EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

From laboratory to patients

How the safety of medicines is ensured in the European Union

An agency of the European Union

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Overview

Medicines can prevent or treat diseases and help manage the symptoms of multiple health conditions. They can change people's lives, make them live longer and improve their quality of life. However, every medicine comes with risks.

Anticipating and reducing side effects caused by medicines are at the core of the mission of the European Medicines Agency (EMA) and national competent authorities. From the moment a medicine is developed, a wide range of activities is in place to ensure the highest level of safety.

Before a medicine is authorised, its risks are studied and then balanced against its benefits. Are the side effects acceptable in view of the disease that is being treated? How can they be minimised? Whether a side effect is seen as acceptable or not depends on how serious the illness is and how much the treatment can help. For example, a serious side effect may be acceptable for a life-threatening disease like cancer but not for a painkiller. **A medicine can only be authorised if data show that its benefits are greater than its risks.**

Once a medicine is on the market, information on the known side effects and recommendations for its safe use are available for patients and healthcare professionals. Medicines are **carefully and continuously monitored after authorisation** to detect any new safety issues. EMA works with national competent authorities in each European Union (EU) country to continuously monitor a wide range of data sources. Scientific studies and patient reports can warn authorities that action is needed to reduce any newly detected risks. This proactive monitoring allows authorities to respond quickly when new risks are identified. The actions they take range from taking steps to reduce a risk, such as including a warning for patients and healthcare professionals about a new side effect, and restricting the use of a medicine or even suspending its use entirely.

How the EU keeps medicines safe: drawing on expertise from across Europe

EMA and the EU Member States work together to supervise the safety of medicines through a unique collaborative network that draws on expertise from across the EU. The Member States conduct a wide range of activities at national level, such as supervising the collection of suspected side effects or collecting safety signals for authorised medicines. For some activities, one Member State carry out assessments on behalf of the EU.

Data gathered from across the EU are centralised and analysed by EMA's safety committee (the Pharmacovigilance Risk Assessment Committee; PRAC), which plays a key role in this system. Each EU Member State, as well as Iceland and Norway, appoints safety experts to the PRAC. The European Commission also nominates six independent scientific experts, as well as members representing patient and healthcare professional organisations. The PRAC meets monthly to provide scientific expertise on all aspects of human medicines' safety.

EMA and national competent authorities regularly update existing information and recommendations about how to use medicines safely. Being aware of and following these recommendations helps maximise a medicine's benefits and minimise its risks.

To understand, monitor and manage the safety of medicines, a strong European system is in place which focuses on:

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1. Understanding a medicine's side effects before approval

- **Evaluation of a medicine's safety starts long before a medicine is authorised and never stops for as long as the medicine is marketed and used.**
- **Before a medicine is approved for use, it undergoes extensive testing to identify possible side effects. Medicine developers must collect strong evidence about its safety through different types of studies.**
- **These tests help identify side effects a medicine can potentially cause and how often they occur.**
- **The information obtained helps medicines regulators determine if the benefits of a medicine in treating a patient's disease are greater than its known risks; this is the key principle behind approving any medicine.**

Medicines go through a lot of testing before they can be approved. First, they are tested in the laboratory to learn as much as possible about the medicine's effects before it gets tested in humans. At this stage, studies will look at different aspects of the safety of a medicine, including how it works, whether it could damage organs or impact the development of a baby during pregnancy or whether long-term use may lead to cancer.

The next phase of development involves studies in people. These typically begin with a small group of healthy volunteers, usually between 20 to 100, in what are known as **phase 1 trials**. The goal is to understand how the body reacts to the treatment, identify any side effects and determine a safe dosage. If successful, the medicine progresses to **phase 2 trials**, where it is tested in a few hundred patients with the condition. These studies evaluate the treatment's effectiveness, continued safety, and optimal dosing. Finally, **phase 3 trials** involve hundreds to thousands of patients to confirm how well the treatment works and to further assess its safety profile. While most medicines follow this general path, the number of participants and the design of each trial can vary significantly depending on the condition being targeted. For rare diseases, trials may involve only a few dozen participants, whereas studies for common conditions like diabetes or hypertension may include several thousand. To support robust and appropriate study designs, EMA has developed numerous guidelines tailored to different medical conditions.

Did you know?

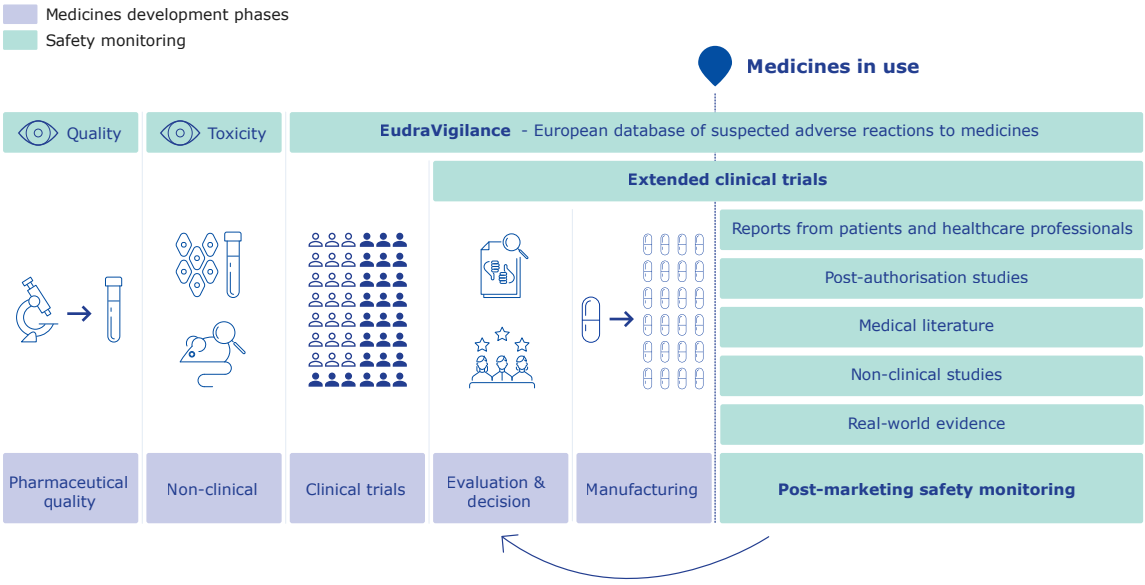
To have a 95% chance of detecting even one case of a very rare side effect (meaning a side effect that may occur in less than 1 in 10,000 people), a clinical trial would need to include at least 30,000 participants. Consequently, very rare side effects are more likely to be identified after the medicine is approved and used more widely.

In every study, medicine developers carefully record any unwanted effects, both serious and non-serious. They then analyse each one to understand whether it may have been caused by the medicine, the illness itself or another disease or whether it occurred simply by chance. They also evaluate how often these side effects occur.

What about vaccines?

Vaccines are slightly different from other medicines because they are given to healthy people to protect against an infectious disease people do not have, rather than to treat it. Studies must show that the benefits in protecting people against the disease are far greater than any risk of side effects. The size of the studies usually depends on whether the vaccine contains components that have been previously authorised or not. As most side effects of vaccines occur within four to six weeks of vaccination, safety data must cover at least six weeks after completion of vaccination.

In general, if a new vaccine contains components not previously included in already authorised vaccines, the number of people included in studies should be sufficient to estimate the frequency of uncommon adverse events (occurring in up to 1 in 1,000 vaccinated persons). However, if there are concerns arising from laboratory data, from historical experience with a similar vaccine or from the available clinical safety data, the number of participants should allow a relatively precise evaluation of the risk of uncommon or even rare adverse events. More information on vaccines is available in the European Vaccination Information Portal.



2. Managing a medicine's side effects at the time of authorisation

- **If the benefits of a medicine have been shown to outweigh the risks in a group of patients, it can be approved for use.**
- **However, approval comes with recommendations and measures to minimise the medicine's risks.**
- **Information about how to use the medicine safely is included in the package leaflet (for patients) and the summary of product characteristics, the SmPC (for healthcare professionals).**
- **Following these recommendations is critical to help prevent side effects, detect them early and reduce harm. If a new safety issue is identified when the medicine is on the market, new measures to mitigate the risks will be introduced and reflected in the information for patients and healthcare professionals.**

The SmPC and the package leaflet are parts of a document called the product information which is available on the EMA website for each centrally authorised medicine. National competent authorities also publish the product information on their websites for nationally authorised medicines.

What does the SmPC include?

This document contains important safety information and recommendations that healthcare professionals should consider when prescribing the medicine.

The SmPC includes information about:

- all known side effects the medicine can cause together with information on how often those effects occur;
- situations in which the medicine must not be used (contraindications);
- special precautions that need to be followed. For example, if there is a need for special laboratory tests or monitoring when used by a patient with kidney or liver disease;
- how the use of the medicine affects the use of other medicines and vice versa;
- special considerations regarding fertility, pregnancy and breastfeeding.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What does the package leaflet include?

This document comes with every medicine that people take. It summarises all the key information about the medicine and is an invaluable reminder of the instructions that the doctor and pharmacist may have given.

Its main sections are:

- What the medicine is used for — this section allows the reader to check what the medicine is for, and it may also briefly explain how it works
- What you need to know before using the medicine — this section explains when the patient must not use the medicine and important precautions to take before or during treatment
- How to use the medicine — this section explains how to take the medicine including how often, how much, when in the day to take it and for how long
- Possible side effects — this section explains all the medicine's known side effects and how likely they are to occur based on the available evidence.

Why are restrictions sometimes put in place?

Some side effects may be more severe or more common in certain people, for example, those with specific health issues, allergies or a genetic trait. If the benefits of a medicine are not greater than the risks for these individuals, they must not use the medicine. This will be clearly stated in the SmPC and package leaflet.

Did you know?

When certain medicines have particularly serious side effects, additional measures are put in place to make sure they are used safely and effectively. These additional risk minimisation measures may include raising awareness about specific side effects, how to detect them and what to do if they occur, through a brochure or a video. They may also help ensure the medicine is only used in people for whom the medicine is authorised, for example through testing before starting treatment. When additional measures are put in place, the materials and details are adapted to meet the national needs of each Member State. Most national medicines agencies publish this information in their official languages.

3. Continuous safety monitoring while a medicine is in use

- **Although detailed safety information must be available when a medicine is approved, some rare or very rare side effects may only emerge after tens or hundreds of thousands of people with different health conditions use it.**
- **Medicines are continuously monitored after approval to detect rarer effects that may only appear when medicines are used by larger, more diverse patient groups in real life.**
- **This monitoring also helps to better understand how often and how severe known side effects are in different groups of people with varying health conditions. A plan is therefore in place for each medicine at the time of approval to proactively generate and collect more information about its safety.**
- **Medicines regulators continuously collect and analyse new data from multiple sources, including patient reports, studies and the scientific literature, to monitor safety and detect any unexpected issues and take action when needed.**

At the time of approval, a plan is put in place for each medicine to prevent or reduce the risk of identified side effects and to generate and collect more information about its safety. This proactive approach allows for early detection of any new safety issue and prompt action when needed.

This plan, called the risk management plan (RMP), includes routine activities that apply to all approved medicines, such as collecting reports of suspected side effects from patients and healthcare professionals, and detecting safety signals.

For some medicines, the RMP may also include specific actions – like additional studies that companies are required to conduct after authorisation – when more information is needed.

The risk management plan of every medicine assessed by EMA is published on the EMA website.

Why not all risks are known at the time of authorisation

Clinical trials are carried out to study a medicine's effects and carefully recruit patients who have only the condition that the medicine is being investigated for. The trials exclude patients with unrelated conditions or those receiving other treatments because this can make it hard to tell whether any changes are caused by the medicine being tested or by something else.

In real life, the medicine will be used in a more diverse population; patients' medical circumstances may be more complicated than those of patients included in trials, treatment may last longer or may be taken together with other medicines. As a result, new side effects may emerge, or some known side effects may appear more often in real life than in the clinical trials. Moreover, side effects that occur only rarely may not be reported until a greater number of people have used the medicine.

This is why medicines are continuously monitored in the wider population after their authorisation.

A range of sources continuously monitored

As soon as a medicine is in use, medicines regulators continuously monitor a wide range of sources to detect any new information about its safety.

Reports of suspected side effects from patients and healthcare professionals: a key pillar of safety monitoring

Patients are encouraged to report any side effects that occur following the use of a medicine even if it may not be caused by the medicine.

They can report them directly to their national medicines agency; alternatively, they can report them to their healthcare professional or to the company marketing the medicine who can report them on their behalf.

These reports are continuously analysed to help identify any new safety issue with a medicine. By reporting suspected side effects, patients help to gather more information about medicines, which will ultimately allow them to be used more safely.

Both national competent authorities and companies submit the reports they receive to the EU database of suspected side effects, called EudraVigilance. Companies are obliged to submit both serious and non-serious reports received from the European Economic Area (EEA) as well as serious reports received from outside the EEA. These data are continuously monitored and analysed by medicines regulators to detect potential safety concerns.

Reporting side effects can make medicines safer for everyone

Anyone can report a suspected side effect on a medicine as long as they have the necessary details; this includes the patient, the patient's carer, a doctor, nurse or pharmacist. Patients can report a suspected side effect themselves, or talk with their healthcare professional during a consultation, who can submit a report on their behalf. Each EU country has a reporting tool and information about how to submit a report is available on the websites of national competent authorities. Information on how to report a suspected side effect can also be found in the package leaflet and the SmPC. Providing clear and detailed information is essential when reporting a suspected side effect. The following key details should be included:

information on the person who has experienced the side effect, including age and sex

the name of the medicine (brand name as well as active substance) suspected to have caused the side effect

dose and duration of treatment with the medicine

how long the treatment had lasted when the suspected side effect occurred

whether the person stopped taking the medicine after the side effect occurred and, if so, did the side effect stop

the batch number of the medicine (found on the packaging)

other medicines taken around the same time (including non-prescription, herbal or birth control medicines)

any other health condition that the person may have

What happens to your suspected side effect after it has been reported?

Once a report is submitted, whether by a patient, healthcare professional or carer, it is first carefully reviewed by the national competent authority to ensure it contains enough information to be assessed. This includes verifying details such as:

the medicine involved (brand and active substance)

the nature and timing of the side effect

patient characteristics (e.g. age, sex, medical history)

other medicines being taken at the same time

If the report is incomplete, the medicine regulator may follow up to request additional information. They are then recorded and stored in the national authority's adverse reaction database.

Regulators classify them based on their severity and impact on health.

These reports are then transferred to the EU database of suspected side effects, which is one of the largest pharmacovigilance databases in the world and contains tens of millions of reports. EMA manages all the reports received, those from the national competent authorities as well as those received from pharmaceutical companies, removing any duplicates and making sure the information is of sufficient quality to allow data analysis.

EMA continuously screens these data to detect unusual or unexpected patterns in the reports received. If a signal is detected for a medicine, it will be assessed along with any other data on the medicine. If there is at least a reasonable possibility that a medicine could have caused a suspected side effect, this is included in the medicine's product information.

As millions of reports are collected and screened in the EU every year, it is not possible to provide individual feedback to patients and healthcare professionals who submitted a report; however, they can check the package leaflet and SmPC for up-to-date information.

Why reports of suspected side effects are not enough to conclude on a possible safety issue

It is important to understand that just because someone experiences an unwanted effect after taking a medicine, it does not necessarily mean the medicine caused it. This is a key difference between correlation (two things happening at the same time) and causation (one thing actually causing the other).

Did you know?

EudraVigilance protects personal data using a method called pseudonymisation. This means it replaces details that could identify someone (like their name or patient ID) with codes. This way, regulators can study medicine safety data without seeing who the person is, in line with EU privacy rules.

For example, a new medicine is approved to treat high blood pressure and becomes widely used in clinical practice and some patients report that they are experiencing headaches. However, headaches are also common in people with high blood pressure, regardless of treatment. Regulators will carefully assess reports of this suspected side effect in EudraVigilance, evaluating important aspects that help them to conclude on causality. For instance, is there a suggestion of a temporal association: do the headaches start soon after the medicine is taken? Do the headaches stop when the medicine is stopped, and return when it is taken again? This may point to a possible link.

Additionally, medicines regulators will also determine if there are any confounders; these are other factors that can be responsible for the suspected side effect other than the medicine itself. A possible confounder in this case, could relate to poor compliance, which means that the patient was not taking their blood pressure medicine every day. The headaches could therefore be due to untreated high blood pressure rather than the medicine itself.


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Furthermore, if higher doses of the medicine lead to more frequent or worse headaches, it supports the idea that the medicine is causing them.

This explains why a single report of a suspected side effect is not enough to confirm that a medicine caused it. More evidence is needed, such as a plausible biological mechanism to explain how the medicine may have caused the effect, a careful evaluation of the case, including the patient's medical history, and data showing if the side effect happens more often than would be expected in this group of people. Medicines regulators carry out detailed assessments of all available data to draw robust conclusions.

Did you know?

Medicines regulators use specialised statistical methods to monitor the data in EudraVigilance. One important approach involves looking for patterns in reported side effects, specifically, whether a suspected side effect is reported more often with a particular medicine than would normally be expected. These patterns are known as signals of disproportionality.

Such signals could mean there is a potential safety signal, although further evaluation is always needed to confirm whether the medicine is actually causing the effect.

To detect such signals, regulators will compare how often a side effect is reported for one medicine with how often it is reported for other medicines, a statistical measure called the reporting odds ratio (ROR). If the ROR is higher than expected, it may point to a possible safety concern that needs closer examination.

During the COVID-19 pandemic, regulators complemented these methods with another type of analysis which compares the number of reported cases of a suspected side effect for a given vaccine to the number expected in the general population based on background rates – this is called observed versus expected (O/E) analyses.

This approach was particularly useful for evaluating suspected side effects following the mass vaccination campaign, given the large volume of data and the need for rapid assessments. To be able to carry out such analyses, even before the vaccination campaigns started, EMA worked very closely with researchers to determine the expected frequency for a wide range of effects in the general population.

Detailed information about how suspected side effects reported during the pandemic were analysed is available in a pharmacovigilance report published on the EMA website.

Understanding data from the EU database of suspected side effects

On EMA's ADR website, anyone can access information on suspected side effects that have been reported by patients and healthcare professionals across the EU for each medicine or active substance. These data come from the EudraVigilance database and users can analyse them by country, age group and type of side effect reported. These reports do not necessarily reflect a real safety issue with a medicine; many of the events reported may have been caused by another illness or be associated with another medicine taken by the patient at the same time. Only a careful assessment will determine if the medicine caused the problem.

During the COVID-19 pandemic, a lot of incorrect figures about reports of suspected side effects and deaths following COVID-19 vaccination circulated on social media and various websites. These figures often resulted from a misunderstanding of how the European database of suspected adverse drug reactions works. Users cannot use the data from this website to calculate the total number of fatal cases reported for a given medicine or the total number of a specific reaction (such as myocardial infarction). This is because one individual case may contain more than one suspected side effect; the sum of the number of suspected side effects will therefore always be higher than the total number of cases.

Post-authorisation studies: a key tool for gathering more information on a medicine's safety profile

Once a medicine has been authorised, studies to further assess its safety are often carried out. They may have been required by medicines regulators at the time of authorisation or carried out by companies on their own initiative. Medicines regulators routinely assess their results.

Post-authorisation safety studies (PASS) are designed to gather additional information about a medicine's safety, particularly in the context of everyday use by a broader and more diverse group of patients than in clinical trials.

A PASS may be used to address concerns related to a suspected side effect, evaluate the risks of a medicine after long-term use or study its safety in patients who were not included in the clinical trials that supported the authorisation, such as older patients, pregnant people or patients with kidney or liver problems.

Did you know?

Medicines regulators can require companies to conduct additional studies to gather more safety data on a medicine. Such studies may be requested at the time of authorisation or at any point afterwards. Companies are legally required to conduct these studies and must submit results within the agreed timeframe.

A PASS may also be used to assess whether risk minimisation measures, such as educational materials for healthcare professionals and patients, are working as intended. The PRAC is responsible for assessing the study protocol (a detailed plan outlining how a study will be conducted) for studies that the EMA has required companies to carry out. The PRAC also assesses the final study results for the PASS.

Medical literature

Scientific journals are an important source of information on a medicine's safety. Healthcare professionals often write about medicines' unexpected effects in medical journals.

These publications contribute to the knowledge about a medicine, particularly about its unwanted effects. Medical journals are systematically scanned for new safety information. Relevant information is included in the EU database of suspected side effects. Information on medical literature monitoring is available on the EMA website.

Non-clinical studies

Non-clinical studies refer to studies that do not involve human beings. For example, they may be conducted on cells or tissues or in animals. Although non-clinical studies are essential during the development of a medicine to understand how a medicine works, they also play a valuable role after a medicine has been authorised.

Non-clinical data can help regulators and pharmaceutical companies better understand how a medicine can cause a suspected side effect. When new safety signals emerge after a medicine is authorised, medicines regulators may request further non-clinical investigations to better understand the nature and severity of the risk, including how the medicine causes it.

For example, if a medicine is suspected of causing liver damage, non-clinical studies can help determine whether the damage is due to the medicine or its breakdown products damaging the cells of the liver directly, whether the medicine blocks transport proteins that help move bile out of the liver or whether it triggers an immune response that mistakenly attacks the liver.

Real-world evidence

EMA and national competent authorities increasingly rely on real-world data to monitor the safety of medicines, as well as their effectiveness, in real life.

These data are collected outside of conventional, planned clinical trials and are generated by sources such as electronic health records, patient registries, pharmacy dispensing databases, insurance claims, health surveys and social media. Real-world evidence can supplement information from clinical trials and help medicines regulators to make evidence-based decisions when approving and monitoring medicines.

In this context, EMA and the EU national competent authorities have established a data network known as DARWIN EU, the Data Analysis and Real-World Interrogation Network, to enhance the monitoring of medicines after they are approved for use. This initiative allows EMA to access and analyse real-world evidence from across the EU, providing insights into diseases, groups of patients and the safety and effectiveness of medicines.

Collaboration with international medicines regulators and organisations

International collaboration plays an important role in safety monitoring activities as it provides invaluable insights into emerging safety issues. EMA routinely exchanges a wide range of information with medicines regulators outside the EU.

EMA liaises with a wide range of countries and international organisations outside the EU through confidentiality agreements. These agreements allow for the secure exchange of information concerning the safety of medicines which is not in the public domain. Such exchanges are often vital for identifying emerging safety issues.

The European Commission and EMA have confidentiality agreements with medicines regulators in Australia, Brazil, Canada, Japan, Republic of Korea, Switzerland, United States, and with the World Health Organization (WHO). These partnerships allow for continuous and structured collaboration, ensuring that safety monitoring is not limited by geographical boundaries.

In addition to these long-term arrangements, EMA can establish ad-hoc confidentiality agreements to address specific public health needs. These are particularly useful during health emergencies or when dealing with novel therapies, allowing for rapid and focused information exchange that supports urgent safety evaluations.

Key tools to assess new data

In the EU, medicines regulators have three main tools that support the continuous monitoring of medicines once they are authorised.

Periodic safety update reports

Every year EMA and the national competent authorities assess thousands of periodic safety update reports (PSURs). These reports must be submitted by companies at regular, predefined intervals. They ensure that all the safety information available on an authorised medicine is regularly reviewed, even if no concerns have been raised from any source.

EMA and national competent authorities assess information in PSURs to determine if there are new risks identified for a medicine or any change to its known safety profile, and if its risk-benefit balance has changed.

PSURs contain all the information on the benefits and risks of a medicine generated worldwide during the period covered by the report. This includes a summary of the suspected side effects reports received from patients and healthcare professionals and new results from clinical trials or any other studies. They must cover all studies carried out, both in authorised and unauthorised indications.

When several medicines contain the same active substance, the related PSURs are assessed together in a so-called PSUR single assessment (PSUSA) procedure. This ensures that all the available data on a given active substance are assessed at the same time across the EU and that harmonised regulatory action is taken across the EU if needed.

Detection of safety signals

Every year, EMA and the national competent authorities review thousands of potential safety signals. A safety signal is information on a new or known side effect that is potentially caused by a medicine and that warrants further investigation.

Such signals often come from the routine screening of suspected side effects reported by patients and healthcare professionals, but they may also come from post-authorisation studies or the medical literature.

The detection and evaluation of safety signals play a central part in the safety monitoring of medicines. The evaluation of a safety signal aims to establish whether there is a causal link between a medicine and an adverse event.

Identification of a safety signal is just the start of a process to discover if the signal is indeed related to the medicine and, importantly, whether the medicine has caused the safety problem. As the next step, EMA or the national competent authority that detected the signal scrutinise all the EudraVigilance data relating to the safety signal and work out if there is sufficient information to warrant investigating it further; this process is called **signal validation**.

A national competent authority or a member of EMA's safety committee, PRAC, will then confirm whether there appears to be enough information to suggest that the medicine might have caused the safety problem under review (referred to as **signal confirmation)**. The signal is then ready for a full assessment by PRAC; new data may be brought to bear, and other bodies may be consulted.

After completing its evaluation, the PRAC concludes if the medicine is likely to have caused the effect or not and decides whether regulatory action is needed.

EMA publishes a summary of the signals evaluated by PRAC, along with the committee's recommendations, each month. These summaries are published in all EU languages on EMA's website to ensure consistent implementation across Member States.

Questions to be answered when assessing data

Figuring out whether a safety signal means that the medicine causes the side effect in question involves answering questions such as:

- Does the safety problem concur with other side effects of the medicine, or information available previously, or the side effects of similar medicines?
- How strong is the evidence? For example:
  - does the safety problem disappear when the medicine is stopped, and does it reappear when the medicine is restarted?
  - does the safety problem occur more often in those using the medicine than in those not using it, taking into account the number of people using the medicine?
  - is the pattern of effects very similar in all the reports (e.g. how soon it appears after starting the medicine, similar test results)?
  - is the severity of the safety problem linked to the size of the dose (higher dose resulting in a more severe effect)?
  - can our understanding of how the medicine works explain the safety problem?

Often medicines regulators need additional information to answer such questions, and they will look at laboratory studies, medical literature, databases holding detailed medical records of a large number of people (registries), scientific opinion of researchers and information from medicines regulators worldwide.

Did you know?

EMA publishes an annual report on EudraVigilance which outlines how many potential signals were reviewed each year. For instance, in 2024, EMA assessed 1,254 potential signals involving 990 different medicines. The report provides a breakdown of the outcomes of the signal assessments. It specifies how many signals were closed following assessment, how many continue to be monitored for additional data, and how many remain under evaluation. It also highlights the number of signals that were prioritised for detailed evaluation by EMA's safety committee, PRAC, as well as the outcomes of these evaluations. In 2024, 32 signals led to a product information update.

This rigorous application of analytical and statistical methods can distinguish unwanted side effects occurring as a result of using the medicine from those occurring because of other reasons.

Safety referrals

Safety concerns cannot always be managed by routine measures. In such instances, the European Commission, a national competent authority, EMA's executive director or a company marketing a medicine can 'refer' a concern to EMA's safety committee, the PRAC. These reviews can concern a single medicine or a class. The PRAC comprehensively reviews all the data available on the concern raised in the context of other risks associated with the medicine and issues recommendations on how to deal with it.

When concerns are considered serious enough to require a coordinated EU-wide response, the issue is formally referred to EMA. EMA is then responsible for conducting a scientific assessment of the medicine in question on behalf of the EU. This process ensures that all Member States receive consistent and evidence-based recommendations on how to manage the safety concern.

Safety referrals are assessed by PRAC, which evaluates all available evidence including data collected from EudraVigilance, the published scientific literature and post-authorisation studies.

Did you know?

You can find the outcome of all referral procedures for human medicines on EMA's website, by selecting referrals on the medicine search page. Past examples of public hearings organised in the context of referrals are available on the EMA website.

To support a thorough and multidisciplinary evaluation, PRAC may also consult outside experts such as patients, healthcare professionals or academics. These groups provide independent, in-depth expertise and contribute to the evaluations by providing insights on complex clinical, scientific, or methodological issues. Their views are considered alongside other evidence to ensure that the final recommendations are robust, balanced, and are more likely to be feasible and proportionate in real-world settings.

For urgent safety referrals, where urgent action is necessary because of a safety issue, the PRAC also consults the public directly. A list of questions is then published on the EMA website so that anyone can send in any relevant data they have to address the topic.

Occasionally, in the course of a safety referral, the PRAC may decide to call a public hearing to hear directly from stakeholders, including patients.

4. Taking measures when needed

- **A key outcome of safety monitoring is action taken to prevent or minimise harm.**
- **The continuous evaluation of new data can lead to different actions.**
- **The choice of action depends on the seriousness of the concern and may take into account whether other treatment options exist.**

No action needed but keep monitoring

Require the company to carry out a new study to gather more data

Add a new side effect or warning to the summary of product characteristics and package leaflet

Change the way a medicine is used, e.g. introduce restrictions or new measures to minimise risks

Suspend the medicine while more information is collected

Cancel the medicine’s marketing authorisation

5. Integrating patients' and healthcare professionals' voices

- **Patients and healthcare professionals are best placed to understand issues arising with medicines 'first hand'.**
- **They are consulted as experts and can share their views and insights during the evaluation of safety concerns in various ways.**

Patients and healthcare professionals are involved in the safety of medicines in many ways. Patients contribute by highlighting, for example, their experience of the disease, their needs and what risks they would consider acceptable in view of the expected benefits. Healthcare professionals may advise on the feasibility of measures proposed to minimise the risks associated with a medicine in clinical practice.

Did you know?

Patients and healthcare professionals review a number of EMA documents before they are published on the EMA website to ensure they are clear and understandable. They review, for example, public health communications when they include safety recommendations, medicine overviews, package leaflets and direct healthcare professional communications.

› They are full members of the PRAC.

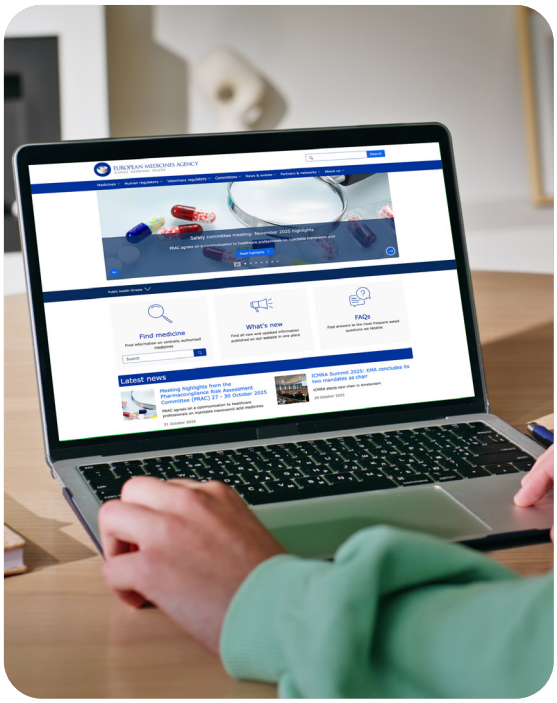
› They are involved as experts in scientific advisory groups or ad-hoc expert groups, and may be consulted during safety reviews.

› They can take part in public hearings, which EMA holds on a case-by-case basis before issuing major public health recommendations.

› They can send their input in writing for consideration during any ongoing review.

6. Providing a high level of transparency

- **EMA provides a high level of transparency about its safety assessments by publishing scientific committees' agendas, minutes, key meeting outcomes, assessment reports, public health communications and the clinical study reports submitted by medicine developers in their applications.**
- **This allows any researchers and members of the public to access the details of EMA's safety assessments and understand how conclusions were reached.**



The agendas and minutes of EMA's committees' meetings include information on the stage of each assessment.

The assessment reports of safety referrals are systematically published once the reviews have concluded.

In addition, EMA publishes the clinical study reports, including safety data, submitted by medicine developers in support of their marketing authorisation applications.

Did you know?

EMA implemented exceptional measures to maximise transparency before, during and after the evaluation of COVID-19 vaccines and treatments. The aim was to provide the public with as much information as possible about its assessments, including its safety monitoring processes. For instance, the full risk management plans of COVID-19 vaccines and medicines are published, together with clinical data supporting marketing authorisations. PSURs and their corresponding assessment reports are also published for COVID-19 vaccines. The exceptional transparency measures devised for the COVID-19 pandemic will apply for all future public health emergencies.

How to read and understand an assessment report?

EMA routinely publishes its assessment reports. These documents contain detailed information about the data assessed and the Agency's assessment and conclusions. For example, the assessment report on the review of risk of suicidal thoughts with finasteride and dutasteride medicines describes the wide range of data available and reviewed by the PRAC. These include an overview of suspected side effects reports from EudraVigilance, data from the medical literature and results from clinical trials and non-clinical studies. The report then presents and discusses the available evidence on the safety issues and the benefit-risk balance of each formulation, taking into account the condition to be treated and existing risk minimisation measures. The PRAC's conclusions and recommendations are then clearly stated with a timeline for implementation.

7. Communicating about medicines safety

- **An essential part of ensuring medicines are used safely is making sure they are prescribed and taken correctly.**
- **End users, such as healthcare professionals and patients, must have access to clear, updated information on their medicines: what side effects could be experienced, how to take the medicine safely, and what to consider before taking it.**
- **For this reason, communicating new safety information to the public, patients and healthcare professionals is a key public health responsibility.**

The SmPC and the package leaflet contain key information on how to use a medicine safely and effectively. These documents are regularly updated to reflect any new information on the medicine, including any new side effects. They are available on EMA's website in all official EU languages plus Icelandic and Norwegian.

Did you know?

Providing the public with factual, complete and up-to-date information about its regulatory activities is a priority for EMA. Each medicine assessed by EMA has a dedicated page describing what the medicine is, links to the package leaflet and SmPC in all EU languages, as well as information on any safety review, past or ongoing, potential shortages or risk of medication errors. You can find these pages on EMA's website.

When necessary, pharmaceutical companies or national competent authorities can deliver important new safety information directly to healthcare professionals via a direct healthcare professional communication (DHPC); when issued by companies, these communications are reviewed and approved by regulatory authorities. The objective is to alert them of the need to take certain actions or adapt their practices in relation to a specific medicine (e.g. recommendations to conduct specific tests before the patient receives the medicine). DHPCs are published on the EMA website and/or in national registers in EU Member States.

EMA's recommendations about the safety of medicines

EMA and the national competent authorities also publish information that helps patients and the public understand the scientific evidence and regulatory actions relating to a safety concern.

For important safety reviews, and all safety referrals, EMA communicates at different stages of the procedure to inform the public about its ongoing assessment. When these reviews are concluded, EMA issues public health communications with key recommendations for healthcare professionals and patients.

Did you know?

A key facts webpage on vaccine-preventable diseases provides information on the benefits of vaccination against serious infectious diseases (such as measles and HPV). It includes data visualisations and statistics that highlight that vaccine benefits have constantly outweighed their risks. A key facts page on common questions and misunderstandings around COVID-19 vaccines is also regularly updated when new concerns arise. The Agency also works closely with fact-checkers across the EU to correct misconceptions.

The main outcomes of the PRAC discussions are published on EMA's website each month after the committee's meetings.

The dangers of false narratives

The large-scale use of social media and artificial intelligence has given rise to an 'infodemic' where huge amounts of information are shared making it hard for people to tell whether the information can be trusted. Mis- and disinformation around the safety of vaccines and medicines impact negatively public health. It is important that all people have access to trusted information so that they can take informed decisions about their health and the medicines they take. To address harmful content circulating online, EMA monitors media and performs listening activities. Information to address concerns is published on the EMA website and communicated through other channels such as media interviews with EMA key experts and live-streamed press briefings when needed, and social media posts to raise awareness of key issues. Webinars and multi-stakeholder workshops are also regularly organised on key topics to increase engagement with the public.

EMA answers any questions from the public in their own language. You can submit your questions via AskEMA.

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