5a COVID-19

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.

Acronyms used in this chapter

AEFI	Adverse event following immunisation
BMI	Body mass index
BTS/SIGN	British Thoracic Society/Scottish Intercollegiate Guidelines Network
CLS	Capillary Leak Syndrome
COPD	Chronic Obstructive Pulmonary Disease
COVID-19	Coronavirus disease 2019
CVST	Cerebral Venous Sinus Thrombosis
EC	European Commission
EMA	European Medicines Agency
GBS	Guillain-Barré Syndrome
HCW	Healthcare worker
HPRA	Health Products Regulatory Authority
HPV	Human Papillomavirus
IGRA	Interferon gamma release assay
INR	International normalised ratio
IM	Intramuscular
MERS	Middle East Respiratory Syndrome
MIS-C	Multisystem Inflammatory Syndrome in Children
mRNA	Messenger RNA
NA	Neutralising antibody
NIAC	National Immunisation Advisory Committee
NIO	National Immunisation Office
PCR	Polymerase Chain Reaction
PEG	Polyethylene glycol
S antigen	Spike antigen
SARS	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SmPC	Summary of Product Characteristics
TST	Tuberculin sensitivity test
TTS	Thrombosis thrombocytopenia Syndrome
VOC	Variants of concern
WHO	World Health Organization

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5a.1 Introduction

Seven coronaviruses cause disease in humans. Four of these generally cause minor respiratory illnesses. Three coronaviruses – Middle East Respiratory Syndrome coronavirus, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), and Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) cause more severe disease. The disease caused by SARS-CoV-2 is termed COVID-19.

As with most RNA viruses, mutations occur and multiple variants strains of SARS-CoV-2 have been identified. The predominant variants of concern (VOCs) circulating at present are Omicron BA.4 and BA.5. VOCs are so termed as they have a significant impact on transmissibility, severity and/or immunity.

5a.2 Epidemiology

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

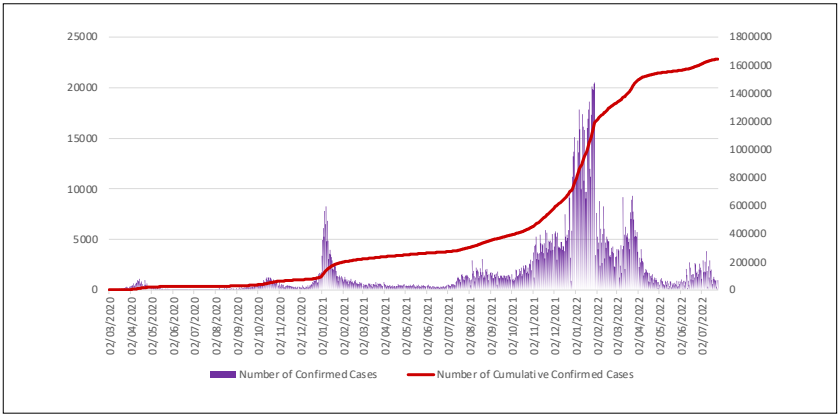
In December 2019, SARS-CoV-2 was identified in humans in Wuhan, China. The disease it causes is called **Co**rona**vi**rus **d**isease 20**19** (COVID-19). On 11 March 2020 , the World Health Organization (WHO) declared the outbreak a pandemic.

By 23 September 2022, 618 million cases and 6.5 million deaths had been reported.

In Ireland, the first laboratory confirmed case of COVID-19 was reported on 29 February 2020. Since then there have been five waves, peaking in April and October 2020, January 2021 , January 2022 and July 2022. Omicron, now the predominant circulating strain, is more transmissible but less virulent than previous strains.

Since the start of the pandemic, Ireland has reported 1.65 million PCR confirmed cases and 7,870 COVID-19 deaths.

Figure 5a.1 Number and cumulative number of confirmed COVID-19 cases notified in Ireland by notification date to midnight 25 July 2022
Source: HPSC



The highest proportion of hospitalisations and deaths have been in those aged 65 years and older. An underlying condition was present in 85% of those admitted to ICU.

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. These include long stay care facilities, meat processing plants, the Traveller community and direct provision centres.

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

The main underlying conditions associated with increased risk of hospitalisation are are listed in Table 5a.2

Transmission

Estimates for the basic reproductive number (R_0) of SARS-CoV-2 ranged from 2-8 before the widespread use of vaccines, masks and social distancing. It also varies depending on the predominant circulating strain. The R_0 in confined settings may be at the higher end of this range.

Transmission occurs mainly to those who have been indoors and within two metres of someone with COVID-19 for a cumulative total of at least 15 minutes over a 24 hour period. Factors that increase the risk of infection include presence in an enclosed space with inadequate ventilation,

increased exhalation of respiratory fluids if an infectious person is e.g., shouting, singing or exercising.

Most transmission occurs in household and community settings. Young children are less likely to transmit infection than adolescents or adults.

SARS-CoV-2 virus can survive on surfaces for up to a few days, depending on the surface and environmental conditions.

The **incubation period** is typically two to five days (range one to 14 days or longer).

Infectious period
Individuals may be infectious from two days before becoming symptomatic, with infectiousness typically peaking within five days of symptom onset. Viable virus is not usually detectable for more than ten days after symptom onset.

5a.3 Effects of COVID-19

5a.3.1. Symptoms

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.

Symptoms include extreme tiredness, coughing spasms, breathlessness and problems with memory and concentration.

With the Omicron variant, fever, loss or altered sense of smell and persistent cough are less prevalent than with previous variants, and sore throat and hoarse voice are more prevalent.

Duration of acute symptoms for those with the Delta variant was longer than those with the Omicron variant (mean duration 9 days versus. 7 days). Regardless of the variant, the duration of symptoms is shorter for those who have received at least three doses of vaccine.

Symptoms among those aged 65 years and older and those with underlying conditions may be atypical, and fever or respiratory symptoms may be absent. While severe illness and death have been reported at all ages, deaths are more likely in those:

- Age 65 and older
- Age 12-64 years with underlying conditions outlined in Table 5a.2.
- From Black, Asian and minority ethnic backgrounds

The majority recover from infection without clinical intervention. Persisting symptoms may result. "Long COVID" occurs usually three months from the onset of COVID-19 with symptoms that last for at least two months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others which generally have an impact on everyday functioning. Symptoms may be new onset, following initial recovery from an acute COVID19 episode, or persist from the initial illness. Symptoms may also fluctuate or relapse over time. Long-term symptoms following COVID-19 are more likely with increasing age, higher BMI and female sex.

5a.3.2 Pregnancy

Pregnant women are at similar risk of COVID-19 infection to non-pregnant women of the same age. However, pregnant women with COVID-19 infection are more likely to be admitted to ICU or to die than similar aged non-pregnant women with COVID-19. Pregnant women from Black, Asian and minority ethnic backgrounds may be more likely to be admitted to hospital with COVID-19 disease than other pregnant women.

COVID-19 in pregnancy may increase the risk of adverse pregnancy outcomes, such as late miscarriage, stillbirth and preterm birth.

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

- Underlying conditions listed in Table 5a.2
- Age over 35 years
- Infection in the third trimester (28 weeks or more)
- BMI of 30 or more

5a.3.3 Children and adolescents

The overwhelming majority of young adolescents who get SARS-CoV-2 infection experience a mild self-limited illness. However, severe disease, ICU admission and extremely rarely death can occur.

The presence of an underlying condition as listed in Table 5a.2 significantly increased the risk of hospitalisation and severe disease.

Multisystem Inflammatory Syndrome in Children (MIS-C) is a rare but serious hyperinflammatory syndrome related to prior SARS-CoV-2 infection, in which different organs can become inflamed. The incidence of MIS-C is about 100/100,000 in those under 21 years of age, with a median age of 9 years old, and 75% of cases with no underlying medical condition. Most children recover with appropriate treatment.

Rarely, adults develop signs and symptoms similar to MIS-C.

5a.3.4 Long COVID

The majority of people who develop COVID-19 feel better in a few days or weeks.

Some people, including children and adolescents, experience physical and/or psychological symptoms lasting more than 12 weeks after developing COVID-19. This is called long COVID.

Onset may occur weeks or months after the initial infection. People who have been hospitalised appear to be at greater risk of experiencing longer-term effects, but it may occur in those who had asymptomatic or only mild infection. The incidence of at least one symptom has been reported in up to 40% of infections.

Symptoms include fatigue, memory problems, sleep disturbances, shortness of breath, anxiety and depression, general pain and discomfort and difficulty thinking or concentrating. Symptoms may fluctuate, and may last for months.

5a.3.5 Other effects of COVID-19

A study in the US showed that people aged 60 years and older who had had COVID-19 were about 40% more likely to develop diabetes up to a year later than those who did not have COVID-19. The chance of developing diabetes rose with increasing severity of COVID-19 and in those with a high BMI. Data on a link between COVID-19 and diabetes in younger adults or children are mixed. Other US studies reported an increased risk of cardiovascular and renal disorders.

5a.4. Vaccines

5a.4.1 Types of vaccine

mRNA vaccines

Messenger RNA vaccines include genetic material (mRNA) that instructs the recipient's antigen-presenting cells to make a spike protein antigen, thus stimulating an immune response. Rapid degradation of mRNA within cells contributes to the safety profile of these vaccines.

Comirnaty and **Spikevax** are authorised by the European Medicines Agency (EMA).

Bivalent mRNA vaccines are adapted versions of the original Comirnaty and Spikevax vaccines which have been modified to target Omicron subvariants in addition to the original strain of SARS-CoV-2.

Comirnaty Original/ Omicron BA.1, Spikevax bivalent Original/Omicron BA.1 and Comirnaty Original/ Omicron BA.4-5 are authorised by the EMA.

Adenoviral vector vaccines
A non-pathogenic virus is genetically modified to encode an antigen which, when expressed by the host cell, provokes an immune response.

Vaxzevria and **JCOVDEN** (formerly COVID-19 vaccine Janssen**)** are authorised by the EMA.

Protein subunit vaccines
These vaccines are based on injection of key viral antigens stimulating the immune response.

Nuvaxovid is authorised by the EMA.

5a.4.2 COVID-19 vaccine safety

To date over 4.9 billion people have received a COVID-19 vaccine. Following close post-marketing monitoring, the benefit/risk of all EMA authorised vaccines remains positive.

Thrombosis with Thrombocytopenia Syndrome (TTS)
A very rare condition involving serious thromboembolic events accompanied by thrombocytopenia (TTS) has been reported after Vaxzevria and JCOVDEN. The thrombi occurred in unusual locations including cerebral venous sinus thrombosis (CVST), the splanchnic vein and in arteries.

TTS generally presents with the following symptoms 3-42 days after vaccination:

- **arterial ischaemia**: changes to limb (pallor and coldness), chest pain, shortness of breath
- **cerebral venous thrombosis**: persistent headache, visual changes, focal neurological symptoms, seizures, coma, confusion
- **deep vein thrombosis**: leg pain, redness or swelling
- **splanchnic vein thrombosis**: abdominal pain
- **pulmonary embolus**: chest pain, shortness of breath
- **thrombocytopoenia**: petechiae, bleeding or bruising

The risk of TTS is higher in those aged under 50 years of age. It is more likely to occur in females aged 30-49 years of age.

It is estimated that 1 in 100,000 people aged 50 years and older and 2 in 100,000 people aged 18-49 years vaccinated with Vaxzevria may develop TTS after the first dose. One in 5 of these may die. The risk of TTS after a second dose of Vaxzevria is much lower.

It is estimated that 1 in 300,000 people vaccinated with JCOVDEN may develop TTS. One in 10 of these may die.

The risk of CVST from COVID-19 is much greater than the risk of TTS associated with the vaccine and increase with age. No specific risk factors for TTS have been identified.

Vaccine recipients should be advised to promptly seek medical attention if they develop symptoms as listed above.

Healthcare professionals should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia. Early recognition and prompt treatment are important in the management of TTS.

Healthcare professionals should seek early expert advice from the National Coagulation Centre about specialised testing and treatment options for patients presenting with thromboembolic events associated with thrombocytopenia (including DIC or CVST) occurring within weeks following adenoviral vector vaccination.

Cerebrovascular venous and sinus thrombosis without thrombocytopenia
Events of cerebrovascular venous and sinus thrombosis without thrombocytopenia have been observed very rarely following vaccination with Vaxzevria. Some cases had a fatal outcome. The majority of these cases occurred within the first four weeks following vaccination. This information should be considered for individuals at increased risk for cerebrovascular venous and sinus thrombosis.

These events may require different treatment approaches than TTS and healthcare professionals should consult applicable guidance.

Capillary leak syndrome
Capillary leak syndrome (CLS) has been reported as an extremely rare event following Spikevax and COVID-19 adenoviral vector vaccines.

It is characterised by acute and severe recurrent attacks of fluid leakage from the capillaries resulting in oedema mainly affecting the limbs, hypotension, haemoconcentration and hypoalbuminaemia.

Healthcare professionals should be aware of the signs and symptoms of CLS and of its risk of recurrence in people previously diagnosed with the condition. Patients with an acute episode of CLS following vaccination require prompt treatment and may require intensive supportive therapy.

Vaccine recipients should be advised to promptly seek medical attention if they develop oedema in the extremities or sudden weight gain in the days after vaccination, which may be associated with feeling faint (due to hypotension).

Myocarditis and pericarditis

Myocarditis and pericarditis are very rare side effects following vaccination with both Comirnaty and Spikevax particularly in males aged under 30 years, and following the second dose of Spikevax.

The risk of myocarditis may be lower in those aged 12-15 years compared to older adolescents. Myocarditis in children aged 5–11 years is very rare.

Studies have shown that after the second dose of Comirnaty there were about 2.6 extra cases of myocarditis per 100,000 males aged 12 - 29 years after seven days and 5.7 extra cases of myocarditis per 100,000 males aged 16 - 24 years after 28 days. The rates for Spikevax were three to five times higher.

The EMA concluded that the overall benefit risk remains favourable.

Available data suggest that the course of myocarditis or pericarditis following vaccination is not different from myocarditis or pericarditis from other causes.

Myocarditis and pericarditis may present with chest pain, shortness of breath, palpitations and fatigue. Most patients respond well to standard treatment, and the prognosis is good. However, it can occasionally progress to dilated cardiomyopathy and chronic heart failure.

Healthcare professionals should be aware of the signs and symptoms of myocarditis and pericarditis.

Vaccine recipients should be advised to promptly seek medical attention if they develop acute and persisting chest pain, palpitations or shortness of breath in the days after vaccination.

Healthcare professionals should consult applicable guidance and/or consult a cardiologist for advice on management.

Guillain-Barré syndrome (GBS)

In July 2021, the EMA included a warning in the licensed documentation of cases of GBS reported following vaccination with Vaxzevria. The available data neither confirms nor rule out a possible association with the vaccine.

Healthcare professionals should be alert to signs and symptom of GBS, allowing early diagnosis, supportive care and treatment. Vaccine recipients should be advised to seek immediate medical attention if they develop weakness and paralysis in the extremities that can progress to the chest and face.

Immune thrombocytopenia (ITP)
Cases of ITP, some with platelet levels below 20,000 per microlitre, have been reported very rarely, usually within four weeks after receiving Vaxzevria or JCOVDEN. Some of these occurred in individuals with a history of ITP.

If an individual has a history of a thrombocytopenic disorder, such as ITP, the risk of developing low platelet levels should be considered before administering the vaccine and platelet monitoring is recommended after vaccination.

Venous thromboembolism (VTE)
In October 2021, the EMA concluded that there is a reasonable possibility that rare cases of VTE (distinct from TTS) are linked to vaccination with JCOVDEN. Most cases observed in the clinical trials occurred in people with at least one risk factor for VTE.

Health care professionals should consider the risk of VTE after JCOVDEN in individuals with VTE risk factors.

5a.4.3 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). 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 are available on the National Immunisation Office (NIO) website at www.immunisation.ie

5a.5 Recommendations

The objective of the COVID-19 vaccination programme 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.

Table 5a.1 Recommendations for COVID-19 vaccines by age and immune status

Group		Primary course*	Additional dose	1st booster	2nd booster	3rd booster
65 years and older		√√		√	√	√
50-64 years		√√		√	√	√**
12-49 years	Underlying medical conditions	√√		√	√	√**
	Residents of long term care facilities	√√		√	√	
	Healthcare workers	√√		√	√	
	Others	√√		√		
Pregnancy		√√		√	√***	
5-11 years		√√				
12 years and older	Immuno-compromise associated with a sub optimal response to vaccines	√√	√	√	√	√
5-11 years		√√	√	√		

*two dose primary course (one dose if JCOVDEN/COVID-19 vaccine Janssen)

** those aged 12-64 years with an underlying medical condition who have not received a bivalent booster vaccine

***at 16 weeks gestation or later if not already boosted in this pregnancy

Table 5a.2 Underlying conditions associated with very high risk or high risk of severe COVID-19 disease.
May also include others, based on clinical judgement and a needs assessment.

Conditions in the shaded areas may be associated with a suboptimal response to vaccines and patients with these conditions should be given an mRNA vaccine if practicable and timely.

Underlying condition	Very high risk	High risk
Cancer	Receiving or within 6 weeks of receiving systemic cytotoxic chemotherapy, targeted therapy, monoclonal antibodies or immunotherapies Receiving treatment or pending treatment for a haematological cancer Undergoing or within 6 weeks of surgery or radical radiotherapy for lung or head and neck cancer Advanced/ metastatic cancer	Haematological[1] - within 5 years of treatment Non haematological cancer within 1 year following immunomodulating treatment All other cancers being treated (excluding hormonal treatment)
Chronic heart and vascular disease		e.g., heart failure, hypertensive cardiac disease
Chronic kidney disease	On dialysis, or eGFR less than 15 ml/min	eGFR less than30ml/min
Chronic liver disease		e.g., cirrhosis or fibrosis
Chronic neurological disease or condition	With evolving respiratory failure requiring non-invasive ventilation e.g., motor neurone disease, spinal muscular atrophy	Significantly compromised 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 conditions e.g. stable cystic fibrosis, severe asthma (continuous or repeated use of systemic corticosteroids), moderate COPD
Diabetes	HbA1c 58mmol/mol or greater	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 - Some B and T cell deficiencies **Treatment e.g.,** - Cyclophosphamide, Rituximab, Alemtuzumab, Cladribine or Ocrelizumab in the last 6 months	Other e.g., High dose systemic steroids[3] HIV, not on treatment or CD4 count less than 200 /10^{6}Lfor adults
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] Includes e.g., leukaemia, lymphomas, blood dyscrasias or other malignant neoplasms affecting the bone marrow or lymphatic systems

[2] APECED - autoimmune polyendocrinopathy candidiasis ectodermal dystrophy

[3] The following doses of prednisolone (or equivalent dose of other glucocorticoid) are likely to be immunosuppressive:

- Adults and children ≥10kg: ≥40mg/day for more than 1 week, or ≥20mg/day for 2 weeks or longer
- Children less than 10 kg: 2mg/kg/day for 2 weeks or longer

EMA authorised COVID-19 vaccines

- **Comirnaty (Pfizer/BioNTech)**
- **Spikevax** (formerly COVID-19 Vaccine Moderna)
- **Vaxzevria** (formerly COVID-19 Vaccine AstraZeneca)
- **JCOVDEN** (formerly COVID-19 Vaccine Janssen)
- **Nuvaxovid**

Table 5a.3 Booster vaccination recommendations by age and vaccine

Vaccine	Dose (mcg)	Age group		
		12-29	30-64	65 and older
Comirnaty	0.3ml (30mcg)	Yes	Yes	Yes
Comirnaty Original/ Omicron BA.1*	0.3ml (30mcg)	Yes	Yes	Yes
Comirnaty Original/ Omicron BA.4-5*	0.3ml (30mcg)	Yes	Yes	Yes
Spikevax	0.25ml (50mcg)	No	Yes	Yes
Spikevax bivalent Original/Omicron BA.1*	0.5ml (50mcg)	No	Yes	Yes

If bivalent vaccine supplies are limited, priority should be given to those:

- aged 65 years and older
- aged 12 years and older with immunocompromise associated with a sub optimal response to vaccines at the time of their primary or booster vaccination
- those aged 12-64 years with an underlying medical condition who have not received a bivalent booster vaccine
- who are pregnant, at 16 weeks gestation or later, and who have not received a booster vaccine in the current pregnancy

mRNA vaccines

Table 5a.4: Contraindications and precautions to an mRNA COVID-19 vaccine

	History	Action
Contraindication	• Anaphylaxis after a previous dose of Comirnaty or Spikevax • Anaphylaxis after polyethylene glycol (PEG, e.g., some bowel preparations for endoscopy, certain laxatives such as Movicol)	Consider vaccination with Nuvaxovid, Vaxzevria or JCOVDEN (formerly COVID-19 vaccine Janssen) in a suitable facility Observe for 30 minutes or Discuss with allergist/ immunologist
	• Anaphylaxis after Trometamol; Spikevax 100 and 50 micrograms and Comirnaty 10 micrograms are contraindicated	Vaccinate with alternate vaccine There is no alternative to Comirnarty 10 micrograms or Spikevax 50 micrograms
	• Previous history of myocarditis after a dose of Comirnaty or Spikevax	Consult with cardiologist
Special precautions	• Anaphylaxis after multiple, different drug classes, with no identified allergen (may indicate PEG allergy) • Anaphylaxis after a vaccine or a medicine known to contain PEG • Unexplained anaphylaxis (may indicate PEG allergy)	Clarify if PEG is tolerated (see FAQs) Discuss with allergist/ immunologist Consider vaccination with Nuvaxovid, Vaxzevria or JCOVDEN Observe for 30 minutes
	Those aged 12-29 years should receive Comirnaty as a subsequent dose	
	• Previous history of pericarditis after a dose of Comirnaty or Spikevax	Consult with cardiologist
	• Children with a previous history of MIS-C	Defer Comirnaty or Spikevax vaccination until clinical recovery or at least 3 months since diagnosis, whichever is the longer
	• Mastocytosis	Vaccinate as scheduled Observe for 30 minutes
	• Idiopathic anaphylaxis • Anaphylaxis after food, venom or medication	Vaccinate as scheduled Observe for 15 minutes
Not a contraindication or a precaution	• Non-anaphylactic food allergy • Family history of allergy, including anaphylaxis • Previous local reaction to any vaccine • Hereditary angioedema • Contact dermatitis to PEG-containing cosmetic product • Underlying asthma • Hay fever • NSAID allergy • Chronic spontaneous urticaria	Vaccinate as scheduled Observe for 15 minutes

5a.5.1 Comirnaty

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.

5a.5.1.1 Comirnaty 30 micrograms (0.3ml, for those aged 12 years and older)

(See Section 5a.5.1.4 Comirnaty 10 micrograms, 0.2ml, for those aged 5-11 years)

The vaccine should be stored in a freezer at -90°C to -60°C. 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, the vaccine can be stored for up to one month (31 days) 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 unopened vial is stable for up to:
- 24 hours when stored at temperatures from -3°C to +2°C
- a total of 4 hours when stored at temperatures from +8°C to +30°C.

The vaccine comes in two presentations
- one which does NOT require dilution (grey cap)
- one which requires dilution with 1.8ml of 0.9% sodium chloride (purple cap). After dilution, the vaccine should be kept at +2°C to +30°C and used within six hours.

Gently mix by inverting the vial 10 times prior to use. Do not shake the vial.

The two formulations are interchangeable.

Licensed indications
Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, for an additional vaccine for those who are immunocompromised and for a booster vaccine in individuals 12 years of age and older.

Vaccine efficacy
Efficacy is 95-100% after two doses in those aged 12 years and older.

Vaccine effectiveness
A large trial in Israel showed two dose effectiveness of 87% against hospitalisation and 92% against severe disease from 7 days after the second dose. This effectiveness may not apply to all variants.

Dose, route and schedule

Primary vaccination

The dose of vaccine is 0.3 ml intramuscularly (IM) into the deltoid muscle. The course consists of 2 doses 21-28 days apart.

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.

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 second dose is given between 17 and 20 days after the first dose, it is a valid dose. If the second dose is given before 17 days, this is not considered a valid dose. A third dose should be given at least 28 days after the second (invalid) dose.

Booster vaccination

The dose of vaccine is 0.3 ml IM.

Additional (3rd dose) vaccination (see Immunocompromised page 24)

The dose of vaccine is 0.3 ml IM.

Interchangeability

The same vaccine should preferably be used for both doses.

Consideration may be given to non-mRNA vaccination after anaphylaxis to a dose of this vaccine if aged 18 years or older, including pregnant women. The alternative vaccine should be given after an interval of at least 28 days and the person should be considered fully vaccinated.

Contraindications (see Table 5a.4)

- Anaphylaxis following a previous dose of the vaccine or any of its constituents (including polyethylene glycol (PEG)).
- Anaphylaxis following another mRNA vaccine.
- Previous history of myocarditis after a dose of an mRNA vaccine (see Section 5a.4.2).

Those with a contraindication to one mRNA COVID-19 vaccine should not receive another mRNA vaccine. Consideration may be given to non-mRNA vaccination for anyone aged 12 years and older following an individual benefit-risk assessment, including pregnant women. This should be given after an interval of at least 28 days and the person should be considered fully vaccinated.

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 (see Table 5a.4)

- Acute severe febrile illness; defer until recovery.
- Previous history of pericarditis after a dose of an mRNA vaccine - seek specialist advice (see Section 5a.4.2).
- There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.
- Consider non mRNA vaccination for those aged 12 years and older, including pregnant women, with:
  - Anaphylaxis after multiple, different drug classes, with no identified allergen (may indicate PEG allergy)
  - Anaphylaxis after a vaccine, or a medicine which contained PEG
  - Unexplained anaphylaxis (may indicate PEG allergy)

If there is a precaution to a booster mRNA vaccine, consideration can be given to boosting with an EMA authorised non-mRNA vaccine following an individual benefit-risk assessment.

For more information see Frequently Asked Questions about COVID-19 vaccines for people with pre-existing allergic conditions.

Patients with planned immunosuppressing 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

Unvacccinated

Those who are unvaccinated and develop laboratory confirmed COVID-19 infection should complete a primary vaccination course, with the first dose 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 with persisting symptoms post COVID-19 may be vaccinated, unless there is evidence of recent clinical deterioration.

Partially vaccinated
Those who have had laboratory confirmed COVID-19 infection between their doses of COVID-19 vaccine should complete their primary vaccination course, with their next dose at least four weeks after diagnosis or onset of symptoms.

Additional or booster vaccination
Those who have had laboratory confirmed COVID-19 infection or a positive COVID-19 antigen test with symptoms after a completed primary vaccine course, additional or booster dose (i.e., a breakthrough infection), should delay further vaccination after the COVID-19 infection for four months.

Serological testing prior to giving an additional or booster dose is not recommended.

Post vaccination observation period
- Vaccine recipients: 15 minutes.
- Those with a history of mastocytosis: 30 minutes
- Those with immediate itching, swelling or urticarial reaction at the vaccination site: 30 minutes or longer as clinically indicated

Immunocompromised *(see Chapter 3)*
Those with severe immunocompromise due to disease or treatment at the time of their primary COVID-19 vaccination do not have adequate protection. Protection can be enhanced by an additional dose (representing an extension of the primary vaccination series).

An additional dose (30 micrograms) should be given to those aged 12 years and older with immunocompromise at the time of vaccination, who have completed their primary course. The additional dose should be given regardless of whether the primary course was of an mRNA or an adenoviral vector vaccine. This is an extended primary vaccination course. The additional vaccine should be given after an interval of four months following the last dose of an authorised COVID-19 vaccine.

A first booster dose (30 micrograms) should be given to all those aged 12 years and older with immunocompromise associated with a suboptimal response to vaccines (Table 5a.2) who have completed a three dose primary series, after an interval of four months.

A second booster dose (30 micrograms) should be given to all those aged 12 years and older with immunocompromise (Table 5a.2) who have completed a three dose primary series and have received a first booster vaccine. The second booster dose should be given after an interval of four months.

A third booster dose (30 micrograms) should be given to all those aged 12 years and older with immunocompromise associated with a suboptimal

response to vaccines (Table 5a.2). The third booster dose should be given after an interval of four months.

Those who developed severe immunocompromise since their primary course, i.e., at the time of their first or second booster COVID-19 vaccination, require a further booster vaccine. No further vaccine is required as they would have mounted a sufficient immune response to the primary course.

See Table 5a.2 for conditions that may be associated with a suboptimal response to vaccines.

Pregnancy
The benefits of vaccination outweigh any know or potential risks of COVID-19 vaccination during pregnancy.

The two doses of the primary course should be given 21-28 days apart at any stage in pregnancy.

To enhance maternal protection and provide optimal benefit to the infant, an additional mRNA COVID-19 booster vaccine is recommended in pregnancy at 16 weeks gestation or later for those who have not received a booster vaccine in the current pregnancy.

Breastfeeding
Comirnaty can be used during breastfeeding. Data from women who were breastfeeding after vaccination have not shown a risk for adverse effects in breastfed infants.

Children from 12 years of age
In a study in adolescents aged 12-15 years without evidence of prior infection, the point estimate for efficacy was 100%.

Reactogenicity occurred at a slightly higher frequency compared to the adult population. No new safety concerns were observed.

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 replacement therapy, 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 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 Uncommon: injection site pruritus
General:	Very common: arthralgia, diarrhoea, fatigue, fever, headache, myalgia Common: nausea, vomiting Uncommon: asthenia, decreased appetite, extremity pain, insomnia, hyperhidrosis, hypersensitivity reactions (e.g. rash, pruritus, angioedema), lethargy, lymphadenopathy in the same arm as vaccination, malaise Rare: acute peripheral facial paralysis Very rare: myocarditis, pericarditis (see Section 5a.4.2) Unknown frequency: erythema multiforme, extensive swelling of the vaccinated limb, facial swelling (in those with a history of dermatological fillers), hypoaesthesia, paraesthesia

The most frequent adverse reactions during clinical trials in those aged 16 years or older were injection site pain (> 80%), fatigue (> 60%), headache (> 50%), myalgia and chills (> 30%), arthralgia (> 20%), pyrexia and injection site swelling (> 10%).

The most frequent adverse reactions in adolescents aged 12-15 years were injection site pain (> 90%), fatigue and headache (> 70%), myalgia and chills (> 40%), arthralgia and pyrexia (> 20%), injection site pain or swelling, fatigue and chills (≥10%).

Symptoms were usually mild or moderate in intensity, and resolved within a few days after vaccination. A lower frequency of adverse events is associated with greater age. A higher rate of pyrexia is seen after the second dose.

Post marketing surveillance showed an anaphylaxis rate of 2-5 per million in the US and 14/million in the UK (the latter figure includes anaphylactoid reactions). These rates are higher than after non COVID-19 vaccines.

First and second booster doses of mRNA vaccines have not shown any unexpected short term safety concerns. Myocarditis and pericarditis are very rare risks of mRNA vaccination, predominantly in males aged under 30 years after the second dose of the primary vaccination course and the risk appears to be comparatively lower following a first booster dose. Data on second booster doses is more limited but preliminary experience from Israel has not revealed any new safety concerns.

Safety data on Comirnaty booster vaccine for those aged 12-15 years is currently limited. In a placebo-controlled trial, 5,081 participants aged 16 years and older received a booster dose of Comirnaty at least six months after the second dose. The safety profile of the booster was similar to that seen after two doses.

In a recent US review of spontaneous reports, Comirnaty was associated with short lived, self-limited side effects. Local and systemic side effects in adolescents and young adults aged 16-24 were generally mild to moderate. They were more commonly reported after the second dose compared to the first and were less common after a booster dose than a second dose. In the US, 2.8 million adolescents aged 12-17 years have safely received a booster dose of Comirnaty vaccine.

Co-administration

COVID-19 vaccines and other vaccines may be administered at the same time or at any interval. Co-administered vaccines should be given in different arms.

COVID-19 and seasonal influenza vaccines should be co-administered where practicable to maximise uptake. A UK study revealed no unexpected safety concerns with co-administration.

Vaccinees should be informed there may be a slight increase in short term mild adverse events after co-administration with a seasonal influenza vaccine. These include pain at the site of injection, fatigue, headache, and myalgia.

There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

No interval is required between a COVID-19 vaccine and a subsequent monkeypox/smallpox vaccine (see Chapter 13a).

TB testing
Testing for TB infection with either the TST or an IGRA can be done at any time in relation to COVID-19 vaccination.

Duration of immunity
There is insufficient information to determine the duration of protection from the vaccine.

Vaccine recipients may not have optimal protection until 7 days after the second dose, and the vaccine may not protect all vaccinees.

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

Booster doses

First booster dose
A first booster dose (30 micrograms, the same dose as the primary schedule) should be given to all those aged 12 years and older.

If a child has received two doses of Comirnaty 10 micrograms and is now 12 years of age, they should receive a booster dose of Comirnaty 30 micrograms.

Second booster dose
A second booster dose should be given to those outlined in Table 5a.1.

Third booster dose
A third booster dose should be given to those outlined in Table 5a.1.

If there is a contraindication or precaution to an mRNA vaccine, consideration can be given to a first or second booster of an EMA authorised non-mRNA vaccine following an individual benefit-risk assessment.

5a.5.2.2 Comirnaty Original/Omicron BA.1 (30 micrograms)
The vaccine should be stored in a freezer at -25°C to -15°C. Each pack contains 10 vials. If the multidose vial is stored frozen it must be thawed prior to use.

Frozen vials should be transferred to an environment of +2°C to +8°C to thaw; a 10 vial pack may take 6 hours to thaw. Ensure vials are completely thawed prior to use.
Unopened vials can be stored for up to 10 weeks at +2 °C to +8 °C. Individual frozen vials may be thawed for 30 minutes at temperatures up to+ 30°C. Prior to use, the unopened vial can be stored for up to 24 hours at temperatures up to +30°C.

The vaccine does not require dilution. Once the multidose vial is punctured the vaccine should be kept at +2°C to +30°C and used as soon as possible and within 12 hours. Gently mix by inverting vials 10 times prior to use. Do not shake the vial.

Licensed indications
Active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 12 years of age and older who have previously received at least a primary vaccination course against COVID-19.

Vaccine efficacy
in a phase 3 clinical trial healthy adults age over 55 years who had previously received three doses of Original Comirnaty vaccine, participants received a booster dose of either Comirnaty original vaccine or Comirnaty original/ Omicron BA.1 bivalent vaccine (n=305 per group). Median interval between third and fourth dose was 6.3 months (range 4.7-12.9 months). In those who received a booster of the bivalent BA.1 vaccine, the neutralising antibody response against Omicron BA.1 strain was 1.56 times the levels of those who received the original vaccine as their trial booster

Dose, route and schedule
Booster vaccination
The dose of vaccine is 0.3 ml intramuscularly (IM) into the deltoid muscle.

The booster vaccine is recommended four to six months after the last COVID-19 vaccine or confirmed SARS-COV-2 infection. In exceptional circumstances an interval of three months may be used (e.g., in a person scheduled to commence chemotherapy). Giving booster vaccination just before or at the beginning of expected high viral circulation (e.g., autumn/winter) is desirable.

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.

Contraindications (see Table 5a.4)
- Anaphylaxis (serious systemic allergic reaction requiring medical intervention) to any of the vaccine constituents (including polyethylene glycol (PEG) and trometamol).
- Previous history of myocarditis after a dose of an mRNA vaccine (see Section 5a.4.2).

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 (see Table 5a.4)
- Acute severe febrile illness; defer until recovery.
- Previous history of pericarditis after a dose of an mRNA vaccine - seek specialist advice (see Section 5a.4.2).
- There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

For more information see Frequently Asked Questions about COVID-19 vaccines for people with pre-existing allergic conditions.

Those for whom a bivalent mRNA vaccine is contraindicated or declined should be offered an alternative vaccine.

Post vaccination observation period
- Those with no history of anaphylaxis: 15 minutes
- Those with a history of mastocytosis: 30 minutes
- Those with immediate itching, swelling or urticarial reaction at the vaccination site: 30 minutes or longer as clinically indicated

Immunocompromised *(see Chapter 3)*
Those who are immunocompromised due to disease or treatment may be vaccinated if they have no contraindications.

The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Comirnaty Original/Omicron BA.1 may be lower in immunocompromised individuals

See Table 5a.2 for conditions that may be associated with a suboptimal response to vaccines.

Pregnancy

No data are available regarding the use of Comirnaty Original/Omicron BA.1 during pregnancy. However, a large amount of observational data from pregnant women vaccinated with the initially approved Comirnaty vaccine during the second and third trimester have not shown an increase in adverse pregnancy outcomes. Since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, Comirnaty Original/Omicron BA.1 can be used during pregnancy.

To enhance maternal protection and provide optimal benefit to the infant, an additional bivalent mRNA COVID-19 booster vaccine is recommended in pregnancy at 16 weeks gestation or later for those who have not received a booster vaccine in the current pregnancy.

Breastfeeding

No data are available yet regarding the use of Comirnaty Original/Omicron BA.1 during breast-feeding. However, no effects on the breast-fed newborn/infant are anticipated since the systemic exposure of breast-feeding woman to the vaccine is negligible. Observational data from women who were breast-feeding after vaccination with the initially approved Comirnaty vaccine have not shown a risk for adverse effects in breast-fed newborns/infants. Comirnaty Original/Omicron BA.1 can be used during breast-feeding.

Vaccination of those with bleeding disorders or on anticoagulants

Those 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.

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 replacement therapy, 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 oral anticoagulants or antiplatelet agents, than with other anticoagulants.

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, swelling
Common:	injection site redness
Uncommon:	injection site pruritus
General:	Very common: arthralgia, chills, diarrhoea, fatigue, headache, myalgia, pyrexia Common: nausea, vomiting Uncommon: asthenia, decreased appetite, hyperhidrosis, hypersensitivity reactions (e.g., angioedema, pruritus, rash, urticaria), injection site pruritus, insomnia, lethargy, lymphadenopathy, malaise, night sweats, pain in extremity Rare: acute peripheral facial paralysis paraesthesia Very rare: myocarditis, pericarditis (see Section 5a.4.2) Unknown frequency: erythema multiforme, extensive swelling of the limb, facial swelling, hypoaesthesia, paraesthesia

No new safety concerns were observed but follow up time has been short. However, the study size did not allow for detection of very rare adverse events.

Co-administration

COVID-19 vaccines and other vaccines may be administered at the same time or at any interval. Co-administered vaccines should be given in different arms.

COVID-19 and seasonal influenza vaccines should be co-administered where practicable to maximise uptake. A UK study revealed no unexpected safety concerns with coadministration.

Vaccinees should be informed there may be a slight increase in short term mild adverse events after co-administration with a seasonal influenza vaccine. These include pain at the site of injection, fatigue, headache, and myalgia.

There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

No interval is required between a COVID-19 vaccine and a subsequent monkeypox/smallpox vaccine (see Chapter 13a).

TB testing
Testing for TB infection with either the TST or an IGRA can be done at any time in relation to COVID-19 vaccination.

Duration of immunity
There is insufficient information to determine the duration of protection from the vaccine.

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

5a.5.2.3 Comirnaty Original/ Omicron BA.4-5 (30 micrograms)
The vaccine should be stored in a freezer at -25°C to -15°C. Each pack contains 10 vials. If the multidose vial is stored frozen it must be thawed prior to use. Frozen vials should be transferred to an environment of +2°C to +8°C to thaw; a 10 vial pack may take 6 hours to thaw. Ensure vials are completely thawed prior to use.

Unopened vials can be stored for up to 10 weeks at +2 °C to +8 °C. Individual frozen vials may be thawed for 30 minutes at temperatures up to+ 30°C. Prior to use, the unopened vial can be stored for up to 24 hours at temperatures up to +30°C.

The vaccine does not require dilution. Once the multidose vial is punctured the vaccine should be kept at +2°C to +30°C and used as soon as possible and within 12 hours. Gently invert the vial 10 times prior to use. Do not shake the vial.

Licensed indications
Active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 12 years of age and older who have previously received at least a primary vaccination course against COVID-19.

Vaccine efficacy
The efficacy of a booster dose of Comirnaty Original/Omicron BA.4-5 is inferred from the immunogenicity of an Omicron BA.1 adapted vaccine.

Dose, route and schedule
Booster vaccination
The dose of vaccine is 0.3 ml intramuscularly (IM) into the deltoid muscle.

The booster vaccine is recommended four to six months from the time of the last COVID-19 vaccine or confirmed SARS-COV-2 infection. In exceptional circumstances an interval of three months may be used (e.g., in a person scheduled to commence chemotherapy).

Giving booster vaccination just before or at the beginning of expected high viral circulation (e.g., autumn/winter) is desirable.

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.

Contraindications (see Table 5a.4)

- Anaphylaxis (serious systemic allergic reaction requiring medical intervention) to any of the vaccine constituents (including polyethylene glycol (PEG) and trometamol).
- Previous history of myocarditis after a dose of an mRNA vaccine (see Section 5a.4.2).

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 (see Table 5a.4)

- Acute severe febrile illness; defer until recovery.
- Previous history of pericarditis after a dose of an mRNA vaccine - seek specialist advice (see Section 5a.4.2).
- There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

For more information see Frequently Asked Questions about COVID-19 vaccines for people with pre-existing allergic conditions.

Those for whom a bivalent mRNA vaccine is contraindicated or declined should be offered an alternative vaccine.

Post vaccination observation period

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

Immunocompromised *(see Chapter 3)*

Those who are immunocompromised due to disease or treatment may be vaccinated if they have no contraindications.

The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Comirnaty Original/Omicron BA.4-5 may be lower in immunocompromised individuals.

See Table 5a.2 for conditions that may be associated with a suboptimal response to vaccines.

Pregnancy

No data are available yet regarding the use of Comirnaty Original/Omicron BA.4-5 during pregnancy. However, a large amount of observational data from pregnant women vaccinated with the initially approved Comirnaty vaccine during the second and third trimester have not shown an increase in adverse pregnancy outcomes. Since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, Comirnaty Original/Omicron BA.4-5 can be used during pregnancy.

To enhance maternal protection and provide optimal benefit to the infant, an additional bivalent mRNA COVID-19 booster vaccine is recommended in pregnancy at 16 weeks gestation or later for those who have not received a booster vaccine in the current pregnancy.

Breastfeeding

No data are available yet regarding the use of Comirnaty Original/Omicron BA.4-5 during breast-feeding. However, no effects on the breast-fed newborn/infant are anticipated since the systemic exposure of breast-feeding woman to the vaccine is negligible. Observational data from women who were breast-feeding after vaccination with the initially approved Comirnaty vaccine have not shown a risk for adverse effects in breast-fed newborns/infants. Comirnaty Original/Omicron BA.4-5 can be used during breast-feeding.

Vaccination of those with bleeding disorders or on anticoagulants
Those 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.

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 replacement therapy, 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 oral anticoagulants or antiplatelet agents, than with other anticoagulants.

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
The safety of a booster dose of Comirnaty Original/Omicron BA.4-5 is inferred from safety data for a booster dose of an Omicron BA.1 adapted vaccine, as well as for a booster dose of Comirnaty Original.

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, swelling
	Common: injection site redness
	Uncommon: injection site pruritus
General:	Very common: arthralgia, chills, diarrhoea, fatigue, headache, myalgia, pyrexia
	Common: nausea, vomiting
	Uncommon: asthenia, decreased appetite,

hyperhidrosis, hypersensitivity reactions(e.g., angioedema, pruritus, rash, urticaria), injection site pruritus, insomnia, lethargy, lymphadenopathy, malaise, night sweats, pain in extremity
Rare: acute peripheral facial paralysis paraesthesia
Very rare: myocarditis, pericarditis (see Section 5a.4.2)
Unknown frequency: erythema multiforme, extensive swelling of the limb, facial swelling, hypoaesthesia, paraesthesia

Co-administration
COVID-19 vaccines and other vaccines may be administered at the same time or at any interval. Co-administered vaccines should be given in different arms.

COVID-19 and seasonal influenza vaccines should be co-administered where practicable to maximise uptake. A UK study revealed no unexpected safety concerns with coadministration.

Vaccinees should be informed there may be a slight increase in short term mild adverse events after co-administration with a seasonal influenza vaccine. These include pain at the site of injection, fatigue, headache, and myalgia.

There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

No interval is required between a COVID-19 vaccine and a subsequent monkeypox/smallpox vaccine (see Chapter 13a).

TB testing
Testing for TB infection with the TST or an IGRA can be done done at any time in relation to COVID-19 vaccination.

Duration of immunity
There is insufficient information to determine the duration of protection from the vaccine.

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

5a.5.1.4 Comirnaty 10 micrograms (0.2ml, for those aged 5-11 years)
The vaccine should be stored in a freezer at -90°C to -60°C. Vials should be transferred to +2°C to +8°C to thaw which may take four 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 ten weeks at +2°C to +8°C and up to 12 hours at up to +30°C. Once thawed, the vaccine cannot be re-frozen.

The unopened vial is stable for up to:

- 10 weeks when stored at temperatures from -2°C to +2°C
- a total of 24 hours when stored at temperatures from +8°C to +30°C.

The vaccine requires dilution with 1.3ml of 0.9% sodium chloride. After dilution, the vaccine should be kept at +2°C to +30°C and used within 12 hours. Gently invert the vial 10 times prior to use. Do not shake the vial.

Licensed indications
Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus in children aged 5-11 years.

Vaccine efficacy
In a study in children aged 5 – 11 years without evidence of prior infection who were given the lower dose of Comirnaty, there were three COVID-19 cases in 1,305 children who received the vaccine, and 16 cases in 663 who received a placebo The point estimate for efficacy was 90.7%. The low dose vaccine demonstrated efficacy against the original and Delta strain.

Approximately 20% enrolled in the trial had an underlying condition associated with severe COVID-19 infection including obesity, but specific risk groups or impact on severe disease were not studied and immunocompromised children were not included.

Dose, route and schedule
Primary vaccination
The dose of vaccine is 0.2 ml intramuscularly (IM) into the deltoid muscle. The course consists of 2 doses 21 days apart.

If more than ten 0.2ml 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 dose of Comirnaty depends on the age at the time of the vaccination, e.g., an 11 year old child who receives the first dose of Comirnaty 10 micrograms and who is 12 years of age at the time of their second dose, should receive a dose of Comirnaty 30 micrograms.

If the interval between doses is longer than 21 days, the second dose should be given as soon as possible. The course does not need to be restarted.

If the second dose is given between 19 or 20 days after the first dose, it is a valid dose. If the second dose is given before 19 days, this is not a valid dose. A third dose should be given 21 days after the second (invalid) dose.

Interchangeability
The same vaccine should be used for both doses.

Contraindications (see Table 5a.4)

- Anaphylaxis following a previous dose of the vaccine or any of its constituents (including polyethylene glycol (PEG) and trometamol).
- Previous history of myocarditis after a dose of an mRNA vaccine (see Section 5a.4.2).

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 (seeTable 5a.4)

- Acute severe febrile illness; defer until recovery.
- Previous history of pericarditis after a dose of an mRNA vaccine - seek specialist advice (see Section 5a.4.2).
- Vaccination should be postponed in children with a previous history of MIS-C, until clinical recovery or until 90 days or more since diagnosis, whichever is the longer.

For more information see Frequently Asked Questions about COVID-19 vaccines for people with pre-existing allergic conditions.

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

Vaccination after COVID-19
Unvaccinated
Vaccination should be deferred until clinical recovery from COVID-19 infection 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 with persisting symptoms post COVID-19 may be vaccinated unless there is evidence of recent clinical deterioration.

Partially vaccinated
Those who have had laboratory confirmed COVID-19 infection between their doses of COVID-19 vaccine should complete their primary vaccination course, with their next dose at least four weeks after diagnosis or onset of symptoms. Serological testing prior to vaccination is not recommended.

Post vaccination observation period
- Vaccine recipients: 15 minutes
- Those with a history of mastocytosis: 30 minutes
- Those with immediate itching, swelling or urticarial reaction at the vaccination site: 30 minutes or longer as clinically indicated

Immunocompromised *(see Chapter 3)*
Immunocompromised individuals due to disease or treatment may be vaccinated if they have no contraindications.

Data indicates that those with severe immunocompromise do not have adequate protection following a primary COVID-19 vaccine course. There is evidence that protection can be enhanced by an additional mRNA vaccine dose, representing an extension of the primary vaccination series.

An additional Comirnaty dose (10 micrograms 0.2ml) should be given to those aged 5-11 years with immunocompromise associated with a suboptimal response to vaccines at the time of vaccination, who have completed their primary course. This is an extended primary vaccination course.

The additional vaccine should be given at least 28 days following the second dose.

Serological testing prior to giving an additional dose is not recommended.

A first booster dose (10 micrograms 0.2ml) should be given to all those aged 5-11 years with immunocompromise associated with a suboptimal response to vaccines who have completed an extended primary vaccination course (three doses) after an interval of four months.

See Table 5a.2 for conditions that may be associated with a suboptimal response to vaccines.

Those who developed severe immunocompromise since their primary course i.e., at the time of their first booster COVID-19 vaccination, require a further booster vaccine. No further vaccine is required as they would have mounted a sufficient immune response to the primary course.

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 parent or guardian about this risk. For those with thrombocytopenia (platelet

count less than $50x10^9$/L), consult the supervising consultant. People with mild bleeding disorders or on maintenance dose Emicizumab (Hemlibra) do not require haemostatic cover for vaccination.

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 replacement therapy, contact the child's supervising consultant.

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 oral anticoagulants or antiplatelet agents, than with other anticoagulants.

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, redness and swelling Uncommon: injection site pruritus
General:	Very common: arthralgia, diarrhoea, fatigue, fever, headache, myalgia, pyrexia Common: nausea, vomiting Uncommon: asthenia, decreased appetite, extremity pain, insomnia, hyperhidrosis, hypersensitivity reactions (e.g., rash, pruritus, angioedema), lethargy, lymphadenopathy in the same arm as vaccination, malaise, night sweats, pain in extremity Rare: acute peripheral facial paralysis Unknown frequency: anaphylaxis, erythema multiforme, extensive swelling of the vaccinated limb, myocarditis, pericarditis (see Section 5a.4.2)

The most frequent adverse reactions in children 5 to 11 years of age were injection site pain (>80%), fatigue (>50%), headache (>30%), injection site redness and swelling (>20%), myalgia and chills (>10%).

These were usually mild or moderate in intensity and resolved within a few days after vaccination. A higher rate of pyrexia was seen after the second dose.

The safety profile in the clinical trials of children aged 5-11 years was similar to that seen in older trial participants. No cases of myocarditis were noted. No new safety concerns were observed. However, the study size did not allow for detection of rare or very rare adverse events or to evaluate whether the characteristics of identified but rarer risks, such as myocarditis, differ compared with the adolescent and adult populations.

Co-administration
COVID-19 vaccines and other vaccines may be administered at the same time or at any interval.

Co-administered vaccines should be given in different arms.

TB testing
Testing for TB infection with either the TST or an IGRA can be done at any time in relation to COVID-19 vaccination.

Duration of immunity
There is insufficient information to determine the duration of protection from the vaccine.

Vaccine recipients may not have optimal protection until seven days after the second dose, and the vaccine may not protect all vaccinees.

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

5a.5.2 Spikevax (formerly 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.

5a.5.2.1 Spikevax 100 micrograms (for those aged 30 years and older)

(See Section 5a.5.2.3 Spikevax 50 micrograms for those aged 6-11 years)

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 two 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 24 hours at +8°C up to +25°C. Once thawed, the vaccine cannot be re-frozen. Do not shake or dilute. Swirl the vial gently after thawing and before each withdrawal. Pierce the stopper preferably at a different site each time.

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 19 hours.

Licensed indications
Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus in individuals 12 years of age and older.

Spikevax is not recommended for those aged 12-29 years.

Vaccine efficacy
Clinical trial data demonstrated a two-dose vaccine efficacy of 94.1% in those aged 18 years and above. This efficacy may not apply to all variants.

Dose, route and schedule
Primary vaccination
The dose of vaccine is 0.5 ml IM, preferably into the deltoid muscle. The course consists of two doses 28 days apart.

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

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 second dose was given between 21 and 27 days after the first dose, it is a valid dose. If the second dose is given before 21 days, this is not considered a valid dose. A third dose should be given 28 days after the second (invalid) dose.

Booster vaccination
The dose of vaccine is 0.25 ml IM (**half the dose of the primary schedule**).

Additional (3rd dose) vaccination (see Immunocompromised)
The dose of vaccine is 0.5ml IM

Interchangeability
The same vaccine should preferably be used for both doses.

Consideration may be given to non-mRNA vaccination after anaphylaxis to a dose of this vaccine if aged 30 years or older, including pregnant women. The alternative vaccine should be given after an interval of at least 28 days and the person should be considered fully vaccinated.

Contraindications (see Table 5a.4)
- Anaphylaxis following a previous dose of the vaccine or any of its constituents (including polyethylene glycol (PEG) and trometamol).

- Anaphylaxis following another mRNA vaccine.
- Previous history of myocarditis after a dose of an mRNA vaccine (see Section 5a.4.2).

Those with a contraindication to one mRNA COVID-19 vaccine should not receive another authorised mRNA vaccine. Consideration may be given to non-mRNA vaccination for anyone 30 years and older following an individual benefit-risk assessment, including pregnant women. This should be given after an interval of at least 28 days and the person should be considered fully vaccinated.

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 (see Table 5a.4)

- Acute severe febrile illness; defer until recovery.
- Previous history of pericarditis after a dose of an mRNA vaccine - seek specialist advice (see Section 5a.4.2).
- There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.
- Consider non-mRNA vaccination for those aged 30 years or older, including pregnant women, with:
  - Anaphylaxis after multiple, different drug classes, with no identified allergen (may indicate PEG allergy)
  - Anaphylaxis after a vaccine or a medicine which contained PEG
  - Unexplained anaphylaxis (may indicate PEG allergy)

If there is a precaution to a booster mRNA vaccine, consideration can be given to boosting with an EMA authorised non-mRNA vaccine following an individual benefit-risk assessment.

For more information see Frequently Asked Questions about COVID-19 vaccines for people with pre-existing allergic conditions.

Patients with planned immunosuppressing 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

Unvacccinated

Those who are unvaccinated and develop laboratory confirmed COVID-19 infection should complete a primary vaccination course, with the first dose 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 with persisting symptoms post COVID-19 may be vaccinated, unless there is evidence of recent clinical deterioration.

Partially vaccinated

Those who have had laboratory confirmed COVID-19 infection between their doses of COVID-19 vaccine should complete their primary vaccination course, with their next dose at least four weeks after diagnosis or onset of symptoms.

Additional or booster vaccination

Those who have had laboratory confirmed COVID-19 infection or a positive COVID-19 antigen test with symptoms after a completed primary vaccine course, additional or first booster dose (i.e., a breakthrough infection) should delay further vaccination after the COVID-19 infection was diagnosed for four months.

Post vaccination observation period

- Vaccine recipients:15 minutes.
- Those with a history of mastocytosis: 30 minutes
- Those with immediate itching, swelling or urticarial reaction at the vaccination site: 30 minutes or longer as clinically indicated

Immunocompromised *(see Chapter 3)*

Immunocompromised individuals due to disease or treatment aged **30 years and older** may be vaccinated if they have no contraindications.

Data indicates that those with severe immunocompromise at the time of their primary COVID-19 vaccination do not have adequate protection. There is evidence that protection can be enhanced by an additional dose, (representing an extension of the primary vaccination series).

An additional dose (100 micrograms) should be given to those aged 30 years and older with immunocompromise associated with a suboptimal response to vaccines at the time of vaccination, who have completed their primary course. The additional dose should be given regardless of whether the primary course was with an mRNA or an adenoviral vector vaccine. This is an extended primary vaccination course. The additional vaccine should be given after an interval of four months following the last dose of an authorised COVID-19 vaccine.

An additional non-mRNA vaccine can be considered for those with a contraindication or precaution to an mRNA vaccine.

A first booster dose (**50 micrograms**) should be given to those aged 30 years and older with immunocompromise associated with a suboptimal response to vaccines (Table 5a.2) who have completed a three dose primary series after an interval of four months.

A second booster dose (**50 micrograms**) should be given to all those aged 30 years and older with immunocompromise associated with a suboptimal response to vaccines (Table 5a.2) who have completed a three dose primary series and a first booster vaccine. The second booster dose should be given after an interval of four months.

A third booster dose (**50 micrograms**) should be given to all those aged 30 years and older with immunocompromise associated with a suboptimal response to vaccines (Table 5a.2) after their second booster vaccine. The third booster dose should be given after an interval of four months.

See Table 5a.2 for conditions that may be associated with a suboptimal response to vaccines.

Those who developed severe immunocompromise since their primary course, i.e., at the time of their first or second booster COVID-19 vaccination, require a further booster vaccine. No further vaccine is required as they would have mounted a sufficient immune response to the primary course.

Pregnancy

The benefits of vaccination outweigh any know or potential risks of COVID-19 vaccination during pregnancy.

The two doses of the primary course should be given 28 days apart at any stage in in pregnancy **to those aged 30 years and older**.

To enhance maternal protection and provide optimal benefit to the infant, an additional mRNA COVID-19 booster vaccine is recommended in pregnancy at 16 weeks gestation or later for **those aged 30 years and older** who have not received a booster vaccine in the current pregnancy.

Breastfeeding

Spikevax can be given **to those aged 30 years and older who are breast feeding.** Data from women who were breastfeeding after vaccination have not shown a risk for adverse effects in breastfed infants.

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 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 replacement therapy, 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 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 erythema, 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 Common: diarrhoea, pain

Uncommon: dizziness
Rare: acute peripheral facial paralysis, facial swelling (in those with a history of dermatological fillers), hypoaesthesia, paraesthesia
Very rare: myocarditis, pericarditis (see Section 5a.4.2)
Unknown frequency: capillary leak syndrome, erythema, extensive swelling of the vaccinated limb

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 similar in those aged 12-17 years.

These 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 lower frequency of adverse events is associated with greater age. A higher rate of local and systemic adverse events are seen after the second dose.

Post marketing surveillance has reported an anaphylaxis rate of 2-5/ million in the US and 21/million in the UK (the latter figure includes anaphylactoid reactions). These rates are higher than after non COVID-19 vaccines.

First and second booster doses of mRNA vaccines have not shown any unexpected short term safety concerns. Myocarditis and pericarditis are very rare risks of mRNA vaccination, predominantly in males aged under 30 years after the second dose of the primary vaccination course and the risk appears to be comparatively lower following a first booster dose. Data on second booster doses is more limited but preliminary experience from Israel has not revealed any new safety concerns.

Co-administration
COVID-19 vaccines and other vaccines, may be administered at the same time or at any interval.

Co-administered vaccines should be given in different arms.

COVID-19 and seasonal influenza vaccines should be co-administered where practicable to maximise uptake. A UK study revealed no unexpected safety concerns with co-administration.

Vaccinees should be informed there may be a slight increase in short term mild adverse events after co-administration. These include pain at the site of injection, fatigue, headache, and myalgia.

There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

No interval is required between a COVID-19 vaccine and a subsequent monkeypox/smallpox vaccine (see Chapter 13a).

TB testing
Testing for TB infection with either the TST or an IGRA, can be done at any time in relation to COVID-19 vaccination.

Duration of immunity
There is insufficient information to determine the duration of protection from the vaccine.

Vaccine recipients may not have optimal protection until 14 days after the second dose, and the vaccine may not protect all vaccinees.

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

Booster doses

First booster dose

A first booster dose (**50 micrograms, half the dose of the primary schedule**) should be given to all those **aged 30 years and older**.

Second booster dose

A second booster dose should be given to those aged 30 years and older as outlined in Table 5a.1.

Third booster dose

A third booster dose should be given to those aged 30 years and older as outlined in Table 5a.1.

If there is a contraindication or precaution to an mRNA vaccine, consideration can be given to a first or second booster of an EMA authorised non-mRNA vaccine following an individual benefit-risk assessment.

5a.5.2.3 Spikevax bivalent Original/Omicron BA.1, 50 micrograms (for those aged 30 years and older)

The vaccine should be stored in a freezer at -50°C to -15°C. Each pack contains 10 vials. If the multidose vial is stored frozen it must be thawed prior to use. Frozen vials should be transferred to an environment of +2°C to +8°C to thaw; a 10 vial pack may take 6 hours to thaw. Ensure vials are completely thawed prior to use.

Unopened vials can be stored for up to 14 days at +2°C to +8°C. Individual frozen vials may be thawed for 30 minutes at temperatures up to+ 30°C.

Prior to use, the unopened vial can be stored for up to 24 hours at temperatures up to +30°C.

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 19 hours.

Do not shake or dilute the vial. Swirl the vial gently after thawing and before each withdrawal. Pierce the stopper preferably at a different site each time.

Licensed indications
Active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 12 years of age and older who have previously received at least a primary vaccination course against COVID-19.

Spikevax bivalent Original/Omicron BA.1, 50 micrograms is not recommended for those aged 12-29 years

Vaccine efficacy
A clinical trial compared a booster dose of Spikevax bivalent BA.1 containing vaccine to a booster dose of Spikevax original vaccine, given at least three months following previous dose (median interval 4.5 months).One month following vaccination the bivalent BA.1 containing booster elicited a higher neutralising antibody response to Omicron BA.1 compared to those who received a booster with the original vaccine, in those with or without prior SARS CoV-2 infection

Neutralising antibodies against the ancestral strain were slightly higher in those who received the bivalent BA.1 containing vaccine compared to the original vaccine. While the bivalent vaccine did effectively boost levels of neutralising antibody to BA.4/BA.5 by a 5.4 fold rise compared to pre booster levels, the geometric mean levels were lower than against Omicron BA.1

Dose, route and schedule
Booster vaccination
The dose of vaccine is 0.5 ml intramuscularly (IM) into the deltoid muscle. The booster vaccine is recommended four to six months from the time of the last COVID-19 vaccine or confirmed SARS-COV-2 infection. In exceptional

circumstances an interval of three months may be used (e.g., in a person scheduled to commence chemotherapy).

Giving booster vaccination just before or at the beginning of expected high viral circulation (e.g., autumn/winter) is desirable.

If more than five 0.5ml 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.

Contraindications (see Table 5a.4)

- Anaphylaxis (serious systemic allergic reaction requiring medical intervention) to any of the vaccine constituents (including polyethylene glycol (PEG) and trometamol).
- In those aged under 30 years of age, previous history of myocarditis after an mRNA vaccine (see Section 5a.4.2).

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 (see Table 5a.4)

- Acute severe febrile illness; defer until recovery.
- Previous history of pericarditis after a dose of an mRNA vaccine - seek specialist advice (see Section 5a.4.2).
- There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

For more information see Frequently Asked Questions about COVID-19 vaccines for people with pre-existing allergic conditions.

Those for whom a bivalent mRNA vaccine is contraindicated or declined should be offered an alternative vaccine.

Post vaccination observation period

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

Immunocompromised *(see Chapter 3)*
Those who are immunocompromised due to disease or treatment **aged 30 years and older** may be vaccinated if they have no contraindications.

The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Comirnaty Original/Omicron BA.4-5 may be lower in immunocompromised individuals.
See Table 5a.2 for conditions that may be associated with a suboptimal response to vaccines.

Pregnancy
No data are available yet regarding the use of Comirnaty Original/Omicron BA.4-5 during pregnancy. However, a large amount of observational data from pregnant women vaccinated with the initially approved Comirnaty vaccine during the second and third trimester have not shown an increase in adverse pregnancy outcomes. Since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, Comirnaty Original/Omicron BA.4-5 can be used during pregnancy for those **aged 30 years and older**.

To enhance maternal protection and provide optimal benefit to the infant, an additional bivalent mRNA COVID-19 booster vaccine is recommended in pregnancy at 16 weeks gestation or later for those who have not received a booster vaccine in the current pregnancy.

Breastfeeding
No data are available yet regarding the use of Comirnaty Original/Omicron BA.4-5 during breast-feeding. However, no effects on the breast-fed newborn/infant are anticipated since the systemic exposure of breast-feeding woman to the vaccine is negligible. Observational data from women who were breast-feeding after vaccination with the initially approved Comirnaty vaccine have not shown a risk for adverse effects in breast-fed newborns/infants. Comirnaty Original/Omicron BA.4-5 can be given during breast-feeding to those **aged 30 years and older**

Vaccination of those with bleeding disorders or on anticoagulants
Those 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.

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 replacement therapy, 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 oral anticoagulants or antiplatelet agents, than with other anticoagulants.

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 erythema, pain, swelling Common: injection site rash, urticaria, delayed injection site reaction Uncommon: injection site pruritus
General:	Very common: arthralgia, chills, fatigue, headache, lymphadenopathy, myalgia, nausea, pyrexia, vomiting Common: diarrhoea, rash Uncommon: abdominal pain, Rare: acute peripheral facial paralysis, facial swelling, hypoaesthesia, paraesthesia Very rare: myocarditis, pericarditis (see Section 5a.4.2) Unknown frequency: erythema multiforme, extensive swelling of the limb, hypersensitivity

Co-administration
COVID-19 vaccines and other vaccines may be administered at the same time or at any interval. Co-administered vaccines should be given in different arms.

COVID-19 and seasonal influenza vaccines should be co-administered where practicable to maximise uptake. A UK study revealed no unexpected safety concerns with coadministration.

Vaccinees should be informed there may be a slight increase in short term mild adverse reactions after co-administration with a seasonal influenza vaccine. These include pain at the site of injection, fatigue, headache, and myalgia.

There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

No interval is required between a COVID-19 vaccine and a subsequent monkeypox/smallpox vaccine (see Chapter 13a).

TB testing
Testing for TB infection with the TST or an IGRA can be done at any time in relation to COVID-19 vaccination.

Duration of immunity
There is insufficient information 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.

5a.5.2.3 Spikevax 50 micrograms (0.25ml) for children age 6-11 years
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 two and a half hours and must sit at room temperature for 15 minutes before administering. Alternatively, frozen vials may be thawed for one 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 24 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 19 hours. Do not shake or dilute. Swirl the vial gently after thawing and before each withdrawal. Pierce the stopper preferably at a different site each time.

Licensed indications
Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in children aged 6-11 years.

Vaccine efficacy
A total of just over 4,000 participants were randomised 3:1 to receive two doses of Spikevax or saline placebo one month apart. Efficacy was evaluated in participants who received two doses (0.25 ml at 0 and 1 month) of either Spikevax (n=2,644) or placebo (n=853) and had a negative baseline

SARS-CoV-2 status. in the Per Protocol Set. COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. There were three COVID-19 cases (0.1%) in the Spikevax group and four COVID-19 cases (0.5%) in the placebo group.

Dose, route and schedule
Primary vaccination
The dose of vaccine is 0.25 ml intramuscularly (IM) into the deltoid muscle. The course consists of 2 doses 28 days apart.

If more than twenty 0.25ml 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 dose of Spikevax depends on the age at the time of the first vaccine. For example, if an 11 year old child received the first dose of Spikevax 50 micrograms (0.25ml) and who is 12 years of age at the time of their second dose, they should receive a further dose of Spikevax 100 micrograms (0.5ml).

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 second dose is given between 21 and 27 days after the first dose, it is a valid dose. If the second dose is given before 21 days, this is not considered a valid dose. A third dose should be given 28 days after the second (invalid) dose.

Interchangeability
The same vaccine should be used for both doses.

Contraindications (see Table 5a.4)
- Anaphylaxis following a previous dose of the vaccine or any of its constituents (including polyethylene glycol (PEG) and trometamol).
- Previous history of myocarditis after a dose of an mRNA vaccine (see Section 5a.4.2).

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 (see Table 5a.4)
- Acute severe febrile illness; defer until recovery.
- Previous history of pericarditis after a dose of an mRNA vaccine - seek specialist advice (see Section 5a.4.3).
- Vaccination should be postponed in children with a previous history of MIS-C, until clinical recovery has been achieved or until 90 days or more since diagnosis, whichever is the longer.

For more information about COVID-19 vaccines for people with pre-existing allergic conditions see Frequently Asked Questions.

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

Vaccination after COVID-19
Unvaccinated
Vaccination should be deferred until clinical recovery from COVID-19 infection 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 with persisting symptoms post COVID-19 may be vaccinated unless there is evidence of recent clinical deterioration.

Partially vaccinated
Those who have had laboratory confirmed COVID-19 infection between their doses of COVID-19 vaccine should complete their primary vaccination course, with their next dose at least four weeks after diagnosis or onset of symptoms. Serological testing prior to vaccination is not recommended.

Post vaccination observation period
- Those with no history of anaphylaxis: 15 minutes
- Those with a history of mastocytosis: 30 minutes
- Those with immediate itching, swelling or urticarial reaction at the vaccination site: 30 minutes or longer as clinically indicated

Immunocompromised (see Chapter 3)
Immunocompromised children due to disease or treatment may be vaccinated if they have no contraindications.

Data indicate that those with severe immunocompromise do not have adequate protection following a primary COVID-19 vaccine course. There is evidence that protection can be enhanced by an additional mRNA vaccine dose, representing an extension of the primary vaccination series.

An additional Spikevax dose (50 micrograms 0.25ml) should be given to those aged 6-11 years with immunocompromise associated with a suboptimal response to vaccines at the time of vaccination, who have completed their primary course. This is an extended primary vaccination course.

The additional vaccine should be given after at least 28 days following the second dose.

Serological testing prior to giving an additional dose is not recommended.

A first booster dose (50 micrograms) should be given to all those aged 6-11 years with immunocompromise associated with a suboptimal response to vaccines who have completed an extended primary vaccination course (three doses) after an interval of four months.

Those who developed severe immunocompromise since their primary course (i.e., at the time of their first booster COVID-19 vaccination), require a further booster vaccine. No further vaccine is required as they would have mounted a sufficient immune response to the primary course.

See Table 5a.2 for conditions that may be associated with a suboptimal response to vaccines.

Vaccination of those with bleeding disorders or on anticoagulants
Children 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.

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 replacement therapy, 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 oral anticoagulants or antiplatelet agents, than with other anticoagulants.

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 <1/10
Rare:	>1/10,000 and <1/1,000
Very rare:	<1/10,000
Local:	Very common: injection site erythema, pain, swelling Common: injection site rash, urticaria Uncommon: injection site pruritus
General:	Very common: arthralgia, axillary lymphadenopathy on the side of injection, chills, fatigue, fever, headache, myalgia, nausea, vomiting Common: abdominal pain, diarrhoea, rash Uncommon: dizziness Rare: hypoaesthesia paraesthesia Very rare: myocarditis, pericarditis (see Section 5a.4.2) Unknown frequency: erythema multiforme

The most frequent adverse reactions in children 6 to 11 years of age following administration of the primary series were injection site pain (>95%), fatigue (>70%), headache (>60%), myalgia (>30%), chills (>30%), nausea/vomiting (>20%), axillary swelling/tenderness (>20%), fever (>20%), arthralgia (>20%) and injection site erythema and swelling (>20%).

No new safety concerns were observed but follow up time has been short. However, the study size did not allow for detection of very rare adverse events.

Co-administration
COVID-19 vaccines and other vaccines may be administered at the same time or at any interval.

Co-administered vaccines should be given in different arms.

TB testing
Testing for TB infection with either the TST or an IGRA can be done at any time in relation to COVID-19 vaccination.

Duration of immunity
There is insufficient information to determine the duration of protection from the vaccine.

Vaccine recipients may not have optimal protection until 14 days after the second dose, and the vaccine may not protect all vaccinees.

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

Adenoviral vector vaccines

Table 5a.5: Contraindications and precautions to a adenoviral vector COVID-19 vaccine

	History	Action
Contraindication	• Anaphylaxis after a previous dose of Vaxzevria • Anaphylaxis after polysorbate 80	Consider vaccination with Comirnaty or Spikevax in a suitable facility Observe for 30 minutes or Discuss with allergist/ immunologist
Special precautions	• Anaphylaxis after a vaccine, injected antibody preparation, or a medicine known to contain polysorbate 80 • Unexplained anaphylaxis (may indicate polysorbate 80 allergy)	Clarify if polysorbate 80 is tolerated (see FAQs) Discuss with allergist/ immunologist Consider vaccination with Comirnaty or Spikevax Observe for 30 minutes
	• Mastocytosis	Vaccinate as scheduled Observe for 30 minutes
	• Idiopathic anaphylaxis • Anaphylaxis after food, venom or medication	Vaccinate as scheduled Observe for 15 minutes
Not a contraindication or a precaution	• Non-anaphylactic food allergy • Family history of allergy, including anaphylaxis • Previous local reaction to any vaccine • Hereditary angioedema • Contact dermatitis to polysorbate 80 containing cosmetic product • Underlying asthma • Hay fever • NSAID allergy • Chronic spontaneous urticaria	Vaccinate as scheduled Observe for 15 minutes

5a.5.3 **Vaxzevria** (formerly 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 an opened vial may be stored in a refrigerator (+2°C to + 8°C) for a maximum of 48 hours if it is immediately returned to the refrigerator following each puncture.

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

Vaccine efficacy
Clinical trial data demonstrated a two-dose vaccine efficacy of 59.5% in those aged 18 years and above. There was insufficient clinical data to allow reliable calculation of efficacy in those aged 55 years and older. However, as a similar immune response was shown in all age groups, including those aged 65 years 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 years and older who received the vaccine.

Clinical trial data published in October 2021 estimated overall vaccine efficacy in adults of 74%. Estimated vaccine efficacy was 83.5% in those aged 65 years or older. There were no severe or critical symptomatic COVID-19 cases in the fully vaccinated cohort.

Vaccine effectiveness
A prospective population study of 5.4 million people from Scotland found that the first dose of vaccine showed effectiveness of 94% for COVID-19 related hospitalisation at 28-34 days post-vaccination. This effectiveness may not apply to all variants.

Dose, route and schedule
The dose of vaccine is 0.5 ml IM, into the deltoid muscle. The vaccine is authorised as a two dose course 4-12 weeks apart.

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.

It is recommended the two doses are given 8-12 weeks apart because of greater efficacy after a longer interval between doses.

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 3 weeks (21 days). If the second dose is given before 21 days, this is not a valid vaccine. A third dose should be given 28 days after the second (invalid) vaccine.

Interchangeability
The same vaccine should preferably be used for both doses.

For those who have already had a first dose of Vaxzevria and who did not complete the vaccination schedule as recommended, an mRNA vaccine should be offered.

If an mRNA vaccine is used as a second dose, it should be given after an interval of at least 28 days and the person should be considered fully vaccinated.

Those who receive a heterologous schedule should be considered fully vaccinated after their second vaccine (seven days after Comirnaty, 14 days after Spikevax).

Contraindications (see Table 5a.5)

- Anaphylaxis following a previous dose of the vaccine or any of its constituents (including polysorbate 80).
- Thrombosis with Thrombocytopenia Syndrome after the first dose. of Vaxzevria or JCOVDEN (see Section 5a.4.2).
- Previous history of capillary leak syndrome (see Section 5a.4.2).

Those with a contraindication to one adenoviral vector vaccine should not receive another adenoviral vector vaccine. They should be offered an alternative vaccine, given at least 28 days later and the person considered fully vaccinated. (see Table 5a.5)

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 (see Table 5a.5)

- Acute severe febrile illness; defer until recovery.
- Consider mRNA vaccination for those with:
  - Anaphylaxis after a vaccine, injected antibody preparation, or a medicine known to contain polysorbate 80
  - Unexplained anaphylaxis (may indicate polysorbate 80 allergy).

For more information see Frequently Asked Questions about COVID-19 vaccines for people with pre-existing allergic conditions.

Those aged **under 50 years,** including those with conditions with very high or high risk of severe COVID-19 disease, should be given an mRNA vaccine.

Patients with planned immunosuppressing 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.

Post vaccination observation period

- Vaccine recipients: 15 minutes
- Those with a history of mastocytosis: 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 or efficacy in these groups. Individuals with immunocompromise due to disease or treatment may be vaccinated if they have no contraindications.

See immunocompromised sections of mRNA vaccines regarding extension of primary vaccination series.

Pregnancy

This vaccine is not recommended for those aged under 50 years.

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

The vaccine may be considered for those with a contraindication or precaution to an mRNA vaccine (see Table 5a.4 and contraindications sections of mRNA vaccines).

Breastfeeding

There is no known reason for vaccinees to avoid breastfeeding.

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 replacement therapy, 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 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: asthenia, diarrhoea, fever >38°C, influenza-like illness, pain in extremity, thrombocytopenia (mild and transient decrease on blood tests), vomiting

Uncommon: abdominal pain, decreased appetite, dizziness, hyperhidrosis, hypoaesthesia, lethargy, lymphadenopathy, muscle spasms, paraesthesia, pruritus, somnolence, rash, tinnitus, urticaria

Very rare: facial paralysis, Guillain-Barré syndrome, thrombosis with thrombocytopenia syndrome (see Section 5a.4.2)

Unknown frequency: angioedema, capillary leak syndrome, cerebrovascular venous and sinus thrombosis without thrombocytopenia and distinct from TTS, immune thrombocytopenia, transverse myelitis (see Section 5a.4.2)

Thrombosis with thrombocytopenia syndrome (TTS), in some cases accompanied by bleeding, has been observed very rarely following vaccination with Vaxzevria. This includes severe cases presenting as venous thrombosis, including unusual sites such as cerebral venous sinus thrombosis, splanchnic vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. Some cases had a fatal outcome. The majority of these cases occurred within the first 3 weeks following vaccination but have also been reported after this period. The reporting rates have been lower after the second dose than after the first dose. Risk factors have not been identified.

Those who developed Guillain-Barré syndrome following Vaxzevria should seek specialist advice regarding a second COVID-19 vaccine.

The most frequent adverse reactions during clinical trials in those aged 18 years and older 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 is associated with older age. The rate and severity of local and systemic adverse reactions is lower after the second dose.

Post marketing surveillance in the UK showed an anaphylaxis rate of 17 per million (the figure includes anaphylactoid reactions). This rate is higher than after non COVID-19 vaccines.

Co-administration
COVID-19 vaccines and other vaccines may be administered at the same time or at any interval.

As it is not known if COVID-19 vaccine reactogenicity is increased with co-administration, vaccines should preferably be given in different limbs.

TB testing
Testing for TB infection with either the TST or an IGRA can be done at any time in relation to COVID-19 vaccination.

Duration of immunity
There is insufficient information to determine the duration of protection from the vaccine.

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). There is no evidence of significant waning of protection for up to 16 weeks after vaccination. Higher efficacy of 82% was reported when the second dose was given after 12 weeks.

Vaccine recipients may not have optimal protection until 15 days after the second dose, and the vaccine may not protect all vaccinees.

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

Booster doses
Those who have received a primary course of Vaxzevria should receive a booster dose of an mRNA vaccine (see sections on booster mRNA vaccines).

5a.5.4 JCOVDEN (formerly 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
Clinical trial data 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 years and above. High efficacy was observed across age and sex, and among persons with underlying medical conditions. This efficacy may not apply to all variants.

Dose and route of administration
The dose of vaccine is 0.5 ml IM, 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
The vaccine may be used as the second dose for a person who had anaphylaxis to an mRNA vaccine and the person should be considered fully vaccinated.

Contraindications (see Table 5a.5)
- Anaphylaxis following a previous dose of the vaccine or any of its constituents (including polysorbate 80).
- Anaphylaxis following another adenoviral vector vaccine.
- Thrombosis with Thrombocytopenia Syndrome (TTS) after the first dose of another adenoviral vector COVID-19 vaccine (see Section 5a.4.2).
- Previous history of capillary leak syndrome (see Section 5a.4.2).

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.
- Consider mRNA vaccination for those with:
  - Anaphylaxis after a vaccine, injected antibody preparation, or a medicine known to contain polysorbate 80
  - Unexplained anaphylaxis (may indicate polysorbate 80 allergy).

mRNA vaccines are recommended for those aged **under 50 years** including those with conditions with very high or high risk of severe COVID-19 disease. Advice from a relevant specialist should be sought for a person with a history of an immediate severe allergic reaction to multiple drug classes with no identified allergen, any other vaccine injected antibody preparation or medicine likely to contain polysorbate 80 or idiopathic anaphylaxis and the risks should be weighed against the benefits of vaccination.

Patients with planned immunosuppressing 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.

Post vaccination observation period

- Vaccine recipients: 15 minutes
- Those with a history of mastocytosis: 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 should be offered an mRNA vaccine.

See immunocompromised sections of mRNA vaccines regarding extension of primary vaccination series.

Pregnancy

This vaccine is not recommended for pregnant women.

The vaccine may be considered for those with a contraindication or precaution to an mRNA vaccine (see Table 5a.4 and contraindications sections of mRNA vaccines).

Breastfeeding

There is no known reason for vaccinees to avoid breastfeeding.

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 replacement therapy, 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 oral anticoagulants or antiplatelet agents, than with other anticoagulants.

Those 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, diarrhoea, hyperhidrosis, malaise, muscular weakness, oropharyngeal pain, pain in extremity, paraesthesia, rash, sneezing, tremor

Rare: hypersensitivity, hypoesthesia, lymphadenopathy, tinnitus, urticaria, venous thromboembolism, vomiting
Very rare: thrombosis with thrombocytopenia, Guillain-Barré syndrome (see Section 5a.4.2).
Unknown frequency: capillary leak syndrome, cutaneous small vessel vasculitis with cutaneous manifestations, immune thrombocytopenia, transverse myelitis (see Section 5a.4.2)

The most frequent adverse reactions during clinical trials in those aged 18 years and older 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
COVID-19 vaccines and other vaccines may be administered at the same time or at any interval.

As it is not known if COVID-19 vaccine reactogenicity is increased with co-administration, vaccines should preferably be given in different limbs.

TB testing
Testing for TB infection with either the TST or an IGRA can be done at any time in relation to COVID-19 vaccination.

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.

Booster doses
Those who have received JCOVDEN should receive a booster dose of an mRNA vaccine after an interval of four months (see sections on booster mRNA vaccines).

Protein sub unit vaccine

5a.5.5 Nuvaxovid

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 between +2°C to +25°C and used within six hours.

Licensed indications
Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus in individuals 12 years of age and older.

Vaccine efficacy
Clinical trial data from Mexico and the US demonstrated vaccine efficacy to prevent the onset of COVID-19 from seven days after dose 2 was 90.4%. A second UK study demonstrated efficacy of 89.7%.

Dose, route and schedule
The dose of vaccine is 0.5 ml IM in 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.

The course consists of two doses three weeks apart.

If the interval between doses is longer than 21 days, the second dose should still be given. The course does not need to be restarted.

If the interval is between 17 and 20 days after the first dose, it is a valid dose.

If the interval between doses is less than 17 days, the dose is invalid. There is insufficient information regarding giving a further dose.

A primary course of Nuvaxovid may be offered to those aged 12 years and over with a contraindication to an mRNA vaccine, or who have chosen not to receive another COVID-19 vaccine course.

Interchangeability
The same vaccine should be used for both doses.

Nuvaxovid may be offered to those with a contraindication/special precaution to to another COVID-19 vaccine or who have chosen not to receive another COVID-19 vaccine to complete a primary course or as an additional dose or a booster vaccine.

Contraindications
Anaphylaxis 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.

There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

Advice from a relevant specialist should be sought for a person with a history of an immediate severe allergic reaction to multiple drug classes with no identified allergen, any other vaccine injected antibody preparation or medicine likely to contain polysorbate 80 or idiopathic anaphylaxis, and the risks should be weighed against the benefits of vaccination.

Vaccination after COVID-19
Unvacccinated
Those who are unvaccinated and develop laboratory confirmed COVID-19 infection should complete a primary vaccination course, with the first dose 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 with persisting symptoms post COVID-19 may be vaccinated, unless there is evidence of recent clinical deterioration.

Partially vaccinated
Those who have had laboratory confirmed COVID-19 infection between their doses of COVID-19 vaccine should complete their primary vaccination course, with their next dose at least four weeks after diagnosis or onset of symptoms

Additional or booster vaccination
Those who have had laboratory confirmed COVID-19 infection or a positive COVID-19 antigen test with symptoms after a completed primary vaccine course, additional or booster dose (i.e., a breakthrough infection), should delay further vaccination after the COVID-19 infection for four months.

Post vaccination observation period
- Vaccine recipients: 15 minutes
- Those with a history of mastocytosis: 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.

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 their immune status and likely immune response to vaccination.

The need for and timing of an additional dose beyond the primary dose series has not yet been established.

If there is a contraindication or precaution to an additional dose of an mRNA vaccine, consideration can be given to an additional dose of Nuvaxovid following an individual benefit-risk assessment. The additional dose should be given after an interval of four months.

Pregnancy
There is limited experience with use of the vaccine in pregnant women.

There is a growing body of evidence on the safety and effectiveness of COVID-19 vaccination, in both animal and human studies, clearly indicating that the benefits of vaccination outweigh any known or potential risks of COVID-19 vaccination during pregnancy.

Administration may be considered when the benefits outweigh the potential risks to the mother or the fetus and when mRNA vaccines are contraindicated or declined.

The pregnant women and a relevant health professional should engage in shared decision-making in advance of vaccination. Counselling should balance the available data on vaccine safety, risks to pregnant women from COVID-19 infection, and a woman's individual risk for infection and severe disease.

The two doses should be given 21 days apart at any stage in pregnancy.

Breastfeeding
There is no known reason for vaccinees to avoid breastfeeding.

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 thrombocytopoenia (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, tenderness Common: injection site erythema, swelling Uncommon: njection site pruritus
General:	Very common: arthralgia, fatigue, headache, malaise, myalgia, nausea, vomiting Common: chills, pain in extremity, pyrexia Uncommon: erythema, hypertension, lymphadenopathy, pruritus, rash, urticaria Unknown frequency: hypoaesthesia, paraesthesia

The most frequent adverse reactions during clinical trials in those aged 18 years and older were injection site tenderness (75%), injection site pain (62%), fatigue (53%), myalgia (51%), headache (50%), malaise (41%),

arthralgia (24%), and nausea or vomiting (15%). A higher frequency of adverse events was observed with the second dose.

Co-administration
COVID-19 vaccines and other vaccines, may be administered at the same time or at any interval. Co-administered vaccines should be given in different arms.

In keeping with international recommendations, COVID-19 and seasonal influenza vaccines should be co-administered where practicable to maximise uptake. A UK study revealed no unexpected safety concerns with coadministration.

Vaccinees should be informed there may be a slight increase in short term mild adverse events after co-administration with a seasonal influenza vaccine. These include pain at the site of injection, fatigue, headache, and myalgia.

There should be an interval of four weeks between monkeypox/smallpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

No interval is required between a COVID-19 vaccine and a subsequent monkeypox/smallpox vaccine (see Chapter 13a).

TB testing
Testing for TB infection with either the TST or an IGRA can be done at any time in relation to COVID-19 vaccination.

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 seven days after the second dose and the vaccine may not protect all vaccinees.

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

If there is a contraindication or precaution to a booster dose of an mRNA vaccine, or a person has chosen not to receive an mRNA COVID-19 booster, consideration can be given to a heterologous booster of Nuvaxovid following

an individual benefit-risk assessment. The booster dose should be given after a minimum interval of four months.

5a.6 COVID-19 vaccination outside Ireland

Those who have documentary evidence of a complete COVID-19 vaccination course with a COVID-19 vaccine authorised by the FDA, MHRA or recommended by WHO should be considered fully vaccinated.

Those who have partially completed a COVID-19 vaccine course with a vaccine authorised by the FDA, MHRA or recommended by WHO should be offered an EMA authorised COVID-19 vaccine to complete the series, and then should be considered fully vaccinated. The minimum interval between the last vaccine dose and an EMA authorised COVID-19 vaccine is 28 days.

Those who have received a partial or complete course of COVID-19 vaccine not authorised by the FDA, MHRA or recommended by WHO should be offered a complete course of an EMA authorised COVID-19 vaccine. The minimum interval between the last dose and an EMA authorised COVID-19 vaccine is 28 days.

5a.7 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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