based vaccines.

Comirnaty® (Pfizer/BioNTech) was granted conditional marketing authorisation by the EC on 21 December 2020.

This vaccine is a nucleoside-modified mRNA vaccine based on the SARS-CoV-2 spike (S) antigen. The vaccine is formulated in lipid nanoparticles, which enables delivery of the RNA into the host cells to allow expression

of the S antigen. The vaccine elicits both neutralising and cellular immune responses to the S antigen. The mRNA is usually degraded within a few days. Data currently available is limited to those aged 16 years and older. The vaccine is administered in a two-dose schedule at least 21 days apart.

Data from the randomised Phase 3 trial, based on 36,621 participants randomised 1:1 to vaccine or placebo in per-protocol efficacy analysis, demonstrated a two-dose vaccine efficacy of 95% (95% confidence interval of 90.3% to 97.6%) in those aged 16 and above. Efficacy was similar in all age groups.

Safety data was based on 43,252 participants enrolled in the Phase 1 / 2 / 3 trial. The most frequent adverse reactions were pain at the injection site (84%), fatigue (63%), headache (30%), chills (38%), arthralgia (24%) and pyrexia (14%). Symptoms were usually mild to moderate in intensity and resolved within a few days. Typically, these reactions were more common after the second dose and in younger patients.

The frequency of serious adverse events was <0.5% and balanced between the two arms of the trial. Four cases of Bell's palsy were reported in those vaccinated, and none in the comparator group. The frequency was similar to the normal background frequency in the population and could represent a chance occurrence. Monitoring will continue in the trials and in post authorisation surveillance.

COVID-19 Vaccine Moderna® was granted conditional marketing authorisation by the EC on 6 January 2021.

This vaccine is a mRNA vaccine, formulated in lipid nanoparticles to enable delivery of the RNA into the host cells and allow expression of the S antigen. The antigen expressed is similar to the that expressed in Comirnaty® Pfizer/ BioNTech vaccine and elicits both NA and cellular immune responses to the S antigen. The mRNA is usually degraded within a few days. The vaccine is administered in a two-dose schedule, 28 days apart.

In a Phase 1 study that included 40 adults aged > 56 years of age, the most common adverse events were headache, fatigue, myalgia, chills, and injection-site pain. Events were more common after the second dose and were generally classed as of moderate severity. Symptoms typically occurred within two days of vaccination and resolved quickly. The vaccine was immunogenic with NA levels similar to those achieved in younger adults.

A Phase 3 trial included 30,000 participants aged 18 years and older. More than 7,000 participants were over 65 years of age and 5,000 were <65 years

of age with comorbidities. Overall, 42% of participants were in a medically high-risk category. Interim analysis showed an efficacy of 94.5%. The vaccine was also effective against severe disease.

The vaccine was generally well tolerated. Most adverse events were mild or moderate. Events categorised as severe after either dose occurred in 2-10% of subjects. They included pain and redness at the injection site, fatigue, myalgia, arthralgia, and headache. Three cases of Bell's palsy were reported in those vaccinated, and one in the comparator group. The frequency was similar to the normal background frequency in the population and could represent a chance occurrence. Monitoring will continue in the trials and in post authorisation surveillance.

Viral vector vaccines

A virus that is non-pathogenic (does not cause infection) in humans, often an adenovirus, is selected to transport key antigens into the recipient's cells to evoke a protective immune response. In the case of SARS-CoV-2, the genome of the vector virus is genetically modified to encode the spike protein of SARS-CoV-2 which, when expressed by the host cell, provokes the immune response stimulating NA production.

ChAdOx1 nCoV-19 vaccine (AZD12222, AstraZeneca/Oxford) was granted conditional marketing authorisation by the EC on 29 January 2021.

This vaccine consists of a non-replicating chimpanzee adenovirus vector in which the genome has been genetically modified to encode the spike protein. Using this adenovirus overcomes the potential limitation of pre-existing immunity to a human adenovirus vector that could impede an effective immune response. The vaccine is administered in a two-dose schedule, 4-12 weeks apart.

In a phase 2/3 trial, 420 adults aged 18 and older were included. Local and systemic reactions (injection-site pain, feeling feverish, muscle ache and headache) occurred in 61 to 88% of recipients, were mild to moderate, were less common in those ≥ 56 years of age, and generally resolved within a few days. Thirteen serious adverse events were reported, none of which was judged as being related to the vaccine. No serious unexpected adverse reactions occurred. The vaccine was immunogenic in all age groups studied.

Over 26,000 participants aged ≥ 18 years are included in an ongoing randomised, active controlled Phase 2/3 trial assessing safety, efficacy and immunogenicity of the COVID-19 vaccine compared with saline or a meningococcal ACWY vaccine. One or two low or standard doses are given.

Participants are healthy or have medically stable chronic diseases and are at increased risk of being exposed to the virus.

In interim analysis, vaccine efficacy was reported at 62-90%, depending on the dose regimen. The vaccine was shown to be highly effective at preventing severe disease and hospitalisation.

Ad26.COVS vaccine, Janssen (Johnson and Johnson) is undergoing an EMA rolling review. This vaccine consists of an adenovirus Type 26 vector in which the genome has been genetically modified to encode the spike protein.

The following are other examples of different platforms used in COVID-19 vaccine trials:

Protein subunit vaccines

These vaccines are based on injection of key viral antigens, e.g., a recombinant spike protein, with or without an adjuvant, thus directly stimulating the immune response.

Virus Like Particle (VLP) vaccines

Viral antigenic proteins produced using recombinant techniques are used to generate an immune response similar to that generated by the virus. Some of these proteins are assembled into VLPs, which mimic the wild virus structure but are not infectious as they contain no genetic material.

Whole virus vaccines

These consist of virus modified either by inactivation by chemical or heat treatment (non-live) or attenuation (live but weakened form of the virus) such that they do not cause the actual disease. These methods of vaccine development are well established. Examples include the whole cell pertussis vaccine (inactivated bacteria) and the BCG, MMR, varicella, and oral polio vaccines.

It is likely that several more COVID-19 vaccines will be authorised within the next 6-12 months.

COVID-19 vaccine safety

To date over over 100 million individuals have received a COVID-19 vaccine. While vaccine development has been rapid, the very high standards for safety monitoring have not been compromised.

Most adverse events following immunisation (AEFI) have onset within 6 weeks following vaccination. Thus, a minimum follow-up time of six to eight weeks is required by the regulatory authorities prior to consideration of vaccines for conditional authorisation.

As with all newly authorised vaccines, clinical trials during the development phase are by necessity limited in the number of selected participants included, with follow up performed under controlled conditions for a defined period of time. It is possible that certain adverse reactions, particularly those that rarely or very rarely occur, may only emerge during real life use in much larger and more diverse populations. It is therefore essential that the safe and effective use of authorised vaccines be continuously monitored.

Vaccine availability and storage

An up-to-date list of licensed vaccines will be available on the Health Products and Regulatory Authority (HPRA) website www.hpra.ie

A list of the vaccines currently available from the National Cold Chain Service can be found at <https://www.hse.ie/eng/health/immunisation/>

Vaccines should be stored at the temperature specified in the Summary of Product Characteristics (SmPC) (either -80°C to -60°C, -20°C, or between +2 to +8°C). Those that require reconstitution must be used within a defined number of hours.

All vaccines are provided in multi-dose vials. Appropriate infection control precautions should always be taken. Specific guidelines will be developed and available on the National Immunisation Office (NIO) website at www.immunisation.ie

5a.5 Recommendations

The objective of the vaccination programme for SARS CoV-2 is to ensure equitable access to a safe and effective vaccine with the goals of limiting mortality and morbidity from COVID-19, protecting healthcare capacity and enabling social and economic activity.

With limited vaccine supplies available initially, NIAC recommends that vaccination is carried out in the following priority order:

NOTE: The order and the groups/individuals may change as more information becomes available. The timeframe of vaccination will depend on several factors, e.g., availability of vaccines and vaccine characteristics.

Group	Rationale
Adults aged ≥ 65 years who are residents of long-term care facilities. Consider offering vaccination to all residents and staff on site	At greatest risk of severe illness and death In Ireland, in the first wave of COVID-19, 56% of deaths occurred in this setting
Frontline HCW ¹ in direct patient contact roles or who risk exposure to bodily fluids or aerosols	At very high or high risk of exposure and/or transmission. In the first wave over 30% of cases were in healthcare workers
Aged 70 and older in the following order: 85 and older 80-84 75-79 70-74	At higher risk of hospitalisation and death
Other HCWs not in direct patient contact	Provide essential health services, protect patients
Aged 65-69. Prioritise those with medical conditions ² which put them at high risk of severe disease	At higher risk of hospitalisation and death
Key workers (to be further refined)	Providing services essential to the vaccination programme
Aged 16-64 years with medical conditions ² which put them at high risk of severe disease	At higher risk of hospitalisation
Residents of long-term care facilities aged 16-64	High risk of transmission
Aged 16-64 years living or working in crowded settings where self-isolation and social distancing may be difficult to maintain	Disadvantaged sociodemographic groups more likely to experience a higher burden of infection
Key workers in essential jobs who cannot avoid a high risk of exposure to COVID-19. They include workers in the food supply system, public and commercial transport and other vital services	High risk of exposure as unable to work without physical distancing
Those who are essential to education and who face disease exposure -primary and second level school staff, childcare workers, maintenance workers, school bus drivers etc.	To maintain the opening of full-time education of all children who have been disproportionately impacted from the pandemic
Aged 55-64 years	Based on risk of hospitalisation

Those in occupations important to the functioning of society, e.g., third level institutions, entertainment and goods-producing industries who work in settings where protective measures can be followed without much difficulty	Moderate risk of exposure
Aged 16-54 years who did not have access to the vaccine in prior phases	If evidence demonstrates the vaccine(s) prevent transmission, those aged 18-34 should be prioritised due to their increased level of social contact and role in transmission
Children and adolescents up to 16 years (to be refined)	If evidence demonstrates vaccine safety and efficacy

Pregnant women who are healthcare workers or who have medical conditions which put them at high risk of severe disease are included in the respective priority groups. The priority for other pregnant women will be determined when more evidence is available.

¹HCW who work in and out of all healthcare settings, including vaccinators

²See Section 5a.3

Authorised COVID-19 vaccines

- **Comirnaty®(Pfizer/BioNTech)**

Conditional marketing authorisation granted by the EC on 21 December 2020.

- **COVID-19 Vaccine Moderna®**

Conditional marketing authorisation granted by the EC on 6 January 2021.

- **COVID-19 Vaccine AstraZeneca®**

Conditional marketing authorisation granted by the EC on 29 January 2021.

Any currently authorised COVID-19 vaccine can be given to adults of all ages, including those aged 70 and older.

Vaccination of those aged 70 and older should not be delayed. Where practicable and timely, those aged 70 and older should be given a mRNA vaccine.

mRNA vaccines

Comirnaty® (Pfizer/BioNTech)

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions to the HPRA.

The vaccine should be stored in a freezer at -80°C to -60°C . Each pack contains 195 vials. Vials should be transferred to $+2^{\circ}\text{C}$ to $+8^{\circ}\text{C}$ to thaw which may take 3 hours. Alternatively, frozen vials may be thawed for 30 minutes at temperatures up to $+30^{\circ}\text{C}$ for immediate use.

After thawing, undiluted vaccine can be stored for up to 120 hours at $+2^{\circ}\text{C}$ to $+8^{\circ}\text{C}$ and up to 2 hours at up to $+30^{\circ}\text{C}$. Once thawed, the vaccine cannot be re-frozen.

The vaccine requires dilution with 1.8ml of 0.9% sodium chloride. After dilution, the vaccine should be kept at $+2^{\circ}\text{C}$ to $+30^{\circ}\text{C}$ and used within 6 hours.

Licensed indications

Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 16 years of age and older.

Dose and route of administration

The dose of vaccine is 0.3 ml intramuscularly (IM) into the deltoid muscle.

The diluted vial contains 2.25 ml if the correct volume of diluent has been used in accordance with the SmPC. If more than six 0.3ml doses can be safely and accurately withdrawn from a diluted vial, they can be used as valid doses. There should be no pooling of different vaccine vials.

The course consists of 2 doses 21-28 days apart.

If the interval between doses is longer than 28 days, the second dose should still be given as soon as possible. The course does not need to be restarted.

If the interval between doses is less than 21 days, a further dose is not required. If the second dose is given between 17 and 20 days after the first dose, it is a valid dose. Evidence of efficacy of doses given before 17 days is lacking.

Interchangeability

There is no data on the interchangeability of COVID-19 vaccines. The same vaccine should be used for both doses.

Contraindications

Anaphylaxis (serious systemic allergic reaction requiring medical intervention) following a previous dose of the vaccine or any of its constituents (including polyethylene glycol (PEG)).

<https://www.hse.ie/eng/health/immunisation/hcinfo/guidelines/anaphylaxis.pdf>

Appropriate support should be available in case of anaphylaxis or fainting after vaccine administration.

Precautions should also be in place to minimise injury from fainting.

Precautions

Acute severe febrile illness; defer until recovery.

Advice from a relevant specialist should be sought for a person with a history of an immediate systemic allergic reaction to any other vaccine, injectable therapy or polysorbate 80 (because of the possibility of cross reactivity with PEG). The risks should be weighed against the benefits of vaccination. The patient should be observed for 30 minutes after vaccination.

Vaccination should be deferred until clinical recovery from COVID-19 and at least four weeks after diagnosis or onset of symptoms, or four weeks from the first PCR positive specimen in those who are asymptomatic.

Vaccination is not contraindicated for those with persisting symptoms post COVID-19 unless there is evidence of recent clinical deterioration.

Post vaccination observation period

- Those with no history of anaphylaxis from any cause: 15 minutes
- Those with a history of anaphylaxis from any cause: 30 minutes
- Those with immediate itching, swelling or urticarial reaction at the vaccination site: 30 minutes or longer as clinically indicated

Immunocompromised

Data are not currently available to establish vaccine safety and efficacy in these groups. Individuals with immunosuppression due to disease or treatment may be vaccinated if they have no contraindications.

Pregnancy

There is limited experience with use of this vaccine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy,

embryo/foetal development, delivery or post-natal development. Although the available data do not indicate any safety concerns or harm to pregnancy, there is insufficient evidence to recommend routine use of COVID-19 vaccines during pregnancy. Administration of this vaccine in pregnancy should be considered when the potential benefits outweigh any potential risks for the mother (e.g. at high risk of severe disease, HCW) and foetus.

Pregnant women who meet the priority criteria for vaccination and their obstetric caregivers should engage in shared decision-making in advance of vaccination. Counselling should balance available data on vaccine safety, risks to pregnant women from SARS-CoV-2 infection, and a woman's individual risk for infection and severe disease.

Where the risk/benefit is favourable, the two doses should be given 28 days apart. The two dose schedule should be given between 14 and 33 completed weeks of gestation.

Breastfeeding

There is no known reason for vaccinees to avoid breastfeeding. Breastfeeding mothers should be vaccinated according to their risk grouping.

Children and adolescents under 16 years of age

There is no data available on vaccine safety and efficacy in children.

Vaccination of those with bleeding disorders or on anticoagulants

Individuals with a bleeding disorder or receiving anticoagulant therapy may develop haematomas in IM injection sites. Prior to vaccination, inform the recipient about this risk. For those with thrombocytopenia (platelet count $<50 \times 10^9/L$), consult the supervising consultant. People with mild bleeding disorders or on maintenance dose Emicizumab (Hemlibra®) do not require haemostatic cover for vaccination. Details of haemostatic cover for all others can be found in the Patient Information tab at

<http://www.stjames.ie/services/hope/nationalcoagulationcentre>

Those with inherited coagulopathies who require factor replacement therapy should receive it on the day of vaccination, prior to the IM vaccination.

If there is uncertainty about the need for cover, contact the patient's Comprehensive Care Centre.

Those receiving long-term anticoagulation with either Warfarin® or heparin are not considered to be at higher risk of bleeding complications following vaccination. There is no reason to expect that there is a greater risk of bleeding complications with the newer direct oral anticoagulants or antiplatelet agents, than with other anticoagulants.

People on Warfarin® should follow their usual schedule for international normalised ratio (INR) testing and can be vaccinated if it is less than 4.0. If the INR is 4.0 or more, follow the advice of the clinic/practice managing Warfarin® and wait until the INR is less than 4.0 to be vaccinated.

See [Chapter 2, sections 2.4.6 and 2.4.7](#) for further information, including technique for IM injection, in this patient group.

Adverse reactions

A full list of adverse reactions may be found in the Summary of Product Characteristics (SmPC).

Terms used for frequency of adverse events

Very common: >1/10

Common: >1/100 and <1/10

Uncommon: >1/1,000 and <1/100

Rare: >1/10,000 and <1/1,000

Very rare: <1/10,000

Local: Very common: injection site swelling and erythema

Common: injection site pain, erythema

Uncommon: injection site pruritus

General: Very common: arthralgia, fatigue, fever, headache, myalgia

Common: nausea

Uncommon: insomnia, lymphadenopathy in the same arm as vaccination, malaise, extremity pain

Rare: acute peripheral facial paralysis

The most frequent adverse reactions during clinical trials in those aged ≥ 16 years were injection site pain (> 80%), fatigue (> 60%), headache (> 50%), myalgia and chills (> 30%), arthralgia (> 20%), pyrexia and injection site swelling (> 10%), which were usually mild or moderate in intensity, and resolved within a few days after vaccination. A slightly lower frequency of adverse events was associated with greater age. A higher rate of pyrexia was seen after the second dose so consideration may be given to staggering healthcare worker vaccinations.

Co-administration

Co-administration with other vaccines has not been studied. It is prudent to leave 14 days between administering COVID vaccine and administering another vaccine.

Duration of immunity

Clinical trial follow-up is ongoing to determine the duration of protection from the vaccine.

Vaccinated persons should continue to follow all current public health guidance to protect themselves and others.

Vaccine effectiveness

Vaccine recipients may not be protected until 7 days after the second dose and the vaccine may not protect all vaccinees.

Booster doses

The need for and timing of booster doses has not been established. No additional doses beyond the two-dose primary series are routinely recommended at this time.

COVID-19 Vaccine Moderna®

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions to the HPRA.

The vaccine should be stored in a freezer at -25°C to -15°C. Each pack contains 10 vials. Vials should be transferred to +2°C to +8°C to thaw which may take 2 and a half hours, and must sit at room temperature for 15 minutes before administering. Alternatively, frozen vials may be thawed for 1 hour at room temperature between +15°C to +25°C for immediate use.

After thawing, the vaccine can be stored for up to 30 days at +2°C to +8°C and up to 12 hours at +8°C up to +25°C. Once thawed, the vaccine cannot be re-frozen.

The vaccine does not require dilution. Once the multidose vial is punctured the vaccine should be kept at +2°C to +25°C and used as soon as possible and within 6 hours.

Licensed indications

Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 18 years of age and older.

Dose and route of administration

The dose of vaccine is 0.5 ml IM, preferably into the deltoid muscle.

If more than ten 0.5ml doses can be safely and accurately withdrawn from a diluted vial, they can be used as valid vaccine doses. There should be no pooling of different vaccine vials.

The course consists of two doses, 28 days apart.

If the interval between doses is longer than 28 days, the second dose should still be given as soon as possible. The course does not need to be restarted.

If the interval between doses is less than 28 days, a further dose is not required. If the second dose was given between 24 and 27 days after the first dose, it is a valid dose. Evidence of efficacy of doses given before 24 days is lacking.

Interchangeability

There is no data on the interchangeability of COVID-19 vaccines. The same vaccine should be used for both doses.

Contraindications

Anaphylaxis (serious systemic allergic reaction requiring medical intervention) following a previous dose of the vaccine or any of its constituents (including polyethylene glycol (PEG)).

<https://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/anaphylaxis.pdf>

Appropriate support should be available in case of anaphylaxis or fainting after vaccine administration.

Precautions should be in place to minimise injury from fainting.

Precautions

Acute severe febrile illness; defer until recovery.

Advice from a relevant specialist should be sought for a person with a history of an immediate systemic allergic reaction to any other vaccine, injectable therapy or polysorbate 80 (because of the possibility of cross reactivity with PEG). The risks should be weighed against the benefits of vaccination. The patient should be observed for 30 minutes after vaccination.

Vaccination should be deferred until clinical recovery from COVID-19 and at least four weeks after diagnosis or onset of symptoms, or four weeks from the first PCR positive specimen in those who are asymptomatic.

Vaccination is not contraindicated for those with persisting symptoms post COVID-19 unless there is evidence of recent clinical deterioration.

Post vaccination observation period

- Those with no history of anaphylaxis from any cause: 15 minutes
- Those with a history of anaphylaxis from any cause: 30 minutes
- Those with immediate itching, swelling or urticarial reaction at the vaccination site: 30 minutes or longer as clinically indicated

Immunocompromised

Data are not currently available to establish vaccine safety and efficacy in these groups. Individuals with immunosuppression due to disease or treatment may be vaccinated if they have no contraindications.

Pregnancy

There is limited experience with use of this vaccine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, delivery or post-natal development. Although the available data do not indicate any safety concerns or harm to pregnancy, there is insufficient evidence to recommend routine use of COVID-19 vaccines during pregnancy. Administration of this vaccine in pregnancy should be considered when the potential benefits outweigh any potential risks for the mother (e.g. at high risk of severe disease, HCW) and foetus.

Pregnant women who meet the priority criteria for vaccination and their obstetric caregivers should engage in shared decision-making in advance of vaccination. Counselling should balance available data on vaccine safety, risks to pregnant women from SARS-CoV-2 infection, and a woman's individual risk for infection and severe disease.

Where the risk/benefit is favourable, the two doses should be given 28 days apart. The two dose schedule should be given between 14 and 33 completed weeks of gestation.

Breastfeeding

There is no known reason for vaccinees to avoid breastfeeding. Breastfeeding mothers should be vaccinated according to their risk grouping.

Children and adolescents under 18 years of age

There is no data available on vaccine safety and efficacy in children.

Vaccination of those with bleeding disorders or on anticoagulants

Individuals with a bleeding disorder or receiving anticoagulant therapy may develop haematomas in IM injection sites. Prior to vaccination, inform the recipient about this risk. For those with thrombocytopenia (platelet count $<50 \times 10^9/L$), consult the supervising consultant. People with mild bleeding disorders or on maintenance dose Emicizumab (Hemlibra[®]) do not require haemostatic cover for vaccination. Details of haemostatic cover for all others can be found in the Patient Information tab at

<http://www.stjames.ie/services/hope/nationalcoagulationcentre>

Those with inherited coagulopathies who require factor replacement therapy should receive it on the day of vaccination, prior to the IM vaccination.

If there is uncertainty about the need for cover, contact the patient's Comprehensive Care Centre.

Those receiving long-term anticoagulation with either Warfarin® or heparin are not considered to be at higher risk of bleeding complications following vaccination. There is no reason to expect that there is a greater risk of bleeding complications with the newer direct oral anticoagulants or antiplatelet agents, than with other anticoagulants.

People on Warfarin® should follow their usual schedule for international normalised ratio (INR) testing and can be vaccinated if it is less than 4.0. If the INR is 4.0 or more, follow the advice of the clinic/practice managing Warfarin® and wait until the INR is less than 4.0 to be vaccinated.

See [Chapter 2, sections 2.4.6 and 2.4.7](#) for further information, including technique for IM injection, in this patient group.

Adverse reactions

A full list of adverse reactions may be found in the Summary of Product characteristics (SmPC).

Terms used for frequency of adverse events

Very common: >1/10

Common: >1/100 and <1/10

Uncommon: >1/1,000 and <1/100

Rare: >1/10,000 and <1/1,000

Very rare: <1/10,000

Local: Very common: injection site pain and swelling

Common: injection site erythema, rash and urticaria

Uncommon: injection site pruritis

General: Very common: arthralgia, axillary lymphadenopathy on the side of injection, chills, fatigue, fever, headache, myalgia, nausea, vomiting

Rare: acute peripheral facial paralysis, facial swelling (in those with a history of dermatological fillers)

The most frequent adverse reactions during clinical trials in those aged ≥18 years were injection site pain (>90%), fatigue (70%), headache (>60%), myalgia (>60%), arthralgia (> 40%), chills (>40%), nausea and vomiting (>20%), axillary swelling/ tenderness, pyrexia and injection site swelling (>15%), which were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of adverse events was associated with greater age.

A higher rate of local and systemic adverse events were seen after the second dose so consideration may be given to staggering healthcare worker vaccinations.

Co-administration

Co-administration with other vaccines has not been studied. It is prudent to leave 14 days between this and another vaccine.

Duration of immunity

Clinical trial follow-up is ongoing to determine the duration of protection from the vaccine.

Vaccinated persons should continue to follow all current public health guidance to protect themselves and others.

Vaccine effectiveness

Vaccine recipients may not be protected until 14 days after the second dose and the vaccine may not protect all vaccinees.

Booster doses

The need for and timing of booster doses has not been established. No additional doses beyond the two-dose primary series are recommended at this time.

Viral vector vaccines**COVID-19 Vaccine AstraZeneca®**

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions to the HPRA.

The vaccine should be stored at +2°C to +8°C. Each pack contains 10 vials.

The vaccine does not require dilution. Once the multidose vial is punctured, the vaccine should be used immediately. If not used, it may be kept for a single period for up to 30°C and used within 6 hours or between +2°C to +8°C and used within 48 hours.

Licensed indications

Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 18 years of age and older.

Dose and route of administration

The dose of vaccine is 0.5 ml IM, preferably into the deltoid muscle.

If more than ten 0.5ml doses can be safely and accurately withdrawn from a diluted vial, they can be used as valid vaccines.

The course consists of two doses 4-12 weeks apart.

For those aged 65 and older an interval of 4-6 weeks is recommended.

For those less than 65 years of age at an interval of 4-12 weeks is recommended.

If the interval between doses is longer than 12 weeks, the second dose should still be given. The course does not need to be restarted.

If the interval between doses is less than 28 days, a further dose is not required. If the second dose was given between 24 and 27 days after the first dose, it is a valid dose.

Interchangeability

There is no data on the interchangeability of COVID-19 vaccines. The same vaccine should be used for both doses.

Contraindications

Anaphylaxis (serious systemic allergic reaction requiring medical intervention) following a previous dose of the vaccine or any of its constituents (including polysorbate 80).

<https://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/anaphylaxis.pdf>

Appropriate support should be available in case of anaphylaxis or fainting after vaccine administration.

Precautions should be in place to minimise injury from fainting.

Precautions

Acute severe febrile illness; defer until recovery.

Advice from a relevant specialist should be sought for a person with a history of an immediate severe allergic reaction to any other vaccine or injectable therapy and the risks should be weighed against the benefits of vaccination. The patient should be observed for 30 minutes after vaccination.

Vaccination should be deferred until clinical recovery from COVID-19 and at least four weeks after diagnosis or onset of symptoms, or four weeks from the first PCR positive specimen in those who are asymptomatic.

Vaccination is not contraindicated for those with persisting symptoms post COVID-19 unless there is evidence of recent clinical deterioration.

Post vaccination observation period

- Those with no history of anaphylaxis from any cause: 15 minutes
- Those with a history of anaphylaxis from any cause: 30 minutes
- Those with immediate itching, swelling or urticarial reaction at the vaccination site: 30 minutes or longer as clinically indicated

Immunocompromised

Data are not currently available to establish vaccine safety and efficacy in these groups. Individuals with immunosuppression due to disease or treatment may be vaccinated if they have no contraindications.

Pregnancy

There is limited experience with the use of this vaccine in pregnant women. Animal reproductive toxicity studies have not yet been completed. Based upon results from the preliminary study, no effects are expected on development of the foetus. Although the available data do not indicate any safety concerns or harm to pregnancy, there is currently insufficient evidence to recommend routine use of this vaccine during pregnancy. Administration of this vaccine in pregnancy should be considered when the potential benefits outweigh any potential risks for the mother (e.g. at high risk of severe disease, HCW) and foetus.

Pregnant women who meet the priority criteria for vaccination and their obstetric caregivers should engage in shared decision-making in advance of vaccination. Counselling should balance available data on vaccine safety, risks to pregnant women from SARS-CoV-2 infection, and a woman's individual risk for infection and severe disease.

Where the risk/benefit is favourable, the two doses should be given 4-12 weeks apart. The two dose schedule should be given between 14 and 33 completed weeks of gestation.

Breastfeeding

There is no known reason for vaccinees to avoid breastfeeding. Breastfeeding mothers should be vaccinated according to their risk grouping.

Children and adolescents under 18 years of age

There is no data available on vaccine safety and efficacy in children.

Vaccination of those with bleeding disorders or on anticoagulants

Individuals with a bleeding disorder or receiving anticoagulant therapy may develop haematomas in IM injection sites. Prior to vaccination, inform the recipient about this risk. For those with thrombocytopenia (platelet count $<50 \times 10^9/L$), consult the supervising consultant. People with mild bleeding disorders or on maintenance dose Emicizumab (Hemlibra[®]) do not

require haemostatic cover for vaccination. Details of haemostatic cover for all others can be found in the Patient Information tab at <http://www.stjames.ie/services/hope/nationalcoagulationcentre>

Those with inherited coagulopathies who require factor replacement therapy should receive it on the day of vaccination, prior to the IM vaccination.

If there is uncertainty about the need for cover, contact the patient's Comprehensive Care Centre.

Those receiving long-term anticoagulation with either Warfarin® or heparin are not considered to be at higher risk of bleeding complications following vaccination. There is no reason to expect that there is a greater risk of bleeding complications with the newer direct oral anticoagulants or antiplatelet agents, than with other anticoagulants.

People on Warfarin® should follow their usual schedule for international normalised ratio (INR) testing and can be vaccinated if it is less than 4.0. If the INR is 4.0 or more, follow the advice of the clinic/practice managing Warfarin® and wait until the INR is less than 4.0 to be vaccinated.

See [Chapter 2, sections 2.4.6 and 2.4.7](#) for further information, including technique for IM injection, in this patient group.

Adverse reactions

A full list of adverse reactions may be found in the Summary of Product Characteristics (SmPC).

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Uncommon:	>1/1,000 and <1/100
Rare:	>1/10,000 and <1/1,000
Very rare:	<1/10,000

<i>Local:</i>	Very common: injection site bruising, pain, pruritus, tenderness, warmth Common: injection site erythema, swelling Uncommon: injection site haematoma
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<i>General:</i>	Very common: arthralgia, chills, fatigue, feverishness, headache, malaise, myalgia, nausea Common: diarrhoea, fever $\geq 38^{\circ}\text{C}$, vomiting Uncommon: decreased appetite, dizziness, hyperhidrosis, lymphadenopathy, pruritus, somnolence, rash
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The most frequent adverse reactions during clinical trials in those aged ≥ 18 years were injection site tenderness ($>60\%$), fatigue, headache, injection site pain (50%), malaise, myalgia ($>40\%$), chills, feverishness, pyrexia ($>30\%$) and arthralgia and nausea ($>20\%$). A lower frequency of adverse events was associated with greater age.

The rate and severity of local and systemic adverse reactions was lower after the second dose.

Co-administration

Co-administration with other vaccines has not been studied. It is prudent to leave 14 days between this and another vaccine.

Duration of immunity

Clinical trial follow-up is ongoing to determine the duration of protection from the vaccine.

Vaccinated persons should continue to follow all current public health guidance to protect themselves and others.

Vaccine effectiveness

Vaccine recipients may not be protected until 15 days after the second dose and the vaccine may not protect all vaccinees.

Booster doses

The need for, and timing of booster doses has not been established. No additional doses beyond the two-dose primary series are recommended at this time.

5a.6 Post-marketing surveillance (Pharmacovigilance)

The HPRA is responsible for managing the national pharmacovigilance system. The HPRA reports nationally occurring adverse reactions to the EMA. Adverse reaction reporting is an important part of the EMA intensive monitoring plan for COVID-19 vaccines, so that any changes in benefit risk balance can be promptly detected and acted upon. This enables the EMA to continue to safeguard public health safety.

Healthcare professionals and members of the public are encouraged to report suspected adverse reactions to the HPRA following the instructions available on the HPRA website www.hpra.ie

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