



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



From laboratory to patient: the journey of a centrally authorised medicine

An agency of the European Union



From laboratory to patient: the journey of a centrally authorised medicine



This booklet covers medicines for human use that are authorised via EMA through the EU [centralised procedure](#). It does not cover medicines authorised through national procedures (including the decentralised procedure and the mutual-recognition procedure) by national medicines authorities in the EU member states.

01

Initial research

Who does initial research on medicines?

The initial research on medicines is usually done by pharmaceutical and biotechnology companies – some big companies develop many medicines, while others are small companies who may only be researching one or two. Doctors and academics also perform research, and may get together to research either new medicines or new uses of old medicines.

Such researchers, either in public institutions or private companies, investigate vast numbers of substances for their potential as medicines each year. However, only a small proportion of the compounds investigated will ever be promising enough to progress to further development.



Did you know?

Developers of innovative treatments can discuss the scientific, legal and regulatory aspects of their medicine with EMA early in the development through the [Innovation Task force](#).

In [2017](#), 16 of 33 such requests for early discussions came from university-based or academic groups.

Can EMA influence which medicines should be developed?

EMA cannot sponsor medicines or fund research studies for a specific medicine, nor can it force companies to research particular medicines or treatments for a particular condition. Being a medicines regulator, EMA has to be neutral and cannot have a financial or other interest in any medicine being developed.

However, EMA can, and does, publicise areas where there is a need for new medicines – for example, new antibiotics – to encourage interested parties to research them. In addition, the EU legislation provides measures to encourage companies to develop [medicines for rare diseases](#). These include for example fee reductions when obtaining scientific advice from EMA.

Also provided by the EU legislation is a system of obligations, rewards and incentives to encourage manufacturers to research and develop [medicines for children](#).

02

Scientific advice



What is scientific advice?

Scientific advice is about advising medicine developers on the most appropriate way to generate robust evidence on a medicine's benefits and risks.

For a medicine to be authorised, medicine developers have to demonstrate that it is effective, safe and of good quality.

During a medicine's development, a developer can ask guidance and direction from EMA on the best methods and study designs to generate robust information on how well a medicine works and how safe it is.

Then, when applying for a marketing authorisation, the developer submits all the data generated on the medicine to EMA. The Agency assesses this information and determines whether or not the medicine is safe and beneficial to patients.

Scientific advice:

- ▶ is not a pre-assessment of the benefits and risks of a medicine
- ▶ does not guarantee that a medicine will receive marketing authorisation

Why does EMA provide scientific advice?

EMA provides scientific advice to support the timely and sound development of high-quality, effective and safe medicines, for the benefit of patients.

EMA provides scientific advice because:

- ▶ Better designed studies are more likely to generate robust and complete data to show whether or not a medicine works and is safe. The sooner it can be shown that a new medicine works and is safe, the sooner it can be made available to patients.
- ▶ Providing advice means that patients are not deprived of beneficial medicines simply because poorly designed trials failed to demonstrate that the medicine works and is safe.
- ▶ Better study designs avoid patients taking part in studies that will not produce useful evidence.



Did you know?

Two out of three development programmes submitted for scientific advice were considered not suitable for a future assessment of the medicine's benefits and risks, according to an analysis done in 2015. Following scientific advice, 63% of these trials were modified to include a better way to assess the medicine's effectiveness or a more appropriate comparator.

- ▶ More effective development means that the limited scientific resources available are used in the best way for the benefit of patients.

Scientific advice is particularly helpful for medicine developers who may have limited knowledge about medicine regulation, such as some academic groups or micro, small and medium sized enterprises (SMEs). Scientific advice is also relevant for innovative therapies for which scientific guidance has not been developed yet or is limited.



Did you know?

For medicines that target conditions for which there are no satisfactory treatments and that have shown promising initial results, EMA provides extra regulatory support, including scientific advice at key development milestones, through an initiative called [PRIME](#) (Priority Medicines).

Why are medicine regulators the ones giving scientific advice?

Medicine regulators have a unique knowledge and experience of how medicines should be developed gained from years of assessment of medicines. It is their duty to share this knowledge and promote a more effective medicine development for the benefit of patients.

Why do we need scientific advice when we have guidelines?

Guidelines provide general advice on the best methods and study designs to be used when developing certain types of medicines, such as vaccines or antibiotics or medicines for certain diseases such as cancer. However, guidelines only address general situations; they cannot cover new

and innovative approaches coming along. In addition, their development takes time.

To complement guidelines, specific scientific advice is therefore provided on request for the development of individual medicines. The advice provided builds on existing scientific guidelines but is tailored to the specific medicine and the group of patients intended to be treated.

The development and update of guidelines in turn incorporate knowledge and experience gained through scientific advice and experience with the assessment of medicines, in particular with innovative medicines. For example when a novel endpoint is recommended in a number of recent scientific advice requests, the relevant guidelines are revised to include reference to the new endpoint. In this way knowledge gained during scientific advice is shared with the wider scientific community.

How is scientific advice paid for?

Applicants pay an administrative fee for scientific advice. The provision of scientific advice by EMA is required by the EU legislation which also defines the administrative fees to be charged to the applicant.

Reductions apply for certain types of medicines and applicants: there is a 75% fee reduction for medicines for rare diseases, known as orphan medicines; micro, small and medium sized companies (SMEs) have a 90% fee reduction.



Did you know?

In 2017, about a third of the 630 scientific advice finalised were provided to SMEs and a quarter related to orphan medicines. Thanks to fee reductions SMEs, who are the originators of a great number of innovative medicines, can access scientific advice during the development of their medicines.

What happens during scientific advice?

During scientific advice, experts respond to specific scientific questions related to the development of a particular medicine.

The developer of a medicine presents the way it plans to develop its medicine and identifies questions and possible solutions. EMA then gives advice on the developer's proposals. During scientific advice EMA does not evaluate the results of the studies and in no way concludes on whether the benefits of the medicine outweigh the risks.

What kind of questions are addressed during scientific advice?

Questions during scientific advice can relate to:

- ▶ quality aspects (manufacturing, chemical, pharmaceutical and biological testing of the medicine),
- ▶ non-clinical aspects (toxicological and pharmacological tests designed to show the activity of the medicine in the laboratory),
- ▶ clinical aspects (appropriateness of studies in patients or healthy volunteers, selection of endpoints, i.e. how best to measure effects in a

study, post-authorisation activities including risk-management plans),

- ▶ methodological issues (statistical tests to use, data analysis, modelling and simulation).

Who's involved in scientific advice?

Dozens of experts from a range of disciplines are involved in responding to the questions asked.

At EMA, the Committee for Medicinal Products for Human Use (CHMP) is responsible for assessing marketing authorisation applications. One of its roles is also to support research and development by providing scientific advice. This task is passed by the CHMP to EMA's Scientific Advice Working Party (SAWP). The answers to the questions asked by the developer are elaborated by the SAWP, and then the final advice is formally adopted and issued by the CHMP.

The SAWP has up to 36 members, who are experts from medicine regulators around the EU, from academia, and from EMA's committees for orphan medicines, advanced therapies, medicines for children and pharmacovigilance and risk assessment. About a fifth of its members are also CHMP members. This overlap allows the longer-term knowledge and expertise gathered on a medicine during scientific advice to be used during the later assessment of the application for marketing authorisation by the CHMP.

Examples of questions addressed during scientific advice

- ▶ Are the patients to be included in a study sufficiently representative of the population for whom the medicine is intended?
- ▶ Are the planned measures to assess the benefits of a medicine valid and relevant?
- ▶ Is the proposed plan to analyse results appropriate?
- ▶ Does the study last long enough and include enough patients to provide the necessary data for the benefit-risk assessment?
- ▶ Is the medicine being compared with an appropriate alternative?
- ▶ Are the plans to follow the long-term safety of the product appropriately designed?

The SAWP members' fields of expertise include non-clinical safety, pharmacokinetics, methodology and statistics, gene and cell therapy, as well as those therapeutic areas where scientific advice is often requested, such as cardiology, oncology, diabetes, neurodegenerative disorders and infectious diseases.

Are patients involved in scientific advice?

Patients are often involved in scientific advice. They are invited to share their real-life perspective and experience in relation to a particular medicine in their disease area. This can help medicine developers and regulators understand better what will work for that patient group and what they consider important.



Did you know?

In 2017, one in five scientific advice procedures involved patients and the SAWP members considered that in almost every case (93%) patients provided added value to the scientific advice. In more than one in four cases, the scientific advice recommended that the development plan be modified to reflect patient advice.

The questions raised during scientific advice and those addressed during the assessment of a medicine are fundamentally different: scientific advice addresses questions related to the most appropriate way to test and study a medicine; during the assessment of a medicine, the CHMP looks at the results of these studies and, based on these, determines whether the benefits of the medicine outweigh its risks and therefore can be authorised for use in patients.

Giving scientific advice should make the evaluation of a medicine easier and quicker because the evidence to be generated is likely to be more robust, appropriate and complete. But it doesn't affect the regulator's stringent assessment of safety and efficacy, nor means that the medicine will automatically pass that assessment. Better evidence means that it is easier to conclude on the benefit-risk balance but does not necessarily mean that the medicine will be authorised – it might show more clearly that a medicine is harmful or not effective. Medicine developers that have had and followed scientific advice may therefore still not get approval for marketing. And conversely, medicine developers who did not follow the advice may still get approval for marketing.

While the scopes of these processes are distinct, the longer-term knowledge and expertise about the medicine that is gathered during scientific advice is useful in understanding more about the medicine and will be of use during the assessment of the application for marketing.

Does giving scientific advice influence EMA's assessment of the medicine?

Scientific advice and the assessment of the benefits and risks of a medicine are different by nature: while scientific advice looks at how a medicine should be tested in studies to generate robust evidence, the assessment at the time of marketing authorisation looks at the evidence generated to determine whether the medicine's benefits outweigh its risks, regardless of any advice previously given.



Did you know?

Complying with scientific advice increases the chances of receiving marketing authorisation but it does not guarantee it. An analysis done in 2015 showed that [15% of companies](#) who complied with scientific advice provided by EMA received a negative opinion at the time of applying for marketing authorisation. This compares with 25% overall.

In both processes, all the decisions taken are collegial and based on extensive discussions and consultations. No single SAWP or CHMP member can force a decision to go a particular way – it has to be agreed by a majority.

What does EMA publish on the outcomes of scientific advice?

During the development and assessment phases, the detailed advice given to a company is not made public. This is because disclosing information at this stage may undermine research and development efforts and so discourage research in new medicines.

However, information is made available as soon as a medicine obtains marketing authorisation.

In June 2018, EMA started publishing more detailed information on the scientific advice provided during the medicine development in the assessment report of medicines that received EMA PRIME support (i.e. medicines that target conditions for which there are no satisfactory treatments and that have shown promising initial results), and this initiative has been rolled out for all medicines with assessment reports finalised after 1 January 2019.

In particular, a summary of the developer's questions is included at the beginning of the assessment report and key elements of the advice provided can be found in the relevant sections of the report. In addition, information on the company's compliance with this advice is included.

Medicines' assessment reports are published on the EMA website as soon as the European Commission has made a final decision on marketing authorisation.

In addition, the full advice can be made available upon [request](#).

Scientific advice is one of the main sources for updating EMA scientific guidelines on medicine development. Disease-specific guidelines are regularly updated to incorporate knowledge and experience gained through scientific advice and

through the assessment of medicines. In this way the outcome of scientific advice becomes available to all.

What are the measures to safeguard experts' independence during scientific advice?

EMA checks every expert's declaration of interests prior to their involvement in scientific advice and restrictions are applied if certain interests are considered to potentially impact impartiality.

[EMA policies on handling competing interests](#) aim to restrict the involvement of members, experts and staff with possible competing interests in the Agency's work while maintaining EMA's ability to access the best available expertise.

Members of the SAWP and any other experts involved submit a declaration of interests prior to any involvement in EMA activities.

The Agency assigns each declaration of interests a level of risk based on whether the expert has any direct or indirect interests (financial or other) that could affect their impartiality. Before the start of a new scientific advice procedure, EMA checks the declaration of interests of every member or expert and if a competing interest is identified, the member or expert will have restricted rights.

Restrictions include no participation in the discussion on a particular topic or exclusion from voting on the topic

Scientific advice, step by step

Two experts, supported by independent teams, conduct separate assessments; additional experts and stakeholders are often consulted.



03

Evaluation of medicines



What happens before a medicine assessment starts?

A few months before the assessment starts, EMA provides guidance to medicine developers to ensure that their applications for marketing authorisation comply with legal and regulatory requirements to avoid unnecessary delays.

To obtain marketing authorisation, medicine developers need to submit specific data on their medicine. EMA then carries out a thorough assessment of these data to decide whether or not the medicine is safe, effective and of good quality and is therefore suitable for use in patients.

EMA provides companies with [guidance](#) on the type of information that needs to be included in a marketing authorisation application.

About 6 to 7 months before submitting an application, medicine developers can meet with EMA to ensure that their application complies with legal and regulatory requirements. This means that the application includes all the different aspects required by [EU legislation](#) and needed to demonstrate that a medicine works as intended.

These meetings involve a range of EMA staff responsible for various areas such as quality, safety and efficacy, risk management or paediatric aspects, who will follow the application throughout the assessment.

EMA encourages developers to request such pre-submission meetings as they aim to increase the quality of the applications and avoid unnecessary delays.

Applicants pay fees upfront

European legislation requires that pharmaceutical companies contribute to the costs of regulation of medicines. As the companies will earn revenues from the sales of medicines, it is fair that they should bear most of the financial costs of regulating them. This means that EU taxpayers do not have to support all the costs of ensuring the safety and effectiveness of medicines.

Companies pay an administrative fee upfront before EMA assessment starts. The administrative fee applicable for each procedure is defined by EU legislation.

What information needs to be submitted in a marketing authorisation application?

The data submitted by medicine developers in their application for marketing authorisation must comply with EU legislation and include information on:

- ▶ the disease concerned, including the number of patients affected and the risk factors for

developing the disease, how patients are being treated and any groups of patients with unmet medical needs;

- ▶ the quality of the medicine including its chemical and physical properties, such as its stability, its purity and biological activity;
- ▶ compliance with international requirements for laboratory testing, medicine manufacture and conduct of clinical trials ([‘good laboratory practice’](#), [‘good clinical practice’](#) and [‘good manufacturing practice’](#));
- ▶ the medicine’s mechanism of action, as investigated in laboratory studies;
- ▶ how the medicine is distributed in, and eliminated by, the body;
- ▶ the benefits observed in the patient group at whom the medicine is aimed;
- ▶ the medicine’s side effects observed in patients, including in special populations such as children or the elderly;
- ▶ the way risks will be managed and monitored once the medicine is authorised;
- ▶ what information is intended to be gathered from follow-up studies after authorisation.

Information about any possible (known or potential) safety concerns with the medicine, the way risks will be managed and monitored once the medicine is authorised and what information is intended to be gathered from follow-up studies after authorisation is described in detail in a document called the ‘risk management plan’ (RMP). The RMP is evaluated by EMA’s safety committee, [PRAC](#), to ensure its suitability.

The information to be provided to patients and healthcare professionals (i.e. the summary of product characteristics or SmPC, labelling and package leaflet) must also be supplied by the developer and is reviewed and agreed by the CHMP.

Where do data on the medicine come from?

Most of the evidence collected on a medicine during its development comes from studies funded by the medicine developer. Any other data available on the medicine (for example from existing studies in the medical literature) must also be submitted by the applicant and will be assessed.

Studies that support the marketing authorisation of a medicine have to comply with strict rules and are conducted in a regulated setting. International standards, called [good clinical practice](#), apply to the study design, recording and reporting to ensure that studies are scientifically sound and conducted in an ethical manner. The study design and the type of evidence needed to determine the benefits and risks of a medicine are defined by EU law and must be adhered to by medicine developers. Inspections can be requested by EMA to verify compliance with these standards.

EMA supports the conduct of high-quality studies through initiatives such as [Enpr-EMA](#) and [ENCePP](#) which bring together expertise from independent academic centres across Europe. Thanks to these initiatives additional sources of evidence can complement the evidence provided by medicine developers, in particular in the context of the continuous safety monitoring of a medicine after its authorisation.

What is the key principle underpinning a medicine's assessment?

The balance between the benefits and risks of a medicine is the key principle guiding a medicine's assessment. A medicine can only be authorised if its benefits outweigh the risks.

All medicines have benefits as well as risks. When assessing the evidence gathered on a medicine, EMA determines whether the benefits of the medicine outweigh its risks in the group of patients for whom the medicine is intended. This is the condition for a medicine to be authorised and made available to patients.

In addition, since at the time of the initial authorisation not everything is known about a medicine's safety, the way [risks will be minimised](#), managed and monitored once the medicine is more widely used is also an integral part of the assessment and is agreed at the time of authorisation. Managing risks of medicines once they are authorised is part of the process called pharmacovigilance, which is key to the availability of safe, effective medicines.

While the authorisation of a medicine is based on an overall positive balance between the benefits and risks at population level, each patient is different and before a medicine is used, doctors and their patient should judge whether this is the right treatment option for them based on the information available on the medicine and on the patient's specific situation.

Who is involved in the assessment of marketing authorisation applications?

A committee of experts, each supported by a team of assessors, evaluates the applications.

EMA's [Committee for Medicinal Products for Human Use](#) (CHMP) assesses applications submitted by medicine developers and recommends whether or not a medicine should be granted marketing authorisation. The committee is composed of one member and an alternate from each EU Member State, as well as from Iceland and Norway. It also has up to five EU experts in relevant fields such as statistics and quality of medicines, who are nominated by the European Commission.

When conducting an assessment, the CHMP members are each supported by a team of assessors in the national agencies, who have a range of expertise and will look at the various aspects of the medicine, such as its safety, quality and the way it works.

The CHMP also works with other EMA committees during the assessment. These include: the [PRAC](#) for aspects related to the medicine's safety and risk management; the [PDCO](#) for aspects related to the medicine's use in children; the [COMP](#) for orphan-designated medicines; and the [CAT](#) for advanced therapy medicines (gene therapy, tissue engineering and cell-based medicines).



Did you know?

In some cases, for example when a medicine is intended to treat a [life-threatening disease](#) for which there is no satisfactory treatment or if the disease targeted is very rare, EMA can recommend marketing authorisation on the basis of less complete or limited evidence on the medicine, provided that further data are provided at a later stage.

Even in these cases, it must be demonstrated that the benefits of the medicine outweigh the risks.

How does the CHMP work?

Peer review and collegial decisions are at the heart of the CHMP assessments.

For each application for a new medicine (excluding generics¹), two committee members – known as rapporteur and co-rapporteur² – from different countries are [appointed](#) to lead the assessment. They are appointed according to objective criteria to make best use of the available expertise in the EU.

The role of the rapporteur and co-rapporteur is to conduct the scientific evaluation of the medicine independently from each other. They each form an assessment team with assessors from their national agency and sometimes from other national agencies.

In their assessment reports, each team summarises the data from the application, presents its judgments of the medicine's effects and its views on any uncertainties and limitations of the data. They also identify questions that will have to be answered by the applicant. The two separate assessments take into account regulatory requirements, relevant scientific guidelines and experience in the evaluation of similar medicines.

In addition to the rapporteur and co-rapporteur, the CHMP also appoints one or more [peer-reviewers](#) from amongst the CHMP members. Their role is to look at the way the two assessments are performed and ensure that the scientific argumentation is sound, clear and robust.

All the CHMP members, in discussion with colleagues and experts in their national agencies, also contribute actively to the evaluation process. They review the assessments made by the rapporteurs, provide comments and identify additional questions to be addressed by the applicant. The initial assessment and the comments received from peer reviewers and other committee members are then discussed during a plenary meeting of the CHMP.

As a result of the discussions and as new information becomes available during the assessment, either from additional experts or from clarifications provided by the applicant, the scientific arguments are refined so that a final opinion, representing the committee's analysis and opinion on the data, is developed. This can sometimes mean, for example, that the committee's view on the benefit and risk of the medicine may change during the evaluation and diverge from the initial assessments performed by the Rapporteurs.

The final CHMP opinion is reached by a formal vote. Ideally, the CHMP will come to a consensus opinion and unanimously recommend either the approval or refusal of the marketing authorisation; such a consensus opinion is reached in 90% of cases. However, when a final opinion by consensus cannot be reached, the committee's final opinion will represent the majority view.

Can the CHMP request more information during the evaluation?

During the medicine evaluation, experts will raise a number of questions that will have to be answered by the applicant within an agreed timeframe.

During the evaluation, the CHMP raises questions on the evidence provided in the application and asks the applicant to provide clarifications or additional analyses to address these questions. Responses have to be provided within an agreed timeframe.

The CHMP can raise objections or concerns which can relate to any aspect of the medicine. If unresolved, major objections preclude marketing authorisation.

Major objections can relate for example to the way the medicine was studied, the way it is manufactured, or to the effects seen in patients such

1 For generics, only a rapporteur is appointed and there is generally no peer-reviewer

2 For advanced therapy medicines, two members of EMA's Committee for Advanced Therapies (CAT) are appointed as rapporteur and co-rapporteur and will lead the assessment. They work with two CHMP coordinators throughout the assessment.

as the magnitude of the benefits or the seriousness of the side effects.

What additional expertise can the CHMP rely on?

Experts with specialised scientific knowledge or clinical experience are often consulted during the evaluation to enrich the scientific discussion.

Additional experts can be called upon by the CHMP at any time during the assessment to provide advice on specific aspects raised during the evaluation.

The CHMP can request the support of and ask specific questions to its working parties which have expertise in a particular field such as biostatistics, or a therapeutic area such as cancer. The members of EMA's [working parties](#) have an in-depth knowledge of the latest scientific developments in their field of expertise.

The committee can also call upon external experts through its [scientific advisory groups](#) or ad-hoc expert groups. These groups, which include healthcare professionals and patients, are asked to respond to specific questions on the potential use and value of the medicine in clinical practice.



Did you know?

EMA regularly exchanges views on ongoing medicines' assessments with other regulatory agencies such as the US FDA, Health Canada and the Japanese regulatory authorities. These [discussions](#) can relate for example to clinical and statistical issues, strategies to manage the risks and studies to be conducted after authorisation.

How are patients and healthcare professionals involved?

Patients and healthcare professionals are involved as experts and provide their views on whether the medicine can address their needs.

Patients and healthcare professionals are invited to take part as experts in scientific advisory groups or ad-hoc expert groups. Patients contribute to discussions 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 groups of patients with unmet needs based on their clinical experience or the feasibility of measures proposed to minimise the risks associated with a medicine in clinical practice.

In addition, since 2014 individual patients can be invited to CHMP plenary meetings in person or via teleconference or consulted in writing (see outcome of pilot [here](#)).



Did you know?

External experts are consulted in about a quarter of the assessments of new medicines (excluding generics).



Did you know?

In 2017, patients and healthcare professionals were involved in the assessment of about one in four new medicines (excluding generics).

What are the measures to safeguard experts' independence?

Independence is safeguarded by a high level of transparency and the application of restrictions if certain interests are considered to potentially impact impartiality.

[EMA policies on handling competing interests](#) have been put in place to restrict the involvement of members, experts and staff with possible competing interests in the Agency's work while maintaining EMA's ability to access the best available expertise.

Members and experts of committees, working parties and scientific advisory groups or ad hoc expert groups submit a declaration of interests prior to any involvement in EMA activities.

The Agency assigns each declaration of interests a level of risk based on whether the expert has any direct or indirect interests (financial or other) that could affect their impartiality. Prior to involvement in a specific EMA activity, EMA checks the declaration of interests. If a competing interest is identified, the member or expert will have restricted rights.

Restrictions include no participation in the discussion on a particular topic or exclusion from voting on the topic. Members' and experts' declarations of interests and information on restrictions applied during scientific committee meetings are publicly available in the [meeting minutes](#).

Rules for experts who are members of scientific committees are stricter than for those participating in advisory bodies and ad-hoc expert groups. This way EMA can call on the best expertise in the context of advisory groups in order to gather the most relevant and complete information, and apply stricter rules when it comes to decision making.

Similarly, requirements for chairs and members in a lead role, e.g. rapporteurs, are stricter than requirements for other committee members.

In addition, members of the committees, working parties, scientific advisory groups (and experts attending these meetings), and EMA staff have to abide by the principles set out in the [EMA Code of Conduct](#).

What information is publicly available during the evaluation of a new medicine and once a decision has been made?

EMA has established a high level of transparency about its medicine assessment with the publication of meeting agendas and minutes, reports describing how the medicine was assessed and the clinical study results submitted by medicine developers in their applications.

The list of new medicines that are being evaluated by the CHMP is available on the EMA website and [updated](#) every month.

EMA also [publishes](#) the agendas and minutes of all its committees' meetings, where information on the stage of the assessment can be found.

Once a decision has been taken on the authorisation or refusal of a marketing authorisation, EMA publishes a comprehensive set of documents called the [European public assessment report \(EPAR\)](#). This includes the public CHMP assessment report, which describes in detail the data assessed and why



Did you know?

The [declarations of interests](#) of all the experts, including patients and healthcare professionals, who take part in EMA activities are published on the EMA website. EMA also publishes [annual reports](#) on its independence which include facts and figures on declared interests and resulting restrictions.

the CHMP recommended authorising or refusing authorisation.

For applications received after 1 January 2015, EMA also publishes the clinical study results submitted by medicine developers in support of their marketing authorisation applications. For older applications, clinical study results can be obtained through [a request for access to the document](#).

Detailed information on what EMA publishes and when on human medicines from the early development to the initial evaluation and the post-authorisation changes can be found in the [Guide to information on human medicines evaluated by EMA](#).



Did you know?

As of October 2018, EMA had published the clinical study results submitted by medicine developers in their applications for over 100 medicines recently assessed by EMA. These are available for public scrutiny on EMA's dedicated [website](#) on clinical data.

The evaluation of medicines, step by step

The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is the time spent by EMA experts to evaluate the evidence provided by the applicant in support of a marketing authorisation application. This time is interrupted by one or two 'clock-stops' during which the applicant prepares the answers to any questions raised by the CHMP. The maximum duration of a clock-stop depends on how long the applicant thinks it will take to respond but must be agreed by the CHMP. The first clock-stop usually lasts 3 to 6 months and the second one 1 to 3 months. Overall, the assessment of a new medicine usually lasts around a year.



Did you know?

The assessment time may be reduced to 150 days instead of 210 days, upon request from the medicine developer ('accelerated assessment'), for medicines considered of major interest for public health, for example those that target a condition for which there is no treatment option.

Initial assessment and list of questions

The rapporteur's and co-rapporteur's³ teams assess the evidence provided on the medicine and independently prepare their assessment reports, where they highlight any issues or concerns to be addressed by the applicant.

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At this stage the rapporteurs may recommend an inspection of the medicine's manufacturing site, of the site of a non-clinical or clinical study or of the pharmacovigilance processes involved in the application. If this is endorsed by the committee, the inspection will be conducted by inspectors of the EU national agencies.

In parallel, two members of EMA's Pharmacovigilance Risk Assessment Committee (PRAC) are appointed as rapporteur and co-rapporteur to assess the company's proposed risk management plan (RMP), which describes the way important risks will be minimised or managed if the medicine is authorised and how more information will be obtained about the medicine's risks and uncertainties (e.g. through post-authorisation safety studies). This assessment is reviewed by all PRAC members.

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Based on their initial evaluation, the CHMP rapporteur and co-rapporteur share their respective assessment reports with all the CHMP and PRAC members, together with a list of questions to be addressed by the applicant. The assessment of the risk management plan, which also contains questions for the applicant, is also shared with the CHMP and PRAC members.

04

The peer-reviewers appointed by the CHMP also review the rapporteurs' assessment reports and send their comments. Peer-reviewers are CHMP members who are appointed to look specifically at the way the two assessments were performed and ensure that the scientific argumentation is sound, clear and robust.

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Comments from all parties, i.e. the rapporteur and co-rapporteur teams, the other CHMP members⁴, the PRAC members, and the CHMP peer-reviewers are discussed during a 'peer-review' meeting. This is a key point in the evaluation of a medicine where the initial viewpoints are integrated and consolidated. This will lead to a single assessment report which will comprise an overview of the assessment and a list of concerns and objections.

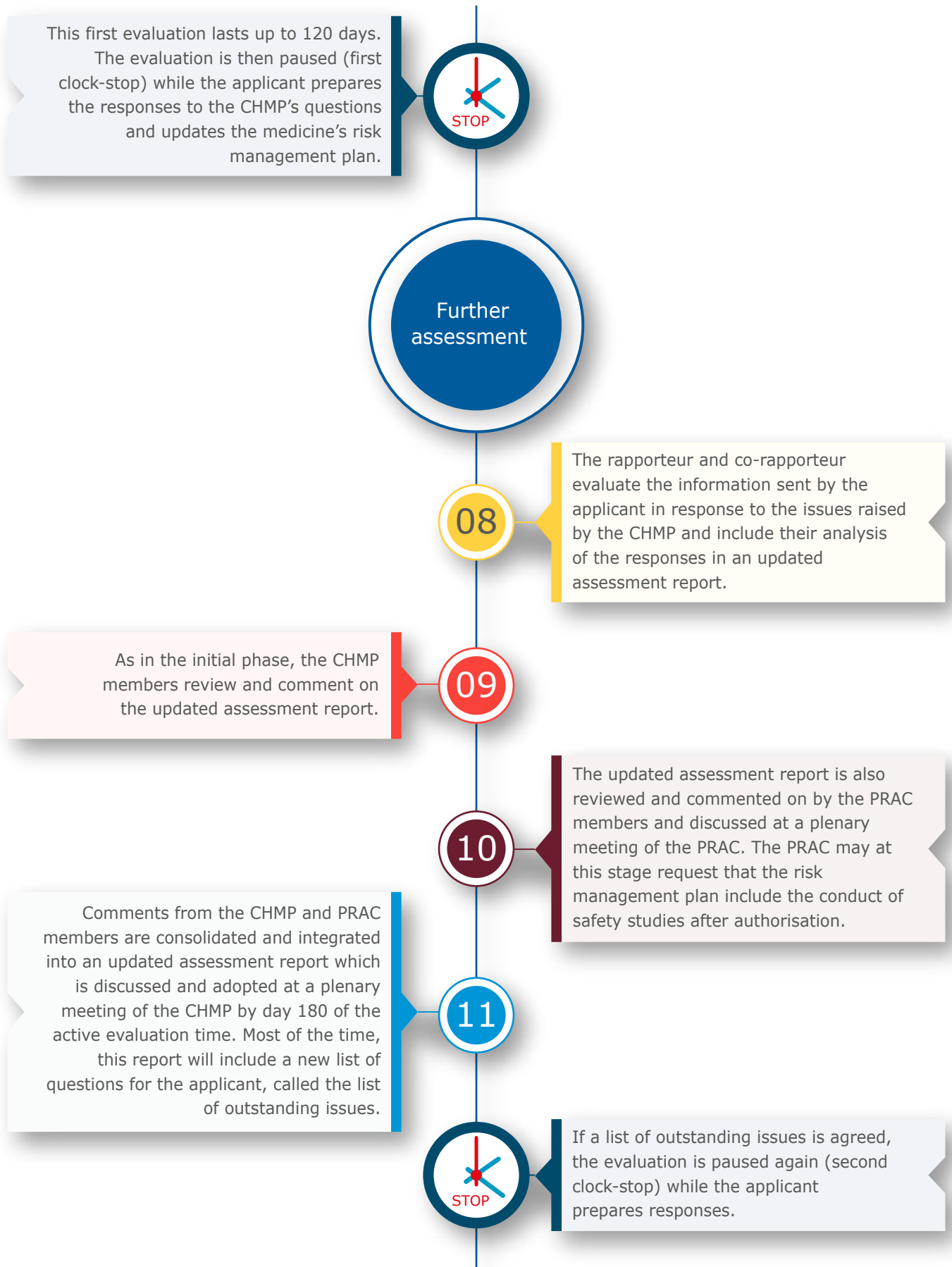
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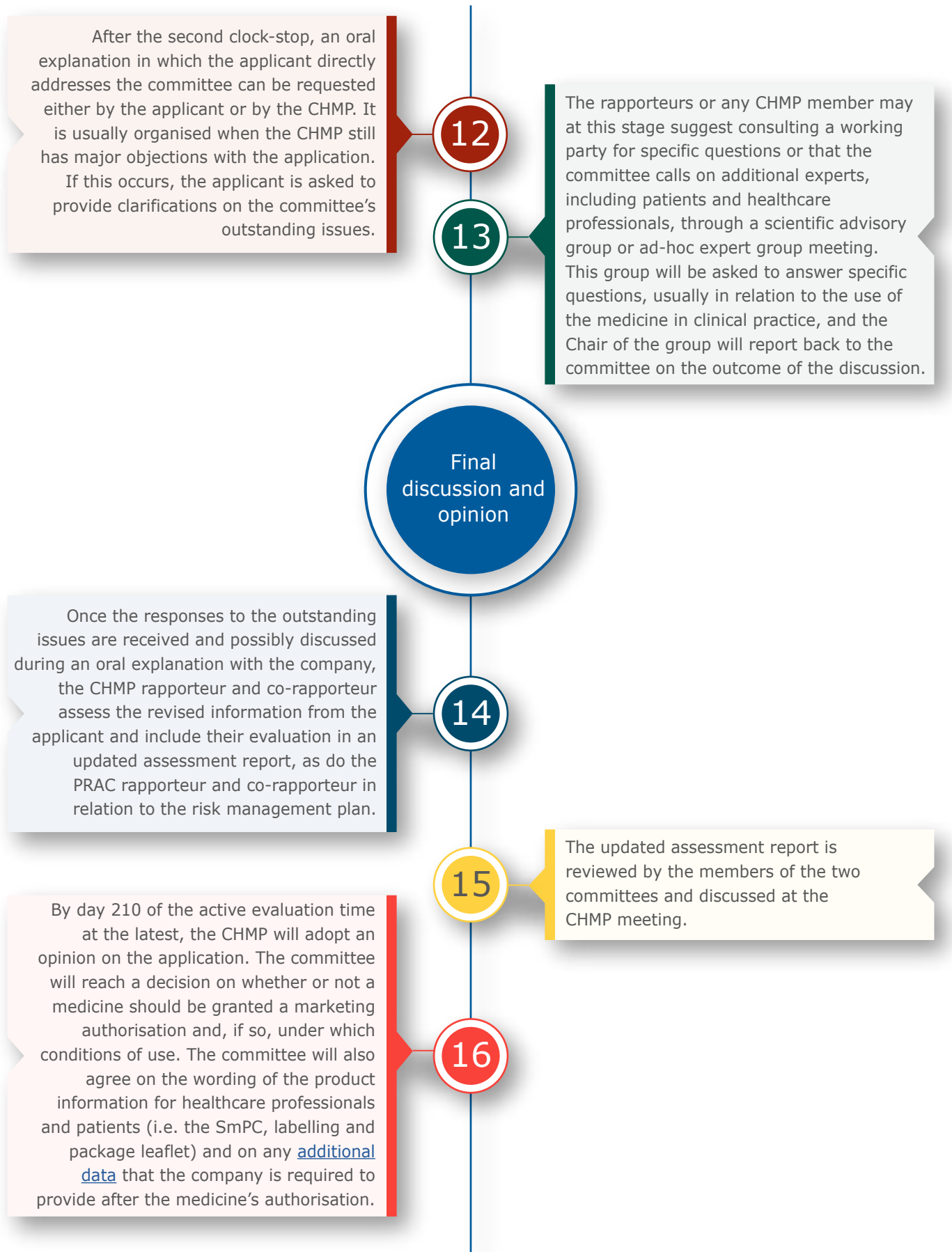
The single assessment report is then discussed at the CHMP plenary meeting. As a result of these discussions, some differing views and issues may be resolved and new concerns may be raised and the report is updated accordingly. Following these discussions, the CHMP adopts the report, which represents a common position in light of the evidence and discussions to date and includes a list of questions to be addressed by the applicant.

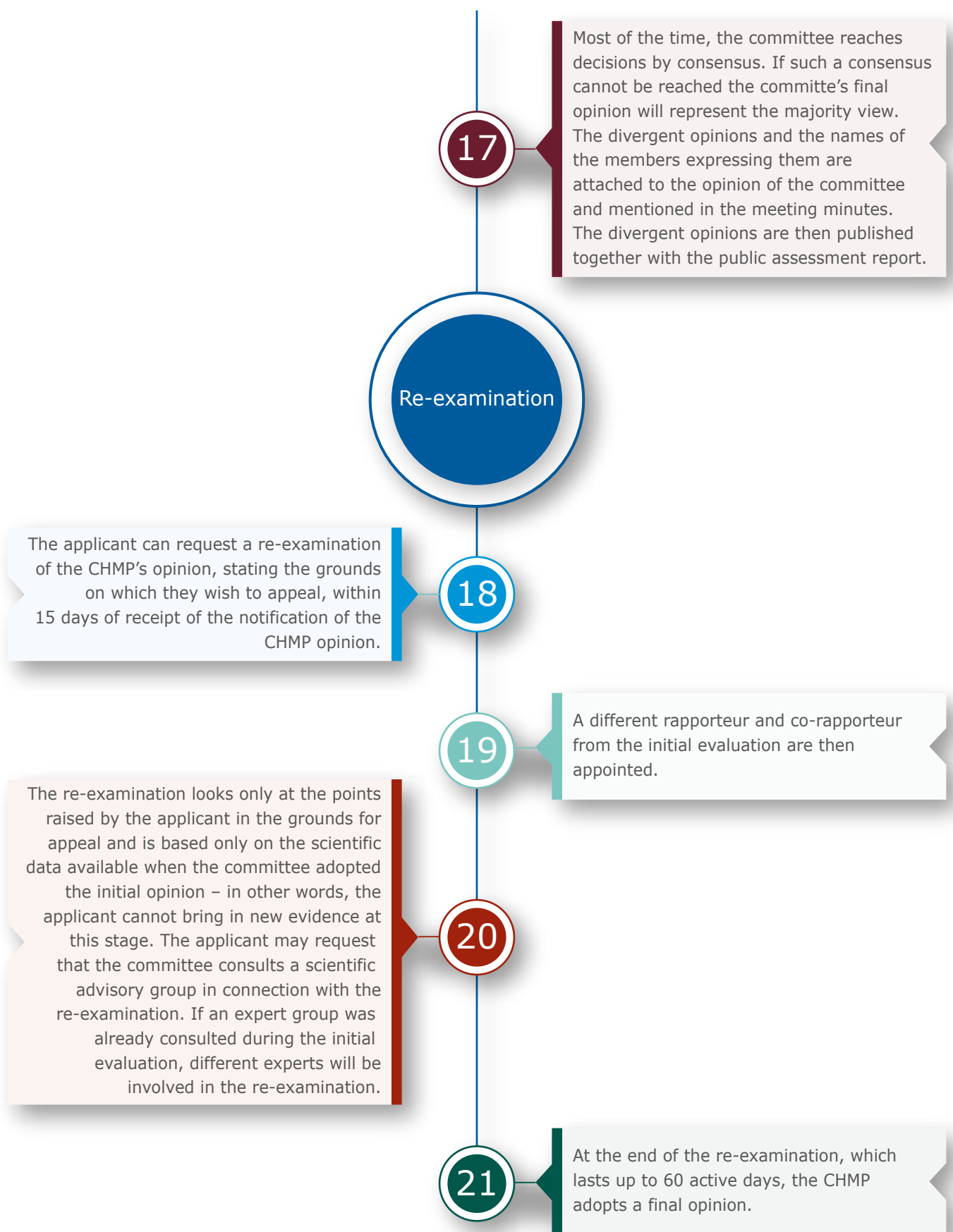
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³ In the case of an advanced therapy medicine the rapporteurs will be appointed amongst EMA's Committee for Advanced Therapies (CAT) members; each of them will work with a CHMP coordinator.

⁴ CAT members are also involved in case of advanced therapies.







04

Commission decision



EMA is a scientific body with the expertise required to assess the benefits and risks of medicines. However, under EU law it has no authority to actually permit marketing in the different EU countries. The role of EMA is to make a recommendation to the European Commission which then takes a final legally binding decision on whether the medicine can be marketed in the EU. This decision is issued within 67 days of receipt of EMA's recommendation. The Commission is thus the authorising body for all centrally-authorized products.

Commission decisions are published in the [Community Register](#) of medicinal products for human use.



Did you know?

While the majority of new, innovative medicines are evaluated by EMA and authorised by the European Commission in order to be marketed in the EU, most generic medicines and medicines available without a prescription are assessed and authorised at national level in the EU. In addition, many older medicines available today were authorised at national level because they were marketed before EMA was created. Most Member States have [registers of nationally authorised medicines](#).

05

Discussion at national level on access and pricing



Medicines that are granted a marketing authorisation by the European Commission can be marketed throughout the EU.

However, before a medicine is made available to patients in a particular EU country, decisions about pricing and reimbursement take place at national and regional level in the context of the national health system of the country.

EMA has no role in decisions on pricing and reimbursement. However, to facilitate these processes, the Agency collaborates with [health technology assessment \(HTA\) bodies](#), which assess the relative effectiveness of the new medicine in comparison with existing medicines, and EU healthcare payers, who look at the medicine's cost-effectiveness, its impact on healthcare budgets and the seriousness of the disease.

The aim of this collaboration is to find ways for developers to address the data needs of medicines regulators as well as those of HTA bodies and EU healthcare payers during the development of a medicine, rather than generating new data after its authorisation. If one set of evidence addressing the needs of all these groups can be generated early during the development of a medicine, it should make decisions on pricing and reimbursement at national level quicker and easier. To achieve this, EMA and the [European Network for Health Technology Assessment \(EUnetHTA\)](#) offer medicine developers the possibility to receive [simultaneous, coordinated advice](#) on their development plans.

Patients' representatives are involved in these consultations on a routine basis so that their views and experiences can be incorporated into the discussions.



Did you know?

In [2017](#) simultaneous advice from EMA and HTA bodies were provided upon request during the development of 27 medicines. Patients were involved in two thirds of these cases.



06

What happens once a medicine is marketed

Once a medicine has been authorised for use in the EU, EMA and the EU Member States constantly monitor its safety and take action if new information indicates that the medicine is no longer as safe and effective as previously thought.

This includes a number of routine activities ranging from: assessing the way risks associated with a medicine will be managed and monitored once it is authorised; continuously monitoring suspected side effects reported by patients and healthcare professionals, identified in new clinical studies or reported in scientific publications; regularly assessing reports submitted by the company holding the marketing authorisation on the benefit-risk balance of a medicine in real life; and assessing the design and results of post-authorisation safety studies which were required at the time of authorisation.

EMA can also carry out a review of a medicine or a class of medicines upon request of a Member State or the European Commission. These are called EU referral procedures; they are usually triggered by concerns in relation to a medicine's safety, the effectiveness of risk minimisation measures or the benefit-risk balance of the medicine.

EMA has a dedicated committee responsible for assessing and monitoring the safety of medicines, the Pharmacovigilance Risk Assessment Committee (PRAC). This ensures that EMA and the EU Member States can move very quickly once an issue is detected and take any necessary action, such as amending the information available to patients and healthcare professionals, restricting use or

suspending a medicine, in a timely manner in order to protect patients.

More information on pharmacovigilance activities can be found [here](#).

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From laboratory to patient: the journey of a centrally authorised medicine.
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