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Pharmacovigilance for COVID-19 Vaccines – Prospects and Plans for 2022

PCWP & HCPWP Joint Meeting
3-4 March 2022

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2021 - One year of strong surveillance

- New strategies to help tailoring existing pharmacovigilance approaches
- Intense work by rapporteurs, the Pharmacovigilance Risk Assessment Committee (PRAC), and the EU regulatory network overall
- Unprecedented international collaboration
- Engagement with the public: stakeholder members in EMA Pandemic Task Force (ETF), 44 vaccines safety updates, press conferences, public meetings, PCWP & HCPWP
- Some new risks and risk minimisation advice for early detection of adverse reactions and prevention of serious outcomes have been identified

Spontaneously reported adverse reaction cases

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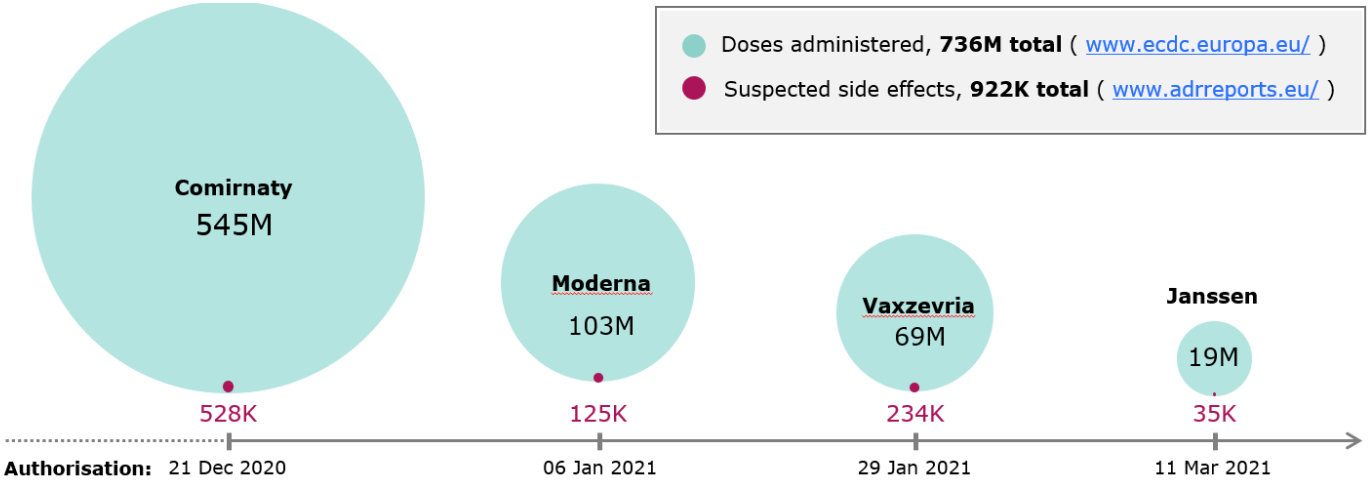
EudraVigilance on 2 January 2022:

More reports received with 4 vaccines than all other centrally authorised products in 1 year

European Economic Area (EEA)



Worldwide

#CASES

1,485,040

Healthcare Professional	482,006
Non HCP	862,349

EudraVigilance strategy for COVID-19 vaccine monitoring

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Eudra-Vigilance Dashboards
for continuous monitoring and communication

Electronic Validation Perpetual Reports
for intensive review of cases

Electronic Reaction Monitoring Reports
with increased frequency (weekly instead of fortnightly)

Algorithms
for ad-hoc data retrieval (e.g. 1st/2nd dose, thrombosis with thrombocyto-penia syndrome (TTS))

Tools

Observed/ Expected stratified by age

Observed/ Expected stratified by age and gender

Reporting rates

Routine Observed/ Expected process

Methods

Structured pharmacovigilance approach

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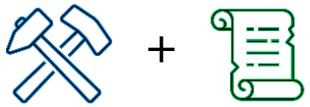
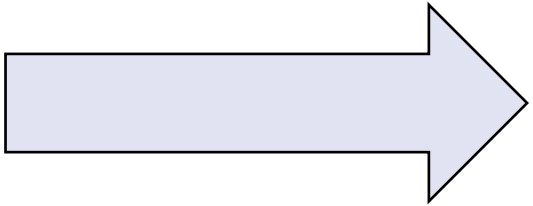
EudraVigilance



Tools Methods

EMA-coordinated studies

Scientific literature



Regulatory procedures:

- ETF/PRAC
- Signal procedure
- Assessment of all data
- Timely transparency

Required from marketing authorisation authorisation holders:

- Risk management plan (RMP)
- Paediatric investigation plan (PIP)
- (Monthly) Summary safety reports
- Periodic safety update reports (PSUR)
- Post-authorisation safety studies (PASS)

Risk minimisation advice to healthcare professionals and individuals

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Comirnaty

Anaphylaxis

- Don't vaccinate if allergic against ingredient
- Talk to your doctor about past allergies to vaccines
- 15 min observation time
- Equipment
- Go to a doctor immediately if swelling, rash, nausea, stomach pain, breathing difficulties or fainting occurs

Spikevax

Myo/pericarditis

- Go to a doctor immediately if breathlessness, strong heartbeat or chest pain occurs

Vaxzevria

Janssen

Capillary leak syndrome

- Don't vaccinate if CLS history
- Go to a doctor immediately if arms and legs swelling, sudden weigh gain or feeling faint occurs
- Intensive care

Vaxzevria

Janssen

TTS

- Don't vaccinate if TTS history after COVID-19 vaccine
- Go to a doctor immediately if breathlessness, chest pain, leg swelling/pain, persistent abdominal pain, severe or persistent headaches, blurred vision, confusion, seizures or skin bruising occurs
- Investigate thrombocytopenia (within three weeks after vaccination) for thrombosis; investigate thrombosis for thrombocytopenia
- Special care

Janssen

Vaxzevria

Venous thrombo-embolism

Cerebral blood clots

- Advice as for TTS

Vaxzevria

Janssen

Immune thrombocytopenia

- If ITP history, consider if to vaccinate and monitor platelets after vaccination
- Go to a doctor immediately if unexplained bleeding, skin bruising or pinpoint round spots beyond site of vaccination occur

Vaxzevria

Janssen

Guillain-Barré syndrome

- Tell your doctor before vaccination if GBS history after Vaxzevria (Vaxzevria package leaflet only)
- Go to a doctor immediately if weakness/paralysis in arms and legs, which can progress to chest and face, occurs

Vaxzevria

Janssen

Transverse myelitis

- Tell your doctor before vaccination if TM history after Vaxzevria (Vaxzevria package leaflet only)
- Go to a doctor immediately if weakness/paralysis in arms and legs, sensory symptoms or problem of bladder or bowel function occur

General

- Talk to your doctor before vaccination about existing severe illness, current severe infection with high fever, existing weakened immune system, bleeding problems, fainting after previous needle injection, vaccination anxiety

Please see full product information

Vaccine use in the EU/EEA

About 570 million doses of Comirnaty were administered in the EU/EEA between 21 December 2020 (EU marketing authorisation date) and 30 January 2022[1].

About 139 million doses of Spikevax were administered in the EU/EEA between 6 January 2021 (EU marketing authorisation date) and 30 January 2022[1].

About 19 million doses of COVID-19 Vaccine Janssen were administered in the EU/EEA between 11 March 2021 (EU marketing authorisation date) and 30 January 2022[1].

About 69 million doses of Vaxzevria were administered in the EU/EEA between 29 January 2021 (EU marketing authorisation date) and 30 January 2022[1].

0 doses of Nuvaxovid were administered in the EU/EEA (as per 22 February 2022); marketing authorisation in the European Union (EU) on 20 December 2021

Footnote 1: The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

2022 - Continued strong surveillance

- Adapted review timetables to data influx
- Established work processes for sustainability
- Further international collaboration
- Continue engagement with the public: stakeholder members in EMA Pandemic Task Force (ETF), vaccines safety updates, press conferences, public meetings, PCWP & HCPWP
- Continue assessing all data, including those in special populations

Ongoing investigations whether causally related

- Very few reports of autoimmune hepatitis after Comirnaty or Spikevax
- Capillary leak syndrome after Comiranty and Spikevax, including data from scientific literature
- Short-lived menstrual disorders after Comiranty and Spikevax, after previous reviews for COVID-19 vaccines have not evidenced such disorders

Comirnaty and Spikevax in pregnancy and breast-feeding

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- A large amount of information from pregnant women vaccinated during the second and third trimester has not shown negative effects on the pregnancy or the newborn baby
- While information on effects on pregnancy or the newborn baby after vaccination during the first trimester is limited, no change to the risk for miscarriage has been seen
- Dissemination of vaccine in breastmilk is not expected
- Vaccines can be used during pregnancy and breast-feeding
- Update of the product information

Public COVID-19 vaccines safety updates – new format in 2022

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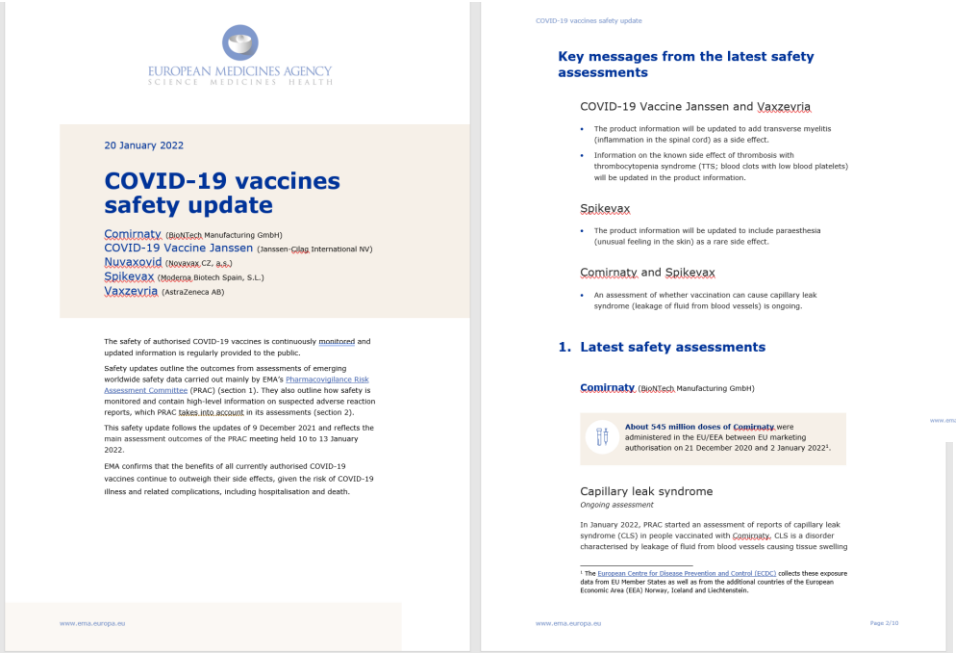

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20 January 2022

COVID-19 vaccines safety update

Comirnaty (BioNTech Manufacturing GmbH)
COVID-19 Vaccine Janssen (Janssen-Cilag International NV)
Nuvaxovid (Novavax CZ, a.s.)
Spikevax (Moderna Biotech Spain, S.L.)
Vaxzevria (AstraZeneca AB)

The safety of authorised COVID-19 vaccines is continuously monitored and updated information is regularly provided to the public.

Safety updates outline the outcomes from assessments of emerging worldwide safety data carried out mainly by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (section 1). They also outline how safety is monitored and contain high-level information on suspected adverse reaction reports, which PRAC takes into account in its assessments (section 2).

This safety update follows the updates of 9 December 2021 and reflects the main assessment outcomes of the PRAC meeting held 10 to 13 January 2022.

EMA confirms that the benefits of all currently authorised COVID-19 vaccines continue to outweigh their side effects, given the risk of COVID-19 illness and related complications, including hospitalisation and death.

www.ema.europa.eu

COVID-19 vaccines safety update

Key messages from the latest safety assessments

COVID-19 Vaccine Janssen and Vaxzevria

- The product information will be updated to add transverse myelitis (inflammation in the spinal cord) as a side effect.
- Information on the known side effect of thrombosis with thrombocytopenia syndrome (TTS; blood clots with low blood platelets) will be updated in the product information.

Spikevax

- The product information will be updated to include paraesthesia (unusual feeling in the skin) as a rare side effect.

Comirnaty and Spikevax

- An assessment of whether vaccination can cause capillary leak syndrome (leakage of fluid from blood vessels) is ongoing.

1. Latest safety assessments

Comirnaty (BioNTech Manufacturing GmbH)

About 545 million doses of Comirnaty were administered in the EU/EEA between EU marketing authorisation on 21 December 2020 and 2 January 2022[1].

Capillary leak syndrome

Ongoing assessment

In January 2022, PRAC started an assessment of reports of capillary leak syndrome (CLS) in people vaccinated with Comirnaty. CLS is a disorder characterised by leakage of fluid from blood vessels causing tissue swelling

[1] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

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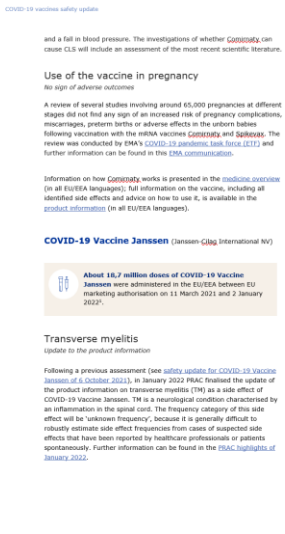

COVID-19 vaccines safety update

and a fall in blood pressure. The investigations of whether Comirnaty can cause CLS will include an assessment of the most recent scientific literature.

Use of the vaccine in pregnancy

No sign of adverse outcomes

A review of several studies involving around 65,000 pregnancies at different stages did not find any sign of an increased risk of pregnancy complications, miscarriages, preterm births or adverse effects in the unborn babies following vaccination with the mRNA vaccines Comirnaty and Spikevax. The review was conducted by EMA's COVID-19 pandemic task force (ETF) and further information can be found in this EMA communication.

Information on how Comirnaty works is presented in the medicine overview (in all EU/EEA languages); full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

COVID-19 Vaccine Janssen (Janssen-Cilag International NV)

About 18,7 million doses of COVID-19 Vaccine Janssen were administered in the EU/EEA between EU marketing authorisation on 11 March 2021 and 2 January 2022[1].

Transverse myelitis

Update to the product information

Following a previous assessment (see safety update for COVID-19 Vaccine Janssen of 6 October 2021), in January 2022 PRAC finalised the update of the product information on transverse myelitis (TM) as a side effect of COVID-19 Vaccine Janssen. TM is a neurological condition characterised by an inflammation in the spinal cord. The frequency category of this side effect will be 'unknown frequency', because it is generally difficult to robustly estimate side effect frequencies from cases of suspected side effects that have been reported by healthcare professionals or patients spontaneously. Further information can be found in the PRAC highlights of January 2022.

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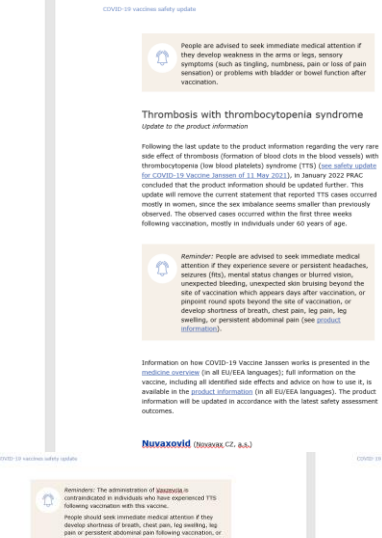


COVID-19 vaccines safety update

People are advised to seek immediate medical attention if they develop weakness in the arms or legs, sensory symptoms (such as tingling, numbness, pain or loss of pain sensation) or problems with bladder or bowel function after vaccination.

Thrombosis with thrombocytopenia syndrome

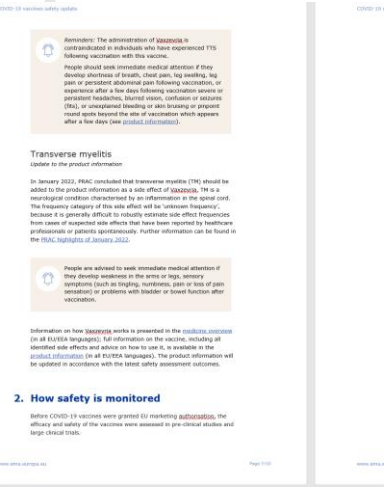
Update to the product information

Following the last update to the product information regarding the very rare side effect of thrombosis (formation of blood clots in the blood vessels) with thrombocytopenia (low blood platelets) syndrome (TTS) (see safety update for COVID-19 Vaccine Janssen of 11 May 2021), in January 2022 PRAC concluded that the product information should be updated further. This update will remove the current statement that reported TTS cases occurred mostly in women, since the sex imbalance seems smaller than previously observed. The observed cases occurred within the first three weeks following vaccination, mostly in individuals under 60 years of age.

Reminder: People are advised to seek immediate medical attention if they experience severe or persistent headaches, seizures (fits), mental status changes or blurred vision, unexpected bleeding, unexpected skin bruising beyond the site of vaccination which appears days after vaccination, or pinpoint round spots beyond the site of vaccination, or develop shortness of breath, chest pain, leg pain, leg swelling, or persistent abdominal pain (see product information).

Information on how COVID-19 Vaccine Janssen works is presented in the medicine overview (in all EU/EEA languages); full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages). The product information will be updated in accordance with the latest safety assessment outcomes.

Nuvaxovid (Novavax CZ, a.s.)



COVID-19 vaccines safety update

Reminders: The administration of Vaxzevria is contraindicated in individuals who have experienced TTS following vaccination with this vaccine.

People should seek immediate medical attention if they develop shortness of breath, chest pain, leg swelling, leg pain or persistent abdominal pain following vaccination, or experience after a few days following vaccination severe or persistent headaches, blurred vision, confusion or seizures (fits), or unexplained bleeding or skin bruising or pinpoint round spots beyond the site of vaccination which appears after a few days (see product information).

Transverse myelitis

Update to the product information

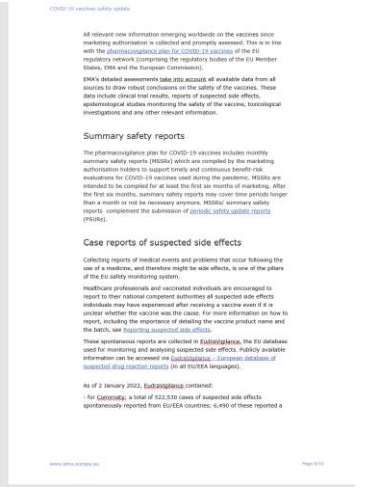
In January 2022, PRAC concluded that transverse myelitis (TM) should be added to the product information as a side effect of Vaxzevria. TM is a neurological condition characterised by an inflammation in the spinal cord. The frequency category of this side effect will be 'unknown frequency', because it is generally difficult to robustly estimate side effect frequencies from cases of suspected side effects that have been reported by healthcare professionals or patients spontaneously. Further information can be found in the PRAC highlights of January 2022.

People are advised to seek immediate medical attention if they develop weakness in the arms or legs, sensory symptoms (such as tingling, numbness, pain or loss of pain sensation) or problems with bladder or bowel function after vaccination.

Information on how Vaxzevria works is presented in the medicine overview (in all EU/EEA languages); full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages). The product information will be updated in accordance with the latest safety assessment outcomes.

2. How safety is monitored

Before COVID-19 vaccines were granted EU marketing authorisation, the efficacy and safety of the vaccines were assessed in pre-clinical studies and large clinical trials.



COVID-19 vaccines safety update

All relevant new information emerging worldwide on the vaccines since marketing authorisation is collected and promptly assessed. This is in line with the pharmacovigilance plan for COVID-19 vaccines of the EU regulatory network (comprising the regulatory bodies of the EU Member States, EMA and the European Commission).

EMA's detailed assessments take into account all available data from all sources to draw robust conclusions on the safety of the vaccines. These data include clinical trial results, reports of suspected side effects, epidemiological studies monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

Summary safety reports

The pharmacovigilance plan for COVID-19 vaccines includes monthly summary safety reports (MSSRs) which are compiled by the marketing authorisation holders to support timely and continuous benefit-risk evaluations for COVID-19 vaccines used during the pandemic. MSSRs are intended to be compiled for at least the first six months of marketing. After the first six months, summary safety reports may cover time periods longer than a month or not be necessary anymore. MSSRs' summary safety reports complement the submission of periodic safety update reports (PSURs).

Case reports of suspected side effects

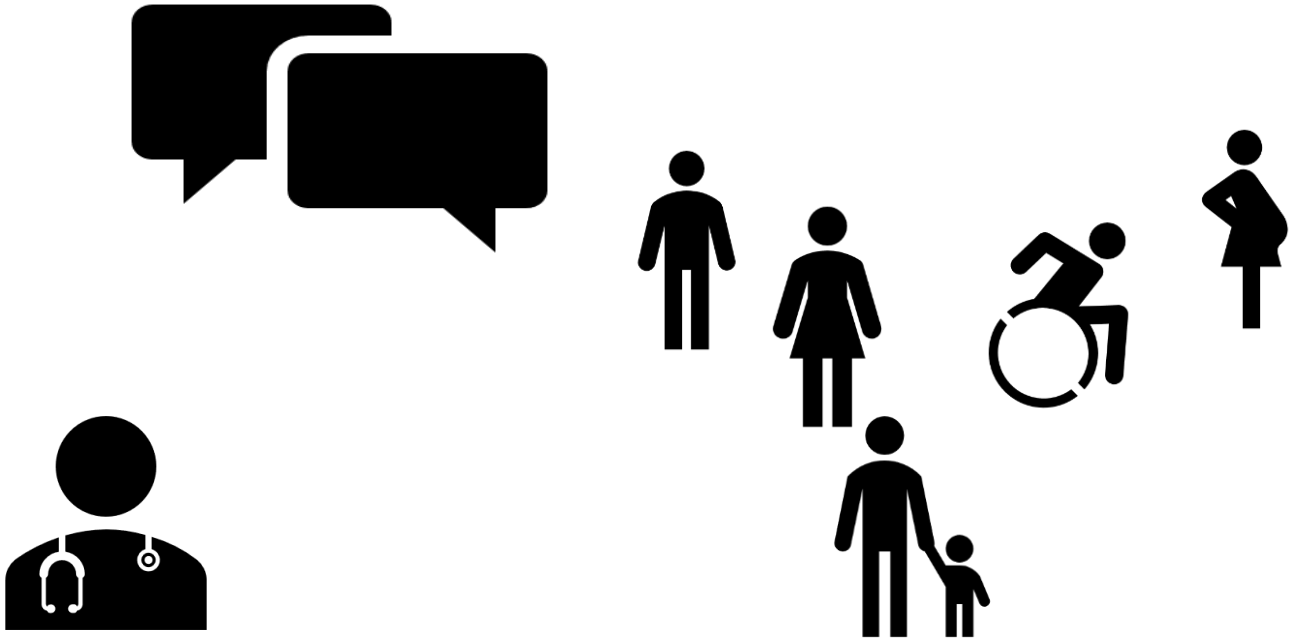
Collecting reports of medical events and problems that occur following the use of a medicine, and therefore might be side effects, is one of the pillars of the EU safety monitoring system.

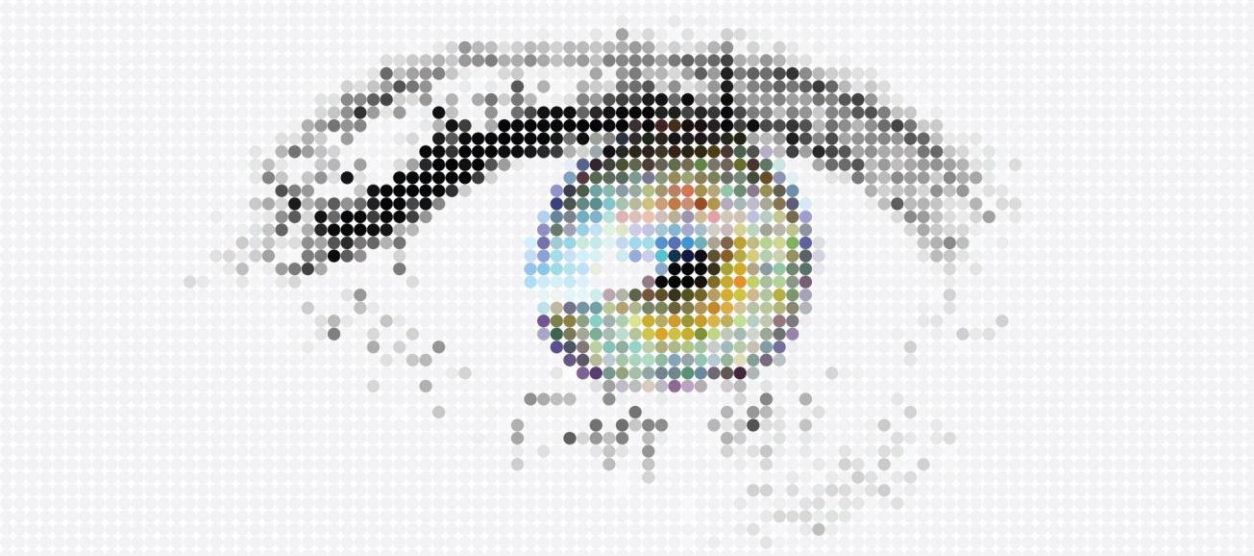
Healthcare professionals and vaccinated individuals are encouraged to report to their national competent authorities all suspected side effects individuals may have experienced after receiving a vaccine even if it is unclear whether the vaccine was the cause. For more information on how to report, including the importance of detailing the vaccine product name and the batch, see Reporting suspected side effects.

These spontaneous reports are collected in EudraVigilance, the EU database used for monitoring and analysing suspected side effects. Publicly available information can be accessed via EudraVigilance – European database of suspected drug reaction reports (in all EU/EEA languages).

As of 2 January 2022, EudraVigilance contained:

- for Comirnaty, a total of 532,539 cases of suspected side effects spontaneously reported from EU/EEA countries; 6,490 of these reported a





Thank you for your attention

Further information

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