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
VOC	Variants of concern
WHO	World Health Organization

Key Updates

Medical conditions associated with very high risk or high risk of severe COVID-19 disease

- high dose systemic steroids

Vaxzevria® COVID-19 vaccine AstraZeneca

- contraindications
- precautions
- thromboembolic events post vaccination
- pregnancy and breastfeeding

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 **S**evere **A**cute **R**espiratory **S**yndrome **Co**rona**V**irus type 2 (SARS-CoV-2). The disease it causes is called **Co**rona**vi**rus **d**isease 20**19** (COVID-19). On March 11th, 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic.

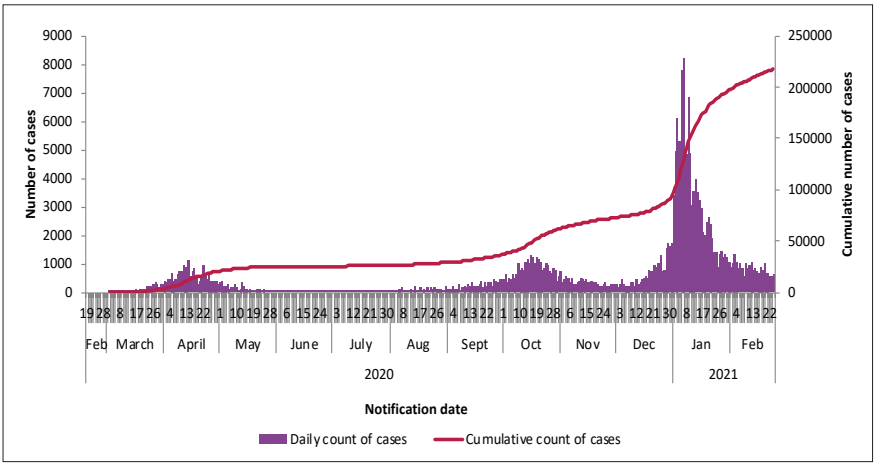
5a.2 Epidemiology

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

As of 16 March, 2021, the WHO has reported almost 120 million cases and over 2.6 million deaths from COVID-19.

The first laboratory confirmed case of COVID-19 in Ireland was on 29 February 2020. As of 24 February 2021, 217,478 confirmed COVID-19 cases and 4,271 deaths (4,012 confirmed) have been reported with a case fatality rate of 1.8%. 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 24/02/2021
Source: HPSC



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. Other conditions that have been associated with a higher risk of having a complicated course include immunocompromise due to disease or treatment, inherited metabolic disorders, intellectual disability (including Down syndrome), severe mental illness and sickle cell disease.

In the first wave, healthcare workers (HCW) accounted for 30% cases and 32% of these cases occurred in those working in long-stay care facilities (nursing homes,residential institutions, community hospitals). Since the start of the pandemic, HCW have accounted for 10% of cases. This figure continues to decline with increasing HCW vaccine uptake.

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.

A number of new more transmissible variants of concern (VOC) have been detected- VOC 202012/01 (B.1.1.7) (UK September 2020), 501Y.V2 ((B.1.351) (South Africa October 2020), P 1 (Brazil late 2020), B.1.427 and B.1.429 (California late 2020). Studies have shown that VOC 202012/01 (B.1.1.7), now the predominant strain in Ireland, is 56-75% more transmissible than previously circulating variants.

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 years with medical conditions outlined in Table 5.2 below.
- 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 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 are 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.

A small number of cases of COVID-19 associated placentitis have been reported in Ireland and are being investigated.

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

- Those with the risk factors listed in Table 5.2 below.
- 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 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 cells 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 is 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 two virus vector vaccines.

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® and **COVID-19 vaccine Moderna®** have been authorised by the EMA (see Section 5a.5).

CVnCoV vaccine (Curevac), is undergoing an EMA rolling review. Phase 2b and Phase 3 randomised, controlled trials are underway in more than 35,000 adults over 18 years of age or older at multiple sites. Vaccinations follow a two-dose schedule on day 0 and day 28. Interim analysis is to be carried out within the first quarter of 2021.

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.

Vaxzevria® COVID-19 Vaccine AstraZeneca and **COVID-19 vaccine Janssen®** have been authorised by the EMA (see Section 5a.5).

Sputnik V (Gam-COVID-Vac), is undergoing an EMA rolling review. Interim analysis of a randomised controlled phase 3 trial in Russia showed vaccine efficacy was 91·6% (95% CI 85·6–95·2). Vaccinations follow a two-dose schedule on day 0 and day 21.

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.

NVX-CoV2373 vaccine (Novavax) is undergoing an EMA rolling review. This vaccine uses recombinant technology combined with an adjuvant (Matrix-M). Final efficacy analysis results of a UK Phase 3 clinical study of more than 15,000 participants between 18-84 years of age, estimated efficacy of 96.4% (95% CI: 73.8, 99.5) against the original virus strain and 86.3% (95% CI: 71.3, 93.5) against the B.1.1.7/501Y.V1 variant

Virus Like Particle 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 virus like particles, 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) so 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 800 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 six 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 following authorisation and their 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 is available on the Health Products 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.

While vaccine supplies are limited it is recommended vaccination is carried out in the following order (although they may be overlap for logistical reasons):

Table 5.1 Priority groups for COVID-19 vaccination

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* 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
Aged 16-69 with medical conditions that put them at very high risk** of disease	At similar very high risk of hospitalisation and death as those aged 70-74
Aged 65-69. Prioritise those with medical conditions** which put them at high risk of severe disease Other HCWs not in direct patient contact Key workers	At higher risk of hospitalisation and death Provide essential health services, protect patients Providing services essential to the vaccination programme
Aged 18-64 years with medical conditions** which put them at high risk of severe disease	At higher risk of hospitalisation
Aged 16 - 64 years Residents of long-term care facilities Traveller and Roma communities People who are homeless Aged 16 - 64 years in descending order e.g. 10-year cohorts 55-64 45-54 35-44 25-34 16-24	Based on risk of ICU admission and death

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.

* HCW who work in and out of all healthcare settings including vaccinators
**See Table 5.2

Table 5.2 Medical conditions and medication associated with very high risk or high risk of severe COVID-19 disease

Conditions in the shaded areas may be associated with a suboptimal response to vaccines and should be given an mRNA vaccine if practicable and timely. However, if preferential selection of an mRNA vaccine will result in delayed vaccination for more than 3 weeks, any benefit of using a higher efficacy vaccine may be lost.

Medical condition[1]	Very high risk	High risk
Cancer	All cancer patients actively receiving (and/or within 6 weeks of receiving) systemic therapy with cytotoxic chemotherapy, targeted therapy, monoclonal antibodies or immunotherapies and surgery or radical radiotherapy for lung or head and neck cancer All patients with advanced/ metastatic cancers	Haematological - within 1 year
		Haematological - within 1 - 5 years Non-haematological - within 1 year All other cancers on non-hormonal treatment
Chronic heart (and vascular) disease		e.g. heart failure, hypertensive cardiac disease
Chronic kidney disease	On dialysis, or eGFR <15 ml/min	With eGFR <30ml/min
Chronic liver disease		e.g. cirrhosis or fibrosis
Chronic neurological disease or condition	With evolving ventilatory failure requiring non-invasive ventilation e.g. motor neurone disease, spinal muscular atrophy	Significantly compromising respiratory function and/or the ability to clear secretions e.g. Parkinson's disease, cerebral palsy
Chronic respiratory disease	Severe e.g. severe cystic fibrosis, severe COPD, severe pulmonary fibrosis	Other e.g. stable cystic fibrosis, severe asthma (continuous or repeated use of systemic corticosteroids), moderate COPD
Diabetes	HbA1c ≥58mmol/mol	All other diabetes (Type 1 and 2)

Immunocompromise due to disease or treatment	Severe e.g. **Transplantation:** - Listed for solid organ or haematopoietic stem cell transplant (HSCT) - Post solid organ transplant at any time - Post HSCT within 12 months **Genetic diseases:** - APECED[2] - Inborn errors in the interferon pathway **Treatment:** - included but not limited to Cyclophosphamide, Rituximab, Alemtuzumab, Cladribine or Ocrelizumab in the last 6 months	Other e.g. High dose systemic steroids[3] Persons living with HIV
Inherited metabolic diseases	Disorders of intermediary metabolism/at risk of acute decompensation e.g. Maple Syrup Urine Disease	Disorders of intermediary metabolism not fulfilling criteria for very high risk
Intellectual disability	Down Syndrome	Intellectual disability excluding Down Syndrome
Obesity	BMI >40 Kg/m^2	BMI >35 Kg/m^2
Severe mental illness		e.g. Schizophrenia, bipolar disorder, severe depression
Sickle cell disease	Sickle cell disease	

[1]May also include other people who have been classed as at very high risk, based on clinical judgement and an assessment of their needs
[2] APECED - autoimmune polyendocrinopathy candidiasis ectodermal dystrophy
[3] The following doses of prednisolone (or equivalent dose of other glucocorticoid) may increase the risk of severe COVID-19 disease:

- ≥10mg per day for more than 4 weeks with one other immunosuppressant
- ≥20mg per day for more than 4 weeks

Pregnant women with any of these high-risk conditions should not be excluded from timely vaccination.

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.
- **Vaxzevria® COVID-19 Vaccine AstraZeneca®**
  Conditional marketing authorisation granted by the EC on 29 January 2021.
- **COVID-19 Vaccine Janssen®**
  Conditional marketing authorisation granted by the EC on 11 March 2021.

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

Comirnaty®(Pfizer/BioNTech) is the only authorised COVID-19 vaccine for those aged 16 and 17 years.

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°C to +8°C to thaw which may take 3 hours. Alternatively, frozen vials may be thawed for 30 minutes at temperatures up to +30°C for immediate use.

After thawing, undiluted vaccine can be stored for up to 120 hours at +2°C to +8°C and up to 2 hours at up to +30°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°C to +30°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.

Vaccine efficacy
Data presented to the European Medicines Agency (EMA) demonstrated a two-dose vaccine efficacy of 95% (95% confidence interval of 90.3% to 97.6%)

in those aged 16 and above. High efficacy was observed across, age, sex and ethnicity categories and among persons with underlying medical conditions.

Vaccine effectiveness
A matched control study of over one million people from Israel showed vaccine effectiveness of 87% (95% CI, 55 to 100) against hospitalisation and 92% (95% CI, 75 to 100) against severe disease at 7 or more days after the second dose of vaccine.

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 the contents of different 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 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/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.

Patients with planned immunosuppressive therapy should ideally complete vaccination two weeks before treatment. The recommended minimum interval may be used. Specialists should consider the individual's risk and likelihood of disease exposure, and provide advice based on knowledge and understanding of the patient's immune status and likely immune response to vaccination.

Vaccination after COVID-19
Those with persisting symptoms post COVID-19 may be vaccinated, unless there is evidence of recent clinical deterioration.

Those aged 65 and older, and those under 65 years who are immunocompromised
Vaccination should be deferred until clinical recovery from COVID-19 and for at least four weeks after diagnosis or onset of symptoms, or four weeks from the first PCR positive specimen in those who are asymptomatic.

Those aged under 65 years
Vaccination should be deferred until clinical recovery from confirmed SARS-CoV-2 infection (symptomatic or asymptomatic).

Vaccination may be deferred for those who are not immunocompromised for up to six months after diagnosis, symptom onset, or from the first PCR or antigen positive specimen

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.

See Table 5.2 for conditions that may be associated with a suboptimal response to vaccines and should be given an mRNA vaccine if practicable and timely. However, if preferential selection of an mRNA vaccine will result in delayed vaccination for more than 3 weeks, any benefit of using a higher efficacy vaccine may be lost.

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 fertility, pregnancy, embryo/foetal development, delivery or post-natal development. There is no biologically plausible reason why the vaccine would affect fertility.

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 36 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 are 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<$50x10^9$/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.

Post marketing surveillance has reported an anaphylaxis rate of 11.1/ million (higher than for other vaccines).

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

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.

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.

Vaccine efficacy
Data presented to the EMA demonstrated a two-dose vaccine efficacy of 94.1% (95% confidence interval of 89.3% to 96.8%) in those aged 18 and above. High efficacy was observed across age, sex, and ethnicity categories and among persons with underlying medical conditions.

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 vial, they can be used as valid vaccines doses. There should be no pooling of the contents 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 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 are 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.

Patients with planned immunosuppressive therapy should ideally complete vaccination two weeks before treatment. The recommended minimum interval may be used. Specialists should consider the individual's risk and likelihood of disease exposure, and provide advice based on knowledge and understanding of the patient's immune status and likely immune response to vaccination.

Vaccination after COVID-19
Those with persisting symptoms post COVID-19 may be vaccinated, unless there is evidence of recent clinical deterioration.

Those aged 65 and older, and those under 65 years who are immunocompromised
Vaccination should be deferred until clinical recovery from COVID-19 and for at least four weeks after diagnosis or onset of symptoms, or four weeks from the first PCR positive specimen in those who are asymptomatic.

Those aged under 65 years:
Vaccination should be deferred until clinical recovery from confirmed SARS-CoV-2 infection (symptomatic or asymptomatic).

Vaccination may be deferred for those who are not immunocompromised for up to six months after diagnosis, symptom onset, or from the first PCR or antigen positive specimen.

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.

See Table 5.2 for conditions that may be associated with a suboptimal response to vaccines and should be given an mRNA vaccine if practicable and timely However, if preferential selection of an mRNA vaccine will result in delayed vaccination for more than 3 weeks, any benefit of using a higher efficacy vaccine may be lost.

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 fertility, pregnancy, embryo/foetal development, delivery or post-natal development. There is no biologically plausible reason why the vaccine would affect fertility.

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 36 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 are 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<$50x10^9$/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.

Post marketing surveillance has reported an anaphylaxis rate of 2.5/ million (higher than for other vaccines).

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

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.

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

Vaxzevria® 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 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.

Vaccine efficacy
Data presented to the EMA demonstrated a two-dose vaccine efficacy of 59.5% (95% confidence interval of 45.8% to 69.7%) in those aged 18 and above. There was insufficient clinical data to allow reliable calculation of

efficacy in those aged 55 and older. However, as a similar immune response was shown in all age groups, including those aged 65 and older, the EMA authorised the vaccine for all adults.

The World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE), subsequently reported the overall vaccine efficacy at 63.1%. There were no cases of COVID-19 hospitalisation, severe disease, or death in those aged 65 and older who received the vaccine.

Vaccine effectiveness
A prospective population study of 5.4 million people from Scotland found that the first dose of vaccine showed effectiveness of 94% (95% CI 73 to 99) for COVID-19 related hospitalisation at 28-34 days post-vaccination.

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 vial, they can be used as valid vaccines. There should be no pooling of the contents of different vials.

The vaccine is authorised as a two dose course 4-12 weeks apart. It is recommended the two doses are given 8-12 apart because of recent evidence which shows that higher efficacy of 82% was reported when the second dose was given after 12 weeks.

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

The minimum interval is 4 weeks (28 days). 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 are 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

A second dose of Vaxzevria® should not be given to anyone who developed thromboembolism with thrombocytopenia after the first dose.

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

Vaxzevria® is not recommended for those aged under 60 years, including those with medical conditions with very high or high risk of severe COVID-19 disease.

However those aged under 60 can be given Vaxzevria® when the benefits clearly outweigh the risk for that individual and the person has made an informed decision based on an understanding of the risks and benefits.

Those who have received a first dose

- *aged 60 and older and aged under 60 years with medical conditions with very high or high risk of severe COVID-19 disease* should receive their second dose 12 weeks later as scheduled. An interval of 4-12 weeks may be used for those with planned immunosuppressive therapy to allow for completion of vaccination before treatment.
- *aged under 60 years without medical conditions with very high or high risk of severe COVID-19 disease* should have the scheduled interval between doses extended to 16 weeks to allow further assessment of the benefits and risks as more evidence becomes available.

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.

Patients with planned immunosuppressive therapy should ideally complete vaccination two weeks before treatment. The recommended minimum interval may be used. Specialists should consider the individual's risk and likelihood of disease exposure, and provide advice based on knowledge and understanding of the patient's immune status and likely immune response to vaccination.

Vaccination after COVID-19

Those with persisting symptoms post COVID-19 may be vaccinated, unless there is evidence of recent clinical deterioration.

Those aged 65 and older, and those under 65 years who are immunocompromised

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

Those aged under 65 years
Vaccination should be deferred until clinical recovery from confirmed SARS-CoV-2 infection (symptomatic or asymptomatic).

Vaccination may be deferred for those who are not immunocompromised for up to six months after diagnosis, symptom onset, or from the first PCR or antigen positive specimen.

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 and Breastfeeding
This vaccine is not recommended for those aged under 60 years, including those with medical conditions with very high or high risk of severe COVID-19 disease.

See Precautions section for those who have received a first dose.

Children and adolescents under 18 years of age
There are 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<$50x10^9$/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.

Thromboembolic events post vaccination
On 7 April 2021, the EMA issued updated advice following the conclusions of their safety reviews following reports of thromboembolic events and thrombocytopenia after vaccination with Vaxzevria®. The cases came mainly from spontaneous reporting in the EEA and the UK, where around 25 million people had received the vaccine. The Pharmacovigilance Risk Assessment Committee carried out an in-depth review of 62 cases of cerebral venous sinus thrombosis and 24 cases of splanchnic vein thrombosis reported to the EMA by 22 March 2021, 18 of which were fatal. Most cases were reported in women under 60 years of age although this may reflect vaccination of healthcare workers in this group.

Available evidence suggests thromboembolism with thrombocytopenia events are very rare (4-10 cases per million vaccines given with an estimated death rate of 1 per million). No specific risk factors have been confirmed. There is no evidence of an increased risk for those with pre-existing clotting or platelet disorders e.g. idiopathic or heparin induced thrombocytopenia, autoimmune conditions, history of cerebral venous sinus thrombosis, acquired or hereditary thrombophilia, or antiphospholipid syndrome.

The EMA has revised the EU product information to include thrombosis in combination with thrombocytopenia as very rare side effects of Vaxzevria®. The EMA and WHO have noted the very low numbers of these reported events overall and acknowledged the challenge in determining incidence and specific risk factors.

The EMA and WHO have reiterated that the overall benefits of the vaccine in protecting against the significant threat of COVID-19 disease, and in preventing hospitalisation and death, continue to outweigh the risk of possible side effects

As the risk/benefits of Vaxzevria® may vary by age and as alternative COVID-19 vaccines are available, NIAC has revised the recommendations for use of this vaccine (see Precautions).

Healthcare professionals should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia. Vaccine recipients should be advised to seek immediate medical attention if they develop symptoms such as shortness of breath, chest pain, leg swelling and/or persistent abdominal pain within weeks of vaccination. Additionally, anyone with neurological symptoms including severe or persistent headaches (particularly 3 or more days after vaccination) or blurred vision, or who develop petechiae or ecchymoses beyond the site of vaccination, should seek prompt medical attention.

Healthcare professionals should seek early expert advice from the National Coagulation Centre about specialised testing and treatment options for patients presenting with thromboembolic events that are associated with thrombocytopenia (including DIC or CVST) occurring within weeks following vaccination with COVID-19 Vaccine AstraZeneca®.

Pregnant women who have had gestational thrombocytopenia or pre-eclampsia are not known to be at higher risk of these rare events and none of the events occurred in pregnant women.

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 bruising, pain, pruritus, tenderness, warmth
	Common: injection site erythema, swelling
	Uncommon: injection site haematoma
General:	Very common: arthralgia, chills, fatigue, feverishness, headache, malaise, myalgia, nausea
	Common: diarrhoea, fever ≥38^{0}C, thrombocytopenia (asymptomatic), vomiting
	Uncommon: decreased appetite, dizziness, hyperhidrosis, lymphadenopathy, pruritus, somnolence, rash
	Very rare: thrombosis in combination with thrombocytopenia

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.

Post marketing surveillance has reported an anaphylaxis rate of 2.5/ million (higher than for other vaccines).

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

Protection starts from approximately three weeks after first dose of vaccine with 76% protection overall against symptomatic COVID-19 disease for up to 90 days (12 weeks). Modelling showed no evidence of waning of protection in the first three months after vaccination. Higher efficacy of 82% was reported when the second dose was given after 12 weeks.

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.

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.

COVID-19 Vaccine Janssen®

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.

After the first dose has been withdrawn, the vaccine should be used immediately. If not used, the vial can be maintained between 2° to 8°C for up to 6 hours or at room temperature (up to 25°C) for up to 3 hours. Discard the vial if vaccine is not used within these times.

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

Vaccine efficacy
Data presented to the EMA demonstrated a vaccine efficacy against severe COVID-19 disease of 76.7% (95% confidence interval 54.6% to 89.1%) 14 days after vaccination, increasing to 85.4% (95% confidence interval 54.2% to 96.9%) 28 days in those aged 18 and above. High efficacy was observed across age and sex, and among persons with underlying medical conditions.

Dose and route of administration
The dose of vaccine is 0.5 ml IM, preferably into the deltoid muscle.

The course consists of one 0.5 ml dose.

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

Interchangeability
There are no data on the use of this vaccine to complete a course of another COVID-19 vaccine. The same vaccine should be used for vaccines with a two dose schedule.

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.

Patients with planned immunosuppressive therapy should ideally receive vaccination two weeks before treatment. Specialists should consider the individual's risk and likelihood of disease exposure, and provide advice based on knowledge and understanding of the patient's immune status and likely immune response to vaccination.

Vaccination after COVID-19
Those with persisting symptoms post COVID-19 may be vaccinated, unless there is evidence of recent clinical deterioration.

Those aged 65 and older, and those under 65 years who are immunocompromised
Vaccination should be deferred until clinical recovery from COVID-19 and for at least four weeks after diagnosis or onset of symptoms, or four weeks from the first PCR positive specimen in those who are asymptomatic.

Those aged under 65 years
Vaccination should be deferred until clinical recovery from confirmed SARS-CoV-2 infection (symptomatic or asymptomatic).

Vaccination may be deferred for those who are not immunocompromised for up to six months after diagnosis, symptom onset, or from the first PCR or antigen positive specimen.

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 the vaccine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to fertility, pregnancy, embryo/foetal development, delivery or post-natal development. There is no biologically plausible reason why the vaccine would affect fertility.

Although the available data do not indicate any safety concern 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 vaccine should be given between 14 and 36 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<$50x10^9$/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
	Common: injection site erythema, swelling
General:	Very common: fatigue, headache, myalgia, nausea
	Common: arthralgia, chills, cough, pyrexia
	Uncommon: asthenia, back pain, hyperhidrosis, malaise, muscular weakness, oropharyngeal pain, pain in extremity, rash, sneezing, tremor
	Rare: hypersensitivity, urticaria

The most frequent adverse reactions during clinical trials in those aged ≥18 years were injection site pain (> 40%), fatigue, headache, myalgia (> 30%), nausea (>10%) and fever (9%). A lower frequency and severity of adverse events was associated with greater age.

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

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.

Booster doses
The need for, and timing of booster doses has not been established. No additional doses beyond one dose 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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