HPRA Safety Update

COVID-19 Vaccines, Overview of National Reporting Experience
Publication date: 09 September 2021 (Update #11)

Highlights from this update:

- Up to 31 August, a total of 14,844 reports of suspected side effects were notified to the HPRA. The number of COVID-19 vaccines administered as of that date was reported as 6,836,122, including 232,600 administered as a single dose, 3,455,838 as a first dose, and 3,147,684 as a second dose.[1]

- Whilst not experienced by everyone, all vaccines have some side effects, the vast majority of which are mild to moderate in nature. These side effects need to be continuously balanced against the benefits in preventing COVID-19 illness. Overall, the national reporting experience continues to support the favourable assessment that the benefits of COVID-19 vaccines outweigh the risks. An overview of national reports received is provided in this safety update on page 5.

- On 03 September, the European Medicines Agency (EMA) published highlights from its monthly safety committee meeting, which included information on COVID-19 vaccines. On 08 September, the EMA published safety update reports for mRNA vaccines (Comirnaty®, Spikevax® [*previously COVID-19 Vaccine Moderna*]) and adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®). These publications describe safety issues under evaluation, as well as any new recommendations.

- The EMA's safety committee is currently assessing whether there is a possible risk of multisystem inflammatory syndrome (MIS), which is an inflammatory condition affecting many parts of the body, with COVID-19 vaccines following a small number of reports. Further information on this review is provided on page 7.

- The next HPRA safety update is due for publication on 07 October.

[1] *https://www.hse.ie/eng/services/news/newsfeatures/covid19-updates/vaccination-programme-dashboard-as-of-31-august-2021.pdf*

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UNDERSTANDING THE DATA PRESENTED WITHIN THIS SAFETY UPDATE

This update includes an overview of reports of ***suspected side effects*** notified to the HPRA safety monitoring system and is provided as an enhanced transparency measure for members of the public and healthcare professionals. All vaccines have some side effects, the vast majority of which are mild to moderate in nature. These side effects need to be continuously balanced against the expected benefits in preventing COVID-19 illness.

Reports included in the overview are those notified to the HPRA on a voluntary basis by healthcare professionals and members of the public, with reporting of suspected side effects to COVID-19 vaccines (www.hpra.ie/report) encouraged. Any reports of Irish cases received by the HPRA from the company (i.e. the licence holder, to date, BioNTech, Moderna, AstraZeneca, Janssen) responsible for the vaccine are also included within this update. This overview provides an up-to-date summary of national reporting experience.

However, it is important to understand that conclusions on the safety of a vaccine cannot be drawn based on the information provided, given well-established and known limitations in interpreting such data in isolation, examples of which are described below.

Causation

- The HPRA receives reports based on ***suspicion*** that an adverse experience may be associated with vaccination. This does not mean the vaccine ***caused*** the adverse experience**.** As such, these are referred to as ***'suspected'*** side effects.
- Reports may describe coincidental events, which have occurred post-vaccination, but would have occurred even if vaccination had not taken place (e.g. they may be due to an underlying medical condition, or be signs and symptoms of another illness).
- Each individual report is carefully reviewed, however, the totality of data from all sources (e.g. clinical and epidemiological studies and literature) must be considered as part of ongoing safety monitoring to ensure ***evidenced based conclusions*** are drawn.

Number/volume

- As the HPRA system is based on voluntary reporting, ***not all*** suspected side effects will be reported. As such, the number and types of reports notified can vary for a variety of reasons.
- An increased number of reports is expected for COVID-19 vaccines, given public interest as well as HPRA calls encouraging reporting. This is known as ***stimulated reporting***.
- A single report may describe more than one suspected side effect in an individual (e.g. headache and nausea reported together), therefore, the number of side effects may exceed the total number of reports received.

Comparisons

- The type and number of reports received for different COVID-19 vaccines are ***not directly comparable*** as, for example, the vaccines have not been used in the vaccination programme for the same length of time, and will have been administered to different numbers of people, with different underlying medical conditions and across different settings.
- Each vaccine is authorised on the basis that its benefits-risk profile has and continues to be favourable.

Changes to data over time

- The description of suspected side effects in this update reflects available information known at the time by the HPRA. These data may undergo changes as more information about individual reports becomes available through follow-up, and as more data are reported and evaluated.

- For these reasons, the information in this report is not sufficient in isolation to draw conclusions on the safety profile of a vaccine. Like all vaccines, some side effects are to be expected, with the vast majority mild or moderate in intensity and resolving within a few days. Vaccines are approved for use on the basis of robust scientific evidence that demonstrates their benefits outweigh any risks.

Always refer to the product information for information on the established safety profile, including known side effects of a COVID-19 vaccine.

This includes the Package Leaflet (for members of the public) and Summary of Product Characteristics (for healthcare professionals)

Product information is accessible from https://www.hpra.ie/homepage/medicines/covid-19-updates/covid-19-vaccines-product-information

AUTHORISED COVID-19 VACCINES

COVID-19 vaccines currently authorised for use in the European Union by the EMA include:

mRNA vaccines:

- Comirnaty® (licence holder: BioNTech Manufacturing GmbH), granted conditional marketing authorisation on 21 December 2020. For further information on this vaccine click here. On 28 May, the EMA extended the marketing authorisation for Comirnaty® beyond the initial authorised use in adults and adolescents aged 16 years and above, to include use in adolescents aged 12 to 15 years.
- Spikevax® (*previously COVID-19 Vaccine Moderna®)* (licence holder: Moderna Biotech Spain, S.L.), granted conditional marketing authorisation on 6 January 2021. For further information on this vaccine click here. On 23 July, the EMA extended the marketing authorisation for Spikevax® beyond the initial authorised use in adults to include use in adolescents aged 12 to 17 years.

Adenoviral vector vaccines:

- Vaxzevria® (licence holder: AstraZeneca AB), granted conditional marketing authorisation on 29 January 2021. For further information on this vaccine click here.
- COVID-19 Vaccine Janssen® (License holder: Janssen-Cilag International NV), granted conditional marketing authorisation on 11 March 2021. For further information on the vaccine click here.

OVERVIEW OF SUSPECTED SIDE EFFECT REPORTS

Number of reports received

Up to 31 August, the HPRA received 14,844 reports describing suspected side effects[2,3] in association with COVID-19 vaccines, as follows:

mRNA vaccines (Comirnaty® and Spikevax® *[previously Moderna]*)	8686
Adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®)	6059
Brand unknown/not specified	99

Doses administered by vaccine type, as of 31 August, were reported as follows:[1]

- mRNA vaccines: 4,852,638 Comirnaty®, 562,394 Spikevax® *(previously Moderna)*.
- Adenoviral vector vaccines: 1,188,490 Vaxzevria®, 232,600 COVID-19 Vaccine Janssen®.

Regularly reported suspected side effects

The most regularly reported suspected side effects notified to the HPRA include the following:[4]

mRNA vaccines (Comirnaty® and Spikevax® *[previously Moderna]*)
10% or more of reports describe side effects such as: ▪ Fever, tiredness ▪ Dizziness, headache ▪ Pain (non-specific) ▪ Nausea **1% to less than 10% of reports describe side effects such as:** ▪ Abdominal pain, diarrhoea, tingling sensation in mouth, vomiting ▪ Drowsy, fainting/feeling faint, migraine, numbness/reduced sensations, tingling/pins and needles/tremor ▪ Back pain, joint/limb pain, muscle pain/weakness/spasm/stiffness, neck pain ▪ Blurred vision ▪ Chest discomfort/pain, chills, general discomfort, feeling unwell, feeling hot/cold, flu-like symptoms, lack of energy/feeling weak/tiredness, swelling including of legs/arms/face, underarm pain ▪ Cough, shortness of breath, sore throat ▪ Difficulty carrying out daily tasks (such as temporarily unable to attend work, need to stay in bed) ▪ Enlarged lymph nodes ▪ Insomnia/trouble sleeping ▪ Increased heart rate/racing heart, increased blood pressure ▪ Injection site redness, pain, itchiness, swelling, rash

[2]A single report may contain more than one suspected side effect for an individual (e.g. rash and hives reported together). Therefore, the total number of suspected side effects will exceed the total number of reports.
[3]In accordance with EU guidance, reports are valid if the minimum reporting criteria are met. These include an identifiable reporter, an identifiable patient, one or more suspected medicine known to have been administered and one or more suspected adverse reaction.
[4]Terms listed as frequently reported are presented according to standard coding classification system (MedDRA) adopted for use in the EU, and grouped by system organ class (SOC) and listed alphabetically. It should be noted that regular reporting of a side effect is not the same as the incidence of occurrence.

- Lack of appetite
- Menstrual disturbances
- Skin reactions, skin red/red rash, sweating, general rash, itching, itchy rash, hives
- Tinnitus (ringing in the ears), vertigo-like symptoms

Adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®)

10% or more of reports describe side effects such as:

- Chills, fever, tiredness
- Dizziness, headache
- Joint pain, muscle pain, other pain (non-specific)
- Nausea

1% to less than 10% of reports received describe side effects such as:

- Abdominal discomfort/pain, diarrhoea, vomiting
- Back pain, bone pain, limb pain, muscle spasms/weakness/stiffness, neck pain
- Chest discomfort/pain, general discomfort, feeling unwell/ill, feeling hot/cold, flu-like symptoms, lack of energy/weakness, swelling including of legs/arms
- Cough, shortness of breath, sore throat, nose bleed
- Difficulty carrying out daily tasks (such as temporarily unable to attend work, need to stay in bed)
- Drowsy, fainting, headache, migraine, numbness/reduced sensations, tingling/pins and needles, tremor
- Ear pain, tinnitus (ringing in the ears), vertigo-like symptoms
- Enlarged lymph nodes
- Eye pain, vision blurred
- Hives, skin red/red rash, general rash, sweating/cold sweat, itching
- Increased heart rate/racing heart
- Injection site pain, redness, swelling, bruising, difficulty moving injected arm
- Insomnia/trouble sleeping
- Lack of appetite
- Menstrual disturbances

The majority of regularly reported suspected side effects are consistent with the types of events typically observed following vaccination, including those described in the product information for the individual vaccine, and are mild to moderate in nature.

In the reports evaluated, which include information on outcome, approximately one third of suspected side effects had resolved or were resolving at the time of reporting. For others, the suspected side effects had not yet resolved, or the outcome was reported as unknown, at the time of initial reporting. Information on reports with a fatal outcome is provided on page 8.

A full breakdown of all suspected side effects described in reports is provided on page 13. Further information on how reports received by the HPRA are processed, including how safety signals are evaluated, is given on page 17.

Links to the most recent updates from EMA's safety committee, including safety issues under evaluation, are provided in the highlights section on the cover page.

TOPICS OF INTEREST, INCLUDING EMA RECOMMENDATIONS

Topics of interest included in this update are listed below:

Common topics

- Multisystem inflammatory syndrome (MIS)
- Menstrual disturbances
- Deaths following vaccination
- Allergic type reactions (also known as hypersensitivity)
- Systemic events

For mRNA vaccines (Comirnaty® and Spikevax® *[previously Moderna]*)

- Vaccination of adolescents (12 to 17 years)
- Myocarditis and pericarditis

For adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®)

- Immune thrombocytopenia (ITP)
- Thrombosis with thrombocytopenia syndrome (TTS)
- Guillain-Barré syndrome (GBS)
- Other product information updates

COVID-19 vaccines - Common topics

Multisystem inflammatory syndrome

- Multisystem inflammatory syndrome (MIS) is a rare but serious inflammatory condition affecting many parts of the body and symptoms can include tiredness, persistent severe fever, diarrhoea, vomiting, stomach pain, headache, chest pain and difficulty breathing. MIS has previously been reported following COVID-19 disease, including in children and adolescents.
- The EMA's safety committee is assessing whether there may be a possible risk of MIS with COVID-19 vaccines, following a case reported in an adolescent and a small number of reports in adults, including in some individuals without a history of COVID-19 disease. The adolescent described as experiencing MIS following vaccination is reported to have fully recovered. To date, no reports of MIS following COVID-19 vaccination have been notified to the HPRA.
- These cases describe medical events that have been observed following vaccination, but which may not necessarily be caused by the vaccine. The EMA's safety committee will fully assess the cases, as well as the available data on MIS, to determine whether the condition can be caused by COVID-19 vaccines and recommend whether any changes to product information are needed. An update on the EMA review is available here.
- Healthcare professionals are encouraged to report any suspected cases of MIS occurring following COVID-19 vaccination.

Reports of menstrual disturbances

- Menstrual disturbances are one of the more regularly reported side effects to the HPRA (see pages 5 & 6). The vast majority of reports received are directly from a vaccinated woman, and describe a recent disturbance in normal menstruation, such as a period arriving earlier or later

than expected, or of a heavier nature than normal. Whilst less frequent, some reports describing a bleeding event in a woman who is post menopausal have also been notified.

- The EMA's safety committee are reviewing reports of menstrual disturbances following COVID-19 vaccination, and have requested further data for all COVID-19 vaccines authorised in the EU. All available evidence, including reports of suspected side effects from vaccinated women, as well as scientific literature, will be examined. However, no causal association or link with vaccination and menstrual disturbances has been found so far.
- Whilst the review is ongong, EMA have highlighted that generally, menstrual disturbances are very common and can occur with or without an underlying medical condition. Women who are concerned about prolonged or severe menstrual disturbances may wish to seek medical advice, in particular if unexpected vaginal bleeding, for example, in a postmenopausal women, is experienced.

Reports of deaths following COVID-19 vaccination

- A total of 86 reports have been received describing an individual who was known to have been vaccinated and subsequently passed away. Of these, 75 were reported with an mRNA vaccine, seven with adenoviral vector vaccines and the remaining four were reported with brand unknown/not specified. The majority of these events were reported in patients aged over 75 and include fatalities often seen in the general population, such as those due to natural causes, progression of underlying disease. For a number of reports, the cause of death was unconfirmed at the time of reporting, with post mortem results awaited.
- Reports describing a death are carefully reviewed. However, it can be expected that fatalities due to progression of underlying disease or natural causes will continue to occur, including following vaccination. This does not mean that the vaccine caused the deaths.
- In most cases, progression of (multiple) pre-existing diseases was considered a plausible explanation. A safety concern has not been identified through an EMA specific review in January or through subsequent EU coordinated reviews, performed as part of continuous monitoring for all vaccines, and which consider the totality of all reports and available data.

Reports of allergic type reactions (also known as hypersensitivity)

- Allergic type reactions are known side effects of both mRNA and adenoviral vector vaccines. The HPRA has received a number of such reports, mainly describing symptoms such as itchiness, hives and rash. In some cases, medical treatment and/or clinical observation of the individual was needed.
- The HPRA continues to monitor reports of anaphylaxis, which is a serious allergic reaction. All reports suggestive of anaphylaxis (e.g. sudden onset of symptoms such as low blood pressure, collapse, rapid heart rate, shortness of breath, swelling of lips/throat and itchy skin) are carefully reviewed. Cases are classified by the HPRA as anaphylaxis using a well-established set of clinical and laboratory criteria however, some reports do not contain sufficient detail for classification purposes.[5] Of the reports reviewed, 12 cases associated with an mRNA vaccine and a small

[5]*Reports classified using Brighton Collaboration case definition for anaphylaxis https://brightoncollaboration.us/category/pubstools/case-definitions/. Some reports contain limited information and therefore it is not possible to classify according to the Brighton Collaboration case definition. In these case, the HPRA follows up with the reporter for the missing information.*

number[6] of cases associated with an adenoviral vector vaccine are currently classified as anaphylaxis. In some cases the individual concerned had recovered at the time of reporting and the remaining cases are being followed-up for further information.

- Anaphylaxis is a known side effect, and information on managing this risk is described in the product information. As for all vaccines, COVID-19 vaccines should be administered under close supervision with appropriate medical treatment available in case of such a reaction. Those vaccinated should discuss any signs/symptoms of allergic reaction that they are concerned about with a healthcare professional.

Reports of systemic events

- In the reports received, reporters sometimes comment on the impact of expected systemic events following vaccination on their normal daily activities (1% to less than 10% of reports). Reporters have described a need to take time off work or to rest in bed, typically for a short period.
- Systemic events can feel similar to flu-like symptoms, and can include fatigue, headache, muscle/joint pain, chills and fever, in the day(s) following vaccination.
- These types of systemic events post vaccination are common, with the vast majority mild to moderate in nature and usually resolve within a few days of vaccination.
- These events may occur after either dose. However, the frequency and intensity observed in clinical trials was increased after the second dose of the mRNA vaccines.[7]
- For Vaxzevria®, these events may occur after either dose. However, adverse reactions reported after the second dose were milder and reported less frequently than after the first dose in clinical trials.[8]
- The product information (package leaflet) for Comirnaty®, Spikevax® *(previously Moderna),* Vaxzevria® and COVID-19 Vaccine Janssen® indicates that some of the possible side effects may temporarily affect ability to operate machinery or drive. Vaccine recipients should be alert to this warning.

mRNA vaccines (Comirnaty® and Spikevax® [*previously Moderna*])

Vaccination of adolescents (12 to 17 years)

- As the national vaccination programme continues, the HPRA are closely monitoring any reports of suspected side effects received in adolescents aged 12 to 17 years.
- As of 31 August, the HPRA has received 78 reports of suspected side effects following vaccination of an adolescent with an mRNA vaccine. A breakdown of all suspected side effects by type, reported in those aged 12 to 17 years are available on page 16. Overall, the reports received are consistent with the types received in adults, with most being mild to moderate in nature.

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[6] *When the relevant number is less than five, it is described as a small number to avoid any potential, inadvertent identification of the individuals concerned.*

[7] *European Public Assessment Report (EPAR) for Comirnaty® available from the EMA website https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty*

[8] *European Public Assessment Report (EPAR) for Vaxzevria® available from the EMA website https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria-previously-covid-19-vaccine-astrazeneca*

Reports of myocarditis and pericarditis

- Myocarditis and pericarditis, which are inflammatory conditions of the heart, are possible side effects of Comirnaty® and Spikevax® *(previously Moderna)*. Cases reported internationally primarily occurred within 14 days, more often in younger men and after the second dose. The clinical course of myocarditis and pericarditis following vaccination has been observed as similar to that which can occur in unvaccinated people, for example, when myocarditis or pericarditis develop after a viral infection, or due to an immune disorder.
- Those vaccinated are reminded to seek immediate medical attention if symptoms indicative of myocarditis or pericarditis occur. These symptoms can vary but often include breathlessness, a forceful heartbeat that may be irregular (palpitations), and chest pain.
- For Comirnaty® and Spikevax®, as of 31 August, the HPRA has received a total of 60 reports, that describe suspected side effects of myocarditis (18 reports), pericarditis (26 reports) or a combination of both (16 reports). In these 60 cases, 35 occurred after the first dose and 25 after the second dose, with most occurring within 14 days of vaccination. Suspected cases were reported in both males and females, with a median age of 39 years (range 12 to 81). A small number[6] of reports received concerned adolescents (aged 12 to 17 years).
- The reports received describe symptoms such as chest pain/discomfort, palpitations, dizziness, irregular heartbeat and shortness of breath. In a number of cases, possible alternative explanations (other than vaccination) for the individual developing the condition were described, or the diagnosis was provisional and not yet finalised at the time of reporting. In the majority of cases, the individuals were still recovering or had ongoing symptoms at the time of initial reporting.
- An additional 13 reports of myocarditis and/or pericarditis have been received following vaccination with Vaxzevria® and COVID-19 Vaccine Janssen®. In the majority of cases, the individuals were still recovering or had ongoing symptoms at the time of initial reporting. A review of reports of this nature following administration of these vaccines by EMA's safety committee is ongoing, however, at this point in time, no causal relationship with myocarditis or pericarditis is established.
- All reports of myocarditis and pericarditis notified to the HPRA are carefully reviewed however, it can be expected that medical events due to various causes will continue to occur, including following vaccination, but which are not all necessarily caused by the vaccine.
- Previous advice issued to healthcare professionals on this topic is available from the HPRA website here.

Adenoviral vector vaccines (Vaxzevria® and COVID-19 Vaccine Janssen®)

Reports of immune thrombocytopenia (ITP)

- Immune thrombocytopenia (ITP) is a condition in which the immune system mistakenly reacts to blood cells called platelets that are needed for normal blood clotting.
- The EMA's safety committee recently assessed very rare reports of ITP which occurred after vaccination with COVID-19 Vaccine Janssen®, together with available scientific evidence, including that from the literature. Following this assessment, the safety committee recommended that product information for COVID-19 Vaccine Janssen® be updated to alert both healthcare professionals and those being vaccinated of ITP as a potential risk. Further details will be included in the anticipated product information.
- As of 31 August, the HPRA has received 11 reports of ITP following COVID-19 vaccination, however, none occurred following administration of COVID-19 Vaccine Janssen®.

Reports of thrombosis with thrombocytopenia syndrome (TTS)

- Thrombosis with thrombocytopenia syndrome (TTS) is a very rare side effect associated with Vaxzevria® and COVID-19 Vaccine Janssen®. The syndrome involves an unusual combination of thrombosis (blood clots) with thrombocytopenia (abnormally low level of the components that help blood to clot, known as platelets). Vaccine recipients are reminded to seek immediate medical attention if they experience any of the following signs and symptoms: shortness of breath, chest pain, leg swelling, leg pain, persistent abdominal pain post vaccination, severe or persistent headaches, blurred vision, confusion, seizures (fits) or bruising beyond the site of vaccination after a few days.
- Healthcare professionals are advised that individuals diagnosed with thrombocytopenia within three weeks after vaccination should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within three weeks of vaccination should be evaluated for thrombocytopenia. Healthcare professionals should be alert to the signs and symptoms of TTS and consult applicable guidance and/or appropriate specialists to diagnose and treat this condition. A second dose of Vaxzevria® is contraindicated in any person who experienced TTS following their first dose.
- As of 31 August, the HPRA has received nine reports that are suspected cases of TTS, and which mostly describe the unusual combination of blood clotting in combination with low platelets. In relation to these suspected TTS cases, symptoms occurred between 1-5 weeks of vaccination with a first dose of Vaxzevria® or single dose of COVID-19 Vaccine Janssen®. The types of symptoms reported include shortness of breath, severe and/or persistent headache, unusual skin bruising, abdominal pain, leg pain and leg swelling. Cases occurred in both males and females, with a median age of 42 (age range, 21 to 63 years). In a small number, blood clots occurred in unusual locations, including in the brain (cerebral venous sinus thrombosis, CVST) and liver (hepatic and portal veins). Based on information currently available, the individuals are either discharged or recovering in hospital after receiving specialist medical care.
- Further information on the ongoing review of other types of blood clotting events (without low blood platelets) is available in EMA safety updates for Vaxzevria® and COVID-19 Vaccine Janssen®. To 31 August, the HPRA received 12 reports describing a blood clotting event (without low platelets), following vaccination with COVID-19 Vaccine Janssen® and 106 reports with Vaxzevria®. The vast majority describe clots typically seen in the general population, such as those that occur in the legs (e.g. deep vein thrombosis), and lung (e.g. pulmonary embolism) with a small number describing CVST, an unusual type of brain clot.
- Previous advise issued to healthcare professionals on this topic is available from the HPRA website here.

Reports of Guillain-Barré syndrome (GBS)

- Guillain-Barré syndrome (GBS) is a very rare and serious immune disorder that affects the nerves, and can result in pain, numbness, tingling sensations, muscle weakness and difficulty walking. Symptoms usually start in the legs, and can spread to the arms and face. GBS is thought to be caused by a problem with the immune system, and whilst the trigger for the condition is not known, it often happens after an infection, especially of the airways, such as flu, or an infection of the digestive system, such as food poisoning or a stomach bug (gastroenteritis). GBS can occur very rarely following vaccination with Vaxzevria® or COVID-19 Vaccine Janssen®.
- Healthcare professionals should be alert to signs and symptom of GBS, in view of the seriousness of the condition, allowing for early diagnosis, supportive care and treatment. Those vaccinated

are advised to seek immediate medical attention if they develop signs and symptoms of GBS which may include weakness in the limbs, chest or face, double vision or difficulty moving eyes, difficulty breathing, chewing, speaking or swallowing, co-ordination problems and unsteadiness, difficulty walking, tingling sensations in the hands and feet and problems with bladder control and bowel function.

- Following a recent review of additional data for Vaxzevria®, the EMA safety committee has recommended that patients who experienced GBS after vaccination with Vaxzevria® should speak to their healthcare professional before receiving another dose.
- As of 31 August, the HPRA has received nine reports of GBS following vaccination with an adenoviral vector vaccine. The cases occurred in both genders, with a median age of 56 years (range 24 to 62), and with symptoms occurring between 1 to 28 days post vaccination. These cases concern suspected side effects, i.e. medical events that have been observed after vaccination, but are not necessarily caused by the vaccine.

Other product information updates for adenoviral vector vaccines

- **COVID-19 Vaccine Janssen®:** the EMA's safety committee has recommended that product information for COVID-19 Vaccine Janssen® be updated to include the following as potential side effects:
    - lymphadenopathy (swollen lymph nodes),
    - paraesthesia (tingling/pins and needles)
    - hypoaesthesia (numbness/reduced sensations in the skin)
    - diarrhoea and vomiting
- Up to 31 August, the HPRA received, a small number[6] of reports of swollen lymph nodes, 21 reports of tingling/pins and needles, 10 reports of numbness/reduced sensations in the skin, 5 reports describing a combination of tingling/pins and needles and numbness/reduced sensations, 14 reports of diarrhoea and 41 reports of vomiting following administration of COVID-19 Vaccine Janssen®.

- **Vaxzevria®**: the EMA's safety committee has recommended that product information for Vaxzevria® will be updated to include the following as potential side effects:
    - general pain (pain in extremities such as arms and legs),
    - abdominal pain (stomach pain),
    - flu-like symptoms (high temperature, sore throat, runny nose, cough and feeling cold)
- Up to 31 August, the HPRA received over 2000 reports of pain in extremities such as arms and legs, 73 reports of stomach pain and over 500 reports of flu-like symptoms following administration with Vaxzevria®.

BREAKDOWN OF SUSPECTED SIDE EFFECTS BY CATEGORY

A full breakdown of all suspected side effects described in reports received by the HPRA is provided below by vaccine type (i.e. mRNA and adenoviral vector vaccines) and by category (i.e. the related body system).

Whilst the vast majority of reports notified to the HPRA describe expected events (i.e. known side effects of a vaccine or vaccination process), reports can also be received for events that are unexpected and/or are considered serious, as they required medical care or intervention. Such reports may describe events not caused by the vaccine and may have occurred coincidentally. However, all reports are carefully reviewed and if there is cause to do so, a further analysis is carried out to determine if a vaccine may have had a contributory role. If it is determined that a vaccine is a contributory factor, the public and healthcare professionals will be informed and the relevant product information will be updated.

Please read the following explanatory note in relation to understanding the data presented in the suspected side effect tables:

- A single report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, which may include more than one category, or more than one in a specific category. For example, a single report that describes chills, fatigue and nausea in an individual, includes three suspected side effects, two in general symptoms (chills and fatigue) and one in gastrointestinal (nausea). As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.
- The breakdown summary includes all suspected side effects as they are reported to the HPRA. This includes cases for which a diagnosis is reported as provisional, or for which there is more than one possible diagnosis at the time of reporting. In other cases, a diagnosis may not be available, and only signs and symptoms or laboratory test results are given. Reports are also received from members of the public, and the HPRA follows up to medically confirm these reports, where consent is provided and more information is required. For each report, all events are 'coded'[9] as suspected side effects in the national pharmacovigilance database using the exact information (verbatim) given in the report. The HPRA follows up with the reporter to collect any further information which may be relevant to the assessment of the case.
- The description of suspected side effects in this update, including the number and category, reflect available information known at the time by the HPRA. These data may undergo changes as more information about individual reports becomes available through follow-up, and as reports are further evaluated.
- Please refer to the section 'Understanding the data presented within this safety update' on page 3 with regard to further interpretation guidance. Background information on the evaluation of suspected side effect reports is available on page 17.

Of the 14,844 reports notified to the HPRA up to 31 August, just over 50% have been submitted to EMA's Eudravigilance database, and as such, additional anonymised information on these reports, is publicly available through the following link www.adrreports.eu. See page 17 for further details.

[9] *Medical Dictionary for Regulatory Activities (MedDRA) https://www.meddra.org/*

Suspected side effects to mRNA vaccines

A breakdown of suspected side effects described in the 8686 reports notified to the HPRA is provided below by category. Each report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, including more than one in a specific category. As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.

Category	Suspected side effects
General symptoms and local reactions *e.g. chills, fatigue, 'flu-like' feeling, fever, injection site pain or swelling*	10313
Nervous system *e.g. dizziness, headache, lack of energy, pins & needles, fainting or feeling faint*	5821
Muscles, tissue, bones or joints *e.g. general muscular pain or weakness*	3971
Gastrointestinal *e.g. nausea, vomiting, diarrhoea*	2952
Skin *e.g. rash, itchy rash*	2363
Reproductive system, obstetrics or gynaecology related *e.g. menstrual disturbance*	1188
Respiratory *e.g. cough, shortness of breath*	1165
Behavioural, emotional and mental health *e.g. insomnia, trouble sleeping*	879
Cardiac (heart) related *e.g. palpitations*	655
Social circumstances *e.g. need to rest in bed or take a break from normal daily activities*	642
Blood and lymphatic system *e.g. swollen glands*	613
Eye *e.g. eye pain, vision blurred*	587
Procedural issues and complications *e.g. injection site bruising*	522
Abnormal clinical or laboratory result (i.e. where information is provided on results of relevant tests) *e.g. high temperature (via thermometer), increased heart rate or blood pressure (via BP monitor)*	511
Blood vessel related (i.e. veins/arteries) *e.g. pale complexion*	432
Infection *e.g. local or general such as influenza or cold sore*	407
Ear related e*.g. earache, tinnitus*	365
Metabolism and nutrition disorders *e.g. decreased appetite*	246
Immune system related *e.g. hypersensitivity, allergic reaction*	125
Kidney related *e.g. change in frequency of urination*	73
Liver related *e.g. jaundice*	17
Endocrine (hormone)	13
Cysts and polyps	7

Suspected side effects to adenoviral vector vaccines

A breakdown of suspected side effects described in the 6059 reports notified to the HPRA is provided below by category. Each report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, including more than one in a specific category. As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.

Category	Suspected side effects
General symptoms and local reactions *e.g. chills, fatigue, 'flu-like' feeling, fever, injection site pain or swelling*	10584
Nervous system *e.g. dizziness, headache, lack of energy, pins & needles, fainting or feeling faint*	5456
Muscles, tissue, bones or joints *e.g. general muscular pain or weakness*	3804
Gastrointestinal *e.g. nausea, vomiting, diarrhoea*	2936
Skin *e.g. rash, itchy rash*	1637
Respiratory *e.g. cough, shortness of breath*	866
Behavioural, emotional and mental health *e.g. insomnia, trouble sleeping*	764
Social circumstances *e.g. need to rest in bed or take a break from normal daily activities*	597
Eye *e.g. eye pain, vision blurred*	454
Metabolism and nutrition disorders *e.g. decreased appetite*	453
Reproductive system, obstetrics or gynaecology related e.g. *menstruation disturbance*	422
Blood vessel related (i.e. veins/arteries) *e.g. pale complexion*	420
Abnormal clinical or laboratory result (i.e. where information is provided on results of relevant tests) *e.g. high temperature (via thermometer), increased heart rate or blood pressure (via BP monitor)*	385
Cardiac (heart) related *e.g. palpitations*	345
Ear related e*.g. earache, tinnitus*	337
Procedural issue or complications *e.g. injection site bruising*	333
Infection *e.g. local or general such as influenza or cold sore*	223
Blood and lymphatic system *e.g. swollen glands*	171
Kidney related *e.g. increased frequency of urination*	68
Immune system related *e.g. hypersensitivity, allergic reactions*	53
Liver related *e.g. jaundice*	9
Endocrine (hormone)	5
Cysts and polyps	<5

Suspected side effects in adolescents (aged 12 to 17 years)

A breakdown of suspected side effects described in the 78 reports notified to the HPRA concerning adolescents aged 12 to 17 years is provided below by category. Each report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, including more than one in a specific category. As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.

Category	Suspected side effects
Nervous system *e.g. dizziness, headache, fainting or feeling faint*	54
General symptoms and local reactions *e.g. tiredness, weakness, chest pain, feeling hot*	47
Gastrointestinal *e.g. nausea, vomiting, abdominal pain*	30
Skin *e.g. rash, sweating*	17
Cardiac (heart) related *e.g. palpitations/racing heart*	13
Respiratory *e.g. shortness of breath, nose bleed*	10
Muscles, tissue, bones or joints *e.g. limb/muscle/joint pain*	9
Behavioural, emotional and mental health *e.g. trouble sleeping*	7
Eye *e.g. vision blurred*	6
Reproductive system, obstetrics or gynaecology related *e.g. menstruation disturbance*	6
Infection *e.g. chest infection*	<5
Abnormal clinical or laboratory result (i.e. where information is provided on results of relevant tests) *e.g. changes in heart rate*	<5
Blood vessel related (i.e. veins/arteries) *e.g. pale complexion*	<5
Blood and lymphatic system *e.g. swollen lymph nodes*	<5
Immune system related *e.g. hypersensitivity, allergic reaction*	<5
Metabolism and nutrition disorders *e.g. decreased appetite*	<5
Procedural issue or complications *e.g. fall*	<5

BACKGROUND INFORMATION ON THE EVALUATION OF SUSPECTED SIDE EFFECT REPORTS

As for all medicines and vaccines, suspected side effect reports in association with COVID-19 vaccines submitted to the HPRA are recorded and stored on the HPRA's national adverse reactions database. They are subsequently submitted (with any personal identifiers and contact details removed) to the EudraVigilance database operated and managed by the European Medicines Agency (EMA). EudraVigilance provides for the transfer of reports from national regulatory agencies such as the HPRA and marketing authorisation holders to the EMA. This supports early detection and monitoring of possible safety signals in relation to reported side effects.

The EMA also make available anonymised information on all reports, based on global safety experience, publically available through the following link www.adrreports.eu. The EMA also publish regular safety updates for COVID-19 vaccines, as well as highlights from meetings of the EMA's safety committee (Pharmacovigilance Risk Assessment Committee), which describe safety issues under review, as well as recommendations to revise product information. These are available via www.ema.europa.eu.

Information from side effect reports, together with additional safety data (e.g. from the scientific literature, cumulative safety data analysis, epidemiological studies etc.) are assessed on an on-going basis, in conjunction with our EU counterparts to consider their impact on the known safety profile of the COVID-19 vaccines and any need for regulatory changes to support safe and appropriate use.

Partially anonymised details of reports are also shared with other bodies also involved in safety monitoring of medicines, in accordance with the legislative provisions, including GDPR (please see the HPRA privacy statement here). These bodies include the World Health Organisation (WHO) and as appropriate, the company(ies) that hold the licence(s) for the medicine(s) concerned (i.e. marketing authorisation holders or 'MAHs'). Sharing of this information ensures that the information is available to all parties responsible for the ongoing safety monitoring of medicines.

Further information to support interpretation of the data provided in this update is available here.