EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Guide to information on human medicines evaluated by EMA

What the Agency publishes and when

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1. Introduction

The European Medicines Agency (EMA) publishes information on human medicinal products at various stages of their life cycles, from the early developmental stages through to EMA's evaluation of authorisation applications, post-authorisation changes, safety reviews and withdrawals of authorisation.

This guide describes the different types of information the Agency currently publishes for both centrally and non-centrally authorised medicines, as well as publication times and location on EMA's website. It aims to help stakeholders know what kind of information to expect on medicines undergoing evaluations and other regulatory procedures.

The same information described in this document is presented in a tabulated format in the Annex.

Whilst reflecting the current practice, the guide is not intended to provide an exhaustive list of EMA publications, and EMA may at its discretion publish additional documents as appropriate. Other non-confidential documents held by EMA which are not published may be provided to stakeholders upon request.

2. Applications for centralised marketing authorisation

2.1. Medicines under initial evaluation

A **list of new medicines that are under evaluation** for a centralised marketing authorisation by EMA's Committee for Medicinal Products for Human Use (CHMP) or the Committee for Advanced Therapies (CAT) is published each month on EMA's medicines under evaluation page. It lists the international non-proprietary name (INN) and therapeutic area(s) of each medicine.

For orphan medicines, information on designated orphan medicinal products under evaluation for a centralised marketing authorisation, including the name of the applicant, is also available in the **monthly meeting reports** of the Committee for Orphan Medicinal Products (COMP) published on the COMP page (see Section 6.1).

2.2. Positive opinions

The CHMP gives opinions on centralised marketing authorisations applications at its monthly plenary meetings, which usually run from a Monday to a Thursday. If the CHMP gives a positive opinion recommending the authorisation of a medicine, a **summary of opinion** document is published in the CHMP meeting highlights and EMA's pending EC decisions page on the Friday following the CHMP plenary meeting (see Table 1). The summary of opinion provides key information about the medicine, including the full recommended indication and its main benefits and risks.

For selected medicines that are likely to address an unmet medical need or represent an important innovation or change in clinical practice, a **dedicated press release** is published on EMA's homepage and also linked to the CHMP meeting highlights to inform the media and general public.

Table 1. Publications on outcomes of applications for initial marketing authorisation

	Initial publications	Full documentation
Withdrawal of application	Withdrawal Q&A plus withdrawal letter [M,W] *(Friday following next CHMP plenary)*	Withdrawal public assessment report [W] *(within 3 months of receipt of withdrawal letter)*
Positive CHMP opinion	Summary of opinion [M,P] Press release (for selected products) [M,H] *(Friday following CHMP plenary)*	New EPAR documents [E] *(2 weeks after EC decision)* EPAR summary Product information List of all authorised presentations Public assessment report Summary of review of orphan designation [O] (for orphan medicines)
Negative CHMP opinion	Refusal Q&A [M,P] *(Friday following CHMP plenary)*	Refusal public assessment report [E] *(2 weeks after EC decision)*

M – Meeting Highlights
W – Withdrawn applications page
H – Homepage
E – EPAR page
P – Pending EC decisions page
O – Rare disease designations page

Around 2 weeks after the European Commission's decision on the marketing authorisation of a new medicine, a comprehensive set of documents called the **European Public Assessment Report (EPAR)** is published on the medicine's EPAR page. The EPAR of each centrally authorised medicine comprises the following:

- the **EPAR summary**, which is a lay-language summary in a question-and-answer format explaining why the medicine is approved in the EU and its conditions of use. This summary serves as the landing page for the medicine on EMA's website. It is published in all official EU languages and its target audience is the general public;
- the approved **product information** (which comprises the summary of product characteristics or SmPC, the product labelling and the package leaflet), and a **list of all authorised presentations**. Both these documents are published in all official EU languages plus Icelandic and Norwegian, under the tab 'Product information' on the medicine's page. The target audience of the SmPC is healthcare professionals, while the package leaflet is for patients;
- the **public assessment report** adopted by the CHMP with any divergent positions annexed to the report. Only information of a commercially confidential nature is redacted. The assessment report is published under the tab 'Assessment history' on the medicine's page;
- the previously published summary of opinion, which is moved under the tab 'Assessment history' on the medicine's page at the time of the EPAR publication (i.e. it will no longer be found on EMA's pending EC decisions page).

For medicines for which additional measures have been included in their risk management plan to reduce the risk of medication errors, a **communication on medication error prevention** is also published in all official EU languages as part of the EPAR as well as on a dedicated page called recommendations on medication errors. The target audience includes patients and healthcare professionals.

For orphan medicines, a **summary of the review of orphan designation** is published at the same time as the EPAR on EMA's rare disease designations page under the tab 'Review of designation' (see Section 6.1).

2.3. Negative opinions

If the CHMP gives a negative opinion on a marketing authorisation application, a **refusal questions-and-answers (Q&A)** document is published in the CHMP meeting highlights and EMA's pending EC decisions page on the Friday following the CHMP plenary meeting (see Table 1). It provides basic information in lay language about the medicine and the reasons why it was not recommended for approval. Its target audience is the general public.

Around 2 weeks after the European Commission's decision refusing the marketing authorisation, a **refusal EPAR** is published on the medicine's EPAR page, comprising:

- the previously published refusal Q&A (which will no longer be found on EMA's pending EC decisions page) and its translations in all official EU languages;
- the **refusal public assessment report**, which is the assessment report as adopted by the CHMP. Only information of a commercially confidential nature is redacted. The assessment report is published under the tab 'Assessment history' on the medicine's page.

2.4. Re-examination of opinions

Applicants may request a re-examination of a CHMP opinion no later than 15 days after receipt of the opinion. If a company requests a re-examination, the refusal Q&A is updated with a note on the start of the re-examination procedure, and this is also mentioned in the CHMP meeting highlights.

After the CHMP has re-examined its original opinion, a **re-examination Q&A** is published in the CHMP meeting highlights on the Friday following the CHMP plenary meeting where the re-examination was concluded. This re-examination Q&A also replaces the original refusal Q&A in EMA's pending EC decisions page. The re-examination Q&A is written in lay language and its target audience is the general public. The original refusal Q&A remains linked to the CHMP meeting highlights where it was first published.

If the outcome of the re-examination is negative (i.e. the CHMP maintains its negative opinion), a refusal EPAR is also published around 2 weeks after the European Commission's decision refusing the marketing authorisation as described in Section 2.3 and will include both the original refusal Q&A and the re-examination Q&A.

If the outcome of the re-examination is positive, a summary of opinion document is published with the re-examination Q&A in the CHMP meeting highlights. Around 2 weeks after the European Commission's decision, the same set of EPAR documents described in Section 2.2 is published and will include both the original refusal Q&A and the re-examination Q&A.

Most cases of re-examinations involve an applicant requesting a re-examination of a negative CHMP opinion. In some cases, an applicant may request a re-examination of a positive opinion if there are

aspects of the opinion with which it does not agree. The publication practice in these cases is the same as for re-examinations of negative opinions: a note on start of the re-examination, an updated summary of opinion at the end of the re-examination (if outcome remains positive), and EPAR documents around 2 weeks after the European Commission's decision (unless the applicant withdraws its application).

2.5. Withdrawal of initial marketing authorisation applications

If an applicant withdraws its application for initial marketing authorisation, a **withdrawal Q&A** is published on EMA's withdrawn applications page on the Friday following the upcoming CHMP plenary meeting (see Table 1). The withdrawal Q&A is also linked to the CHMP meeting highlights.

For applications withdrawn during a CHMP meeting, the Q&A is published on the Friday following the next CHMP meeting. The withdrawal Q&A contains information in lay language on the scientific assessment of the product up to the time of the withdrawal. Its target audience is the general public.

EMA also publishes the **withdrawal letter** sent by the applicant, which is linked to the withdrawal Q&A and includes the reason for the withdrawal (in line with Article 11 of Regulation EC 726/2004). All personal contact information (addresses, emails, phone numbers and signatures) in the letter will be redacted. The withdrawal letter is also published separately on the medicine's withdrawn applications page.

Within 3 months of receipt of the withdrawal letter, EMA publishes the **withdrawal public assessment report**, which is the last adopted CHMP assessment report available at time of withdrawal. All information of a commercially confidential nature is redacted. The assessment report is published under the tab 'All documents' on the medicine's withdrawn applications page. Translations of the withdrawal Q&A in all official EU languages are also published at the same time as the assessment report.

3. Changes to centralised marketing authorisations

3.1. Extensions of indication[1]

The documents published on the outcome of extension of indication applications closely mirror those published for initial authorisation applications, and are summarised in Table 2.

Positive opinions

If the CHMP gives a positive opinion on an extension of indication application, **a summary of opinion** is published in the CHMP meeting highlights and EMA's pending EC decisions page on the Friday following the CHMP plenary meeting[2]. For selected extension of indications, a **dedicated press release** may also be published at the same time on EMA's homepage to inform the media and general public of important extensions of indication that address unmet medical needs.

Around 2 weeks after the European Commission's decision, the summary of opinion is moved to the medicine's EPAR page, where updated documents related to the extension of indication are published. These include the updated **product information** and, if applicable, the **updated EPAR summary**.

[1] List of ongoing evaluations of extension of indication applications not currently published. EMA will publish such a list in the near future. Until then this information can be provided upon request.
[2] Summaries of opinion for extensions of indications are not published for generic or biosimilar medicines.

The **assessment report** related to the extension of indication as adopted by the CHMP is also always published under the tab 'Assessment history'. All information of a commercially confidential nature is redacted and any divergent positions of CHMP members are annexed to the report.

A document called **procedural steps taken and scientific information after authorisation** is also published (under the tab 'Assessment history') or updated if the document was already available. This document provides an overview of all the changes made to the marketing authorisation since the medicine's initial authorisation.

If the medicine was designated an orphan medicine, a **summary of the review of orphan designation** related to the new indication is also published at the same time as the updated EPAR on EMA's rare disease designations page under the tab 'Review of designation' (see Section 6.1).

Table 2. Publications on outcomes of applications for extensions of indication

	Initial publications	Full documentation
Withdrawal of application	Withdrawal Q&A plus withdrawal letter [M,W] *(Friday following next CHMP plenary)*	Withdrawal public assessment report [W] *(within 3 months of receipt of withdrawal letter)*
Positive CHMP opinion	Summary of opinion [M,P] Press release (for selected products) [M,H] *(Friday following CHMP plenary)*	New or updated EPAR documents [E] *(2 weeks after EC decision for extension of indications)* EPAR summary Product information List of all authorised presentations Public assessment report Procedural steps document Summary of review of orphan designation [O] (for orphan medicines)
Negative CHMP opinion	Refusal Q&A [M,E] *(Friday following CHMP plenary)*	Refusal public assessment report [E] *(4 to 5 weeks after CHMP opinion for extension of indications)*

M – Meeting Highlights
W – Withdrawn applications page
H – Homepage
E – EPAR page
P – Pending EC decisions page
O – Rare disease designations page

Negative opinions

If the CHMP's opinion on an extension of indication application is negative, a **refusal Q&A** is published in the CHMP meeting highlights and the medicine's EPAR page on the Friday following the CHMP plenary meeting.

Around 4 to 5 weeks after the CHMP's negative opinion, the translations of the refusal Q&A in all official EU languages are published in the medicine's EPAR page. The **refusal public assessment report** is also published on the same page under the tab 'Assessment history' and the document **procedural steps taken and scientific information after authorisation** is also published, or updated if the document was already available.

Re-examinations

If an applicant requests a re-examination of a negative opinion, the refusal Q&A is updated with a note on the start of the re-examination procedure and this is also mentioned in the CHMP meeting highlights. At the end of the re-examination, a **re-examination Q&A** is published in the CHMP meeting highlights and in the medicine's EPAR page on the Friday following the CHMP plenary meeting in which the re-examination was concluded.

If the outcome of the re-examination is negative, the same set of documents as for negative opinions described above are published around 2 weeks after the CHMP's opinion on the re-examination.

If the outcome of the re-examination is positive, a summary of opinion is published together with the re-examination Q&A in the CHMP meeting highlights and the pending EC decisions page on the Friday following the CHMP plenary. Around 2 weeks after the European Commission's decision, the summary of opinion and the re-examination Q&A are moved to the medicine's EPAR page, and the same set of documents as for positive opinions described above are published.

Withdrawn applications

If the applicant withdraws its application for an extension of indication, a **withdrawal Q&A**, **withdrawal letter** and **withdrawal public assessment report** are published in the same way as for initial applications on EMA's withdrawn applications page (see Section 2.5). The document **procedural steps taken and scientific information after authorisation** is also published, or updated if the document was already available, on the medicine's EPAR page.

Changes of scope during extensions of indication applications

There are cases where an applicant applies for an extension of indication but the extension of indication aspect is later removed from the application. The CHMP may then issue an opinion recommending changes to the product information that do not include the extension of indication initially applied for.

In such cases EMA publishes a **Q&A document** on the Friday following the CHMP plenary on medicine's EPAR page, explaining the scientific assessment of the extension of indication application up to the point it was removed. Around 2 weeks after the European Commission's decision, the updated **product information** is published on the same page under the tab 'Product information'. The **public assessment report** is published under the tab 'Assessment history', reflecting the initial scope applied for and the opinion finally granted. The document **procedural steps taken and scientific information after authorisation** is also published, or updated if the document was already available.

3.2. Other variations, annual re-assessments, renewals and line extensions

Publications at time of CHMP opinion

For some changes to the marketing authorisation (other than extensions of indication), EMA publishes a **summary of opinion** in the CHMP meeting highlights and the pending EC decisions page on the Friday following the CHMP plenary meeting. These include changes to contra-indications and changes that will significantly alter the way the medicine is used (i.e. new route of administration, switch of prescription status e.g. from prescription-only to OTC, moving from multiple doses to a single dose or vice versa, extension to use in combination).

If a change to the marketing authorisation is of major public health importance, EMA may also publish in the CHMP meeting highlights and the medicine's EPAR page on the Friday following the CHMP

plenary meeting a **public health communication** containing advice for patients and healthcare professionals.

Update of the EPAR

For variations that result in an updated **product information**, the medicine's EPAR is updated around 2 weeks after the European Commission's decision if an immediate decision is expected, or 4-5 weeks after the CHMP's opinion or notification when no immediate European Commission's decision is issued.

In addition to the updated product information, the EPAR update may include an updated **EPAR summary** (if needed). The **procedural steps taken and scientific information after authorisation** is published or updated in all cases.

Finally, the EPAR update also includes the publication of the **public assessment report** for those changes that are considered to be of significant clinical relevance. In particular, public assessment reports are published for line extension applications (Annex I applications) when they contain new non-clinical or clinical data and for conditional marketing authorisations when they are switched to full authorisations.

Public assessment reports are also published for paediatric studies submitted under Article 46 of paediatric regulation (Regulation (EC) No 1901/2006).

All assessment reports are published under the tab 'Assessment history' with commercially confidential information redacted.

There are cases where a CHMP evaluation of a variation or line extension application does not ultimately result in a change to the marketing authorisation, either because the CHMP decided no change was needed (negative opinion) or the applicant withdrew its application. The scope of the application may also be changed during the procedure. In most of these cases, the only EPAR update concerns the **procedural steps taken and scientific information after authorisation**.

In all cases where the only change to the EPAR concerns the document **procedural steps taken and scientific information after authorisation**, this updated document is published with the next EPAR update.

4. Withdrawal / expiry of centralised marketing authorisations

A marketing authorisation may be withdrawn at the request of a marketing authorisation holder if it no longer wishes to market a medicine or chooses not to renew its authorisation. In some cases, a marketing authorisation may expire because of the so-called 'sunset clause' that comes into force when a product has not been marketed in any EU country for three consecutive years.

In these instances, EMA publishes a **public statement** on the medicine's EPAR page at the time of the authorisation's expiry or the official withdrawal of the authorisation by the European Commission. The EPAR documents already published remain on the website but are watermarked to indicate that the medicine is no longer authorised.

The European Commission may also withdraw or suspend a medicine's authorisation when a medicine is deemed to have an unfavourable benefit-risk balance. Such withdrawals or suspensions usually take place within the context of an EU referral. Section 5 describes the documents EMA publishes for EU referrals. The EPAR documents for the medicines concerned are also watermarked as described above.

5. EU referrals

A referral is a procedure used to resolve issues such as concerns over the safety or benefit of a medicine or a class of medicines. The matter is 'referred' to EMA, so that it can make a recommendation for a harmonised position across the European Union. Information on referral procedures is published on EMA's referrals page.

The referrals described below are grouped according to the extent of information published about them.

5.1. Article 20, 31 and 107i referrals[3]

At the start of an Article 20, 31 or 107i referral, EMA publishes an **announcement of start of referral** in lay language to inform the general public of the reasons for the safety/efficacy review (see Table 3). Depending whether or not the referral is triggered on the basis of pharmacovigilance data, EMA's Pharmacovigilance Risk Assessment Committee (PRAC) or EMA's CHMP carries out the assessment, and the announcement of the start is published on the Friday following the plenary meeting where the referral is initiated. The official **notification**, the draft **list of products** affected by the procedure (annex I), a **list of questions** intended for marketing authorisation holders, and a **timetable** for the referral are also published.

In addition, for Article 107i referrals EMA also publishes the **rationale for the triggering of the procedure** and the **PRAC list of questions addressed to stakeholders** inviting stakeholders (e.g. healthcare professionals, patients' organisations and the general public) to submit data relevant to the procedure.

For those referrals that involve the PRAC, a lay-language **summary of PRAC recommendations** is published on the Friday following the PRAC plenary meeting where the recommendations were adopted. If the medicines included in the review were all authorised through national procedures, the PRAC recommendations are then sent to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which adopts a final position. When the CMDh position is agreed by consensus, the position is directly implemented in all EU Member States. If, however, the CMDh position is agreed by majority it is sent to the European Commission, which issues a final decision applicable throughout the EU. For reviews that include centrally authorised medicines, the PRAC recommendations are sent to the CHMP, which adopts the Agency's final opinion.

On the Friday following the CHMP opinion or CMDh position, a **public health communication** is published. This document comprises 3 sections: a high-level summary targeting the media and general public and dedicated sections with information targeting patients and healthcare professionals. The **text of the updated product information** (annex III) in English is also published at the same time. In addition, when there is a CMDh consensus position, EMA publishes a **timetable for implementation** of the CMDh position. The **public assessment report** is published around 1 week after the European Commission's decision or CMDh consensus position.

[3] Article 20 of Regulation (EC) 726/2004; Article 31 of Directive 2001/83/EC; Article 107i of Directive 2001/83/EC.

Table 3. EMA publications for Article 20, 31 and 107i referrals

	Documents
Start of referral	Start of referral announcement [M,R] Notification [R] List of questions [R] Timetable [R] Draft list of products [R] Rationale for Art. 107i procedure [R] *(Friday following CHMP/PRAC plenary)*
PRAC recommendation *(if applicable)*	Summary of PRAC recommendations [M,R] *(Friday following PRAC plenary)*
CHMP opinion/CMDh position	Public health communication [M,R,H] Text of updated product information [R] Timetable for implementation of CMDh consensus position [R] *(Friday following CHMP/CMDh plenary)*
EC decision	Public assessment report [R,*] *(1 week after EC decision)* Updated public health communication [R,§] Annexes [R,§] *(around 4 weeks after EC decision)*

M – Meeting Highlights
R – Referrals page
H – Homepage
***** - If the CMDh position is agreed by consensus, there is no EC decision and the public assessment report is published 1 week after the CMDh consensus position.
§ - If the CMDh position is agreed by consensus, there is no EC decision and the updated public health communication and Annexes are published 8 weeks after the CMDh consensus position.

Finally, around 4 weeks after the European Commission's decision is issued or 8 weeks after CMDh consensus position, the public health communication is updated saying that the review is now final, and translations in all official EU languages are also published together relevant **annexes** in all official EU languages (containing, as applicable, the final list of medicines affected by the referral, the scientific conclusions, the text of the updated product information and the conditions of the marketing authorisation).

All the documents related to referral procedures are published on EMA's referrals page. The start of referral announcement, the summary of PRAC recommendations and public health communication are also linked to the meeting highlights of the relevant committees, and the public health communication is also published on EMA's homepage. For centrally authorised medicines, the referral page is linked to the EPAR page of the medicine and EPAR documents are updated as applicable (see Section 3.2).

5.2. Article 13(2), 29(4) and 30 referrals[4]

For Article 13(2), 29(4) and 30 referrals, assessment is carried out by the CHMP. The start of these referrals is made public in a table called **Start of community reviews**, which is published as a link to

[4] Article 13(2) of Regulation (EC) 1234/2008; Article 29(4) and Article 30 of Directive 2001/83/EC.

the CHMP meeting highlights on the Friday after the CHMP plenary meeting where the referrals are initiated.

For Article 30 referrals, an **announcement of start of referral**, the official **notification**, the draft **list of products** affected by the procedure (annex I), a **list of questions** intended for marketing authorisation holders, and a **timetable** for the referral are also published on the Friday after the CHMP plenary meeting where the referrals are initiated.

On the Friday following the CHMP plenary where the CHMP assessment is concluded, EMA publishes a **Q&A document** in lay language and, if applicable, the **text of the updated product information** (annex III) in English. The **public assessment report** is then published around 1 week after the European Commission's decision is issued.

Finally, around 4 weeks after the European Commission's decision, the Q&A in all official EU languages is published along with relevant **annexes** in all official EU languages (containing, as applicable, the list of medicines affected by the referral, the agency's scientific conclusions, the text of the updated product information and the conditions of the marketing authorisation).

All these documents are published on EMA's referral page. In addition, the Q&A and the announcement of the start of Article 30 referrals are also linked to the CHMP meeting highlights.

5.3. Article 5(3) opinions

In accordance with Article 5(3) of Regulation (EC) No 726/2004, the CHMP may at the request of EMA's Executive Director, the European Commission or an EU Member State draw up opinions on scientific matters related to the evaluation of a medicine or a group of medicines.

The start of an Article 5(3) review is made public in the table **Start of community reviews**, which is published as a link to the CHMP meeting highlights on the Friday following the CHMP plenary meeting where the review is started.

The **public assessment report** is published on EMA's Article 5(3) opinions page 15 days after the CHMP opinion. For those reviews that are considered to be of public interest, a press release is also published. It will be published at the start and at the end of the review on the Friday following the CHMP plenary meeting, linked to the CHMP meeting highlights.

5.4. Article 29 (Paediatrics) opinions

In accordance with Article 29 of Regulation (EC) No 1901/2006, the CHMP issues opinions on non-centrally authorised medicines concerning applications for new indications, pharmaceutical forms or routes of administration intended for children.

On the Friday following the CHMP plenary where the CHMP opinion is issued, EMA publishes a **summary** of the CHMP conclusion on EMA's referral page. The **public assessment report** is then published around 1 week after the European Commission's decision is issued. Finally, around 4 weeks after the European Commission's decision relevant **annexes** (containing, as applicable, the list of medicines affected by the referral, the agency's scientific conclusions, the text of the updated product information and the conditions of the marketing authorisation) are published in all official EU languages.

6. Other documents and procedures

6.1. Orphan designations

When EMA's Committee for Orphan Medicinal Products (COMP) has evaluated an application for orphan designation, a summary of the COMP's opinion (known as a **public summary of opinion on orphan designation**) is published on EMA's rare disease designations page around 4 weeks after the European Commission has issued a final decision. This public summary of opinion on orphan designation is written in lay language. It explains the rationale for the medicine's designation and provides basic information about the medicine and its stage of development.

Orphan designations are reviewed when an application for marketing authorisation or extension of indication application for an orphan medicine is successful. The COMP reviews the designation to determine whether the medicine still meets the necessary criteria and a **summary of the review of orphan designation** is published at the same time as the EPAR on the page of the original summary of orphan designation, under the tab 'Review of designation' (see also Section 2.2). In addition, the orphan designation can be further reviewed upon request of a Member State within the first 5 years of receipt of the marketing authorisation. In such cases, a new summary of the review of orphan designation will be published in the same place 6-8 weeks after COMP opinion.

6.2. ATMP classification

Companies can request a recommendation from EMA's Committee for Advanced Therapies (CAT) on whether a medicine they are developing is an advanced-therapy medicinal product (ATMP). The CAT has 60 days to issue its recommendation on ATMP classification, following which a summary (known as **summary of scientific recommendations on classification of advanced-therapy medicinal products**) is published on EMA's advanced-therapy classification page. The summary includes a brief description of the product and its proposed indication and the CAT's conclusion on whether the product falls within the definition of any of the different types of ATMPs (gene therapy medicinal products, somatic cell therapy medicinal products or tissue engineered products).

6.3. Paediatric investigation plans

All applications for marketing authorisation for human medicines have to include the results of studies in children as described in an agreed paediatric investigation plan (PIP), unless the applicant has been granted a deferral or waiver. The requirement for a PIP also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorised.

EMA's Paediatric Committee (PDCO) is responsible for agreeing or refusing PIPs, deferrals and waivers. The **decisions on PIPs** and **waivers** are published 6-8 weeks after adoption on EMA's paediatrics page, together with a **summary of the PDCO evaluation**. The summary is written in lay language and contains an overview of process leading to the decision, and the reasons for any deferrals or waivers.

Once an applicant has completed an agreed PIP, it may request EMA to perform a compliance check. EMA's paediatrics page is updated twice a year to indicate the outcome (positive or negative) of the compliance checks performed by EMA. In addition, the PIP compliance statement is published on the medicine's EPAR page around 2 weeks after the European Commission's decision if an immediate

decision is expected, or 4-5 weeks after the CHMP's opinion or notification when no immediate European Commission's decision is issued.

6.4. Safety signals

A safety signal is information on a new or known adverse event that is potentially caused by a medicine that warrants further investigation. The PRAC assesses safety signals for both centrally and non-centrally authorised medicines and makes recommendations to the CHMP or CMDh. The recommendations are then published within a month of the PRAC plenary meetings on the page PRAC recommendations on safety signals. In addition to publishing the **PRAC recommendations on signals**, EMA also publishes the document **recommendations for updates of product information**. This document captures the proposed changes to the product information following the assessment of a signal and is translated into all official EU languages.

6.5. Medicines under additional monitoring

A medicine can be included in the list of medicines under additional monitoring (i.e. medicines that are monitored particularly closely) when it is approved for the first time or in certain cases during its life cycle. It remains under additional monitoring for five years or until the PRAC decides to remove it from the list. Every month, the PRAC reviews the **list of medicines under additional monitoring**, and the up-to-date list is published on the page List of medicines under additional monitoring. The list contains the invented name and active substance of the medicine, the reason why the medicine is on the list, the name of the marketing authorisation holder, a link to the European public assessment report (for centrally authorised medicines) and the date of inclusion in the list. The list is available in both a PDF and Excel format.

6.6. Compassionate use

The CHMP can provide recommendations on how to administer, distribute and use certain medicines for compassionate use, although these recommendations do not create a legal framework and compassionate use programmes remain under the responsibility of individual Member States. After the CHMP opinion on a compassionate use, EMA publishes on the page Compassionate use a **Summary of compassionate use** and a document called '**Conditions of use, conditions for distribution and patients targeted and conditions for safety monitoring**'.

6.7. Shortages

EMA maintains a Catalogue on shortages of medicines that are likely to affect more than one EU Member State and where EMA has made specific recommendations to patients and healthcare professionals. Each catalogue entry includes information on the reason for the shortage, the countries affected as well as the recommendations for patients and healthcare professionals during the shortage. The information is updated when the shortage is resolved.

6.8. Periodic safety update reports

Periodic safety update reports (PSURs) are periodic reports on the benefit-risk balance of an active substance or combination of active substances contained in medicines authorised in the EU. PSURs are submitted by companies and evaluated by the PRAC and CHMP/CMDh at defined time points after a medicine's authorisation.

A single assessment of related PSURs (PSUSAs) is carried out for medicines containing the same active substance or combination of active substances, as included in the list of EU reference dates (EURD list published on the PSUR page).

PSUSAs for active substances found only in centrally authorised medicines will result in an update of relevant EPAR documents, as described in Section 3.2. In addition, when a PSUSA leads to a change to the product information, a document called **The scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation** is always published on the medicine's EPAR page under the tab 'Assessment history'.

Information on PSUSAs for active substances found only in nationally authorised medicines is published on the page Outcomes of periodic safety update report single assessments. If the PSUSA results in no change to the marketing authorisation (maintenance), the **List of medicines** that were assessed in the PSUSA is made available on this page 1 week after the end of the procedure. For PSUSAs which result in changes to the marketing authorisation (i.e. a variation), EMA publishes on the same page the **List of medicines** together with the **Scientific conclusions and grounds for variation to the terms of the marketing authorisations** within 2 months of the conclusion of the PSUSA procedure. This latter document, which shows the changes made to the product information of the medicines concerned, is available in all official EU languages. An **Assessment report** is only published when changes are considered to be of significant clinical relevance.

6.9. Imposed non-interventional post-authorisation safety studies

Post-authorisation safety studies (PASS) are studies carried out after a medicine has been authorised in order to obtain further information on the medicine's safety, or to measure the effectiveness of risk-management measures. The PRAC assesses both the protocols and the final study results of all imposed non-interventional PASS.

All procedures to assess final results of imposed non-interventional PASS result in a change to the marketing authorisation (i.e. a variation).

The assessment of results from imposed non-interventional PASS for active substances found only in centrally authorised medicines will result in an update of relevant EPAR documents, as described in Section 3.2. A document called **Scientific conclusions, amendments to product information and implementation timetable** is also published on the medicine's EPAR page under the tab 'Assessment history'.

The outcomes of assessments of imposed non-interventional PASS results for active substances found only in nationally authorised medicines are published on the page Outcomes of imposed non-interventional post-authorisation safety studies within 2 months of the conclusion of the procedure. EMA publishes on this page the **List of medicines** that were assessed in the PASS together with the **Scientific conclusions, amendments to product information and implementation timetable.** This latter document is available in all official EU languages. An **Assessment report** is only published when changes are considered to be of significant clinical relevance.

6.10. Medicines for use outside the EU (Article 58)

The CHMP evaluates applications for some medicines that are not intended for use in the EU, in accordance with Article 58 of Regulation (EC) No 726/2004. Medicines eligible for an Article 58 evaluation are those used to prevent or treat diseases of major public-health interest, including vaccines used in the WHO Expanded Programme on Immunization or for protection against a public-

health priority disease, and medicines for WHO target diseases such as HIV/AIDS, malaria or tuberculosis.

Article 58 evaluations are part of EMA's co-operation with WHO. When the evaluation is complete, EMA publishes similar documents to those described in Section 2 and 3 on positive and negative opinions and withdrawals within 2 months of the CHMP's opinion. These documents are published in English only on a dedicated webpage for Medicines for use outside the EU.

6.11. Ancillary medicinal substances

The CHMP evaluates applications for consultations on ancillary medicinal substances or ancillary human blood derivatives incorporated in a medical device, in accordance with Article 1(4) of Directive 93/42/EEC as amended and Article 1(4) of Directive 90/385/EEC as amended.

When the evaluation is completed and the EMA has received confirmation from the notified body of the issuing of a CE mark for the medical device, EMA publishes the **Consultation public assessment report** on the Ancillary medicinal substances webpage. Publication of reports occurs around 2 weeks after receipt of this confirmation. The reports are only published for positive opinions.

6.12. Agendas, minutes and reports of meetings of EMA's scientific committees

In addition to the documents focusing on individual medicines or groups of medicines, EMA publishes several documents on the activities of its scientific committees.

Agendas are published in advance of the meetings and list the medicines and other topics to be discussed. The **Minutes**, which are published after the meeting (usually the following month), contain information on the outcomes of procedures discussed or concluded by the committees, including those described above in sections 2 to 6 of this document.

For CHMP and PRAC, EMA also publishes **Meeting highlights** on the Friday following their monthly plenary meetings to highlight outcomes of major public interest.

For CAT, COMP and PDCO, EMA publishes **Monthly meeting reports** in the week following the committee's plenary meeting.

These documents can be found on the respective Committee pages. The meeting highlights are also published on EMA's homepage.

6.13. Medical literature monitoring

EMA monitors medical literature on a number of active substances. The objective is to identify suspected adverse reactions with medicines authorised in the EU and to enter the relevant information into the EudraVigilance database. The list of substance groups (chemical and herbal) which are subject to the monitoring activities by the Agency are published in the document **Medical literature monitoring: substance and herbal substance groups** which is available on the page Medical literature monitoring. The list is reviewed annually.

7. Information on non-centrally authorised medicines

Although most of the information published on EMA's website relates to centrally authorised medicines, EMA also publishes information on non-centrally authorised medicines, particularly on those medicines

that are included in reviews by its scientific committees. Such reviews include the PRAC's review of safety signals (see Section 6.4), referral procedures (see Section 5) and PSUSAs (see Section 6.8).

8. Coordination of information on medicines

It is important that adequate mechanisms are in place to ensure that accurate information reaches the EU public in a timely manner. This is especially relevant for information which might be sensitive or which may generate significant public interest.

Marketing authorisation holders, applicants and third parties are generally expected to refrain from making public announcements, which cannot be independently verified, on the expected outcomes of evaluations carried out by EMA's scientific committees until the committees have formally adopted their opinions (i.e. on the last day of the committee meeting).

Some committees (the CHMP and PRAC) make use of the so-called meeting highlights to communicate information considered to be of major public interest. Meeting highlights are usually published the day after a committee meeting ends. As a matter of good practice, marketing authorisation holders, applicants and third parties should wait until EMA communication is published before publishing their own communication related to the committee's outcome.

With regard to communication on safety, EMA has procedures for giving advance notice of their safety-related publications to national competent authorities in the EU, the European Commission and the concerned marketing authorisation holders. This is to ensure that the same message reaches all patients and healthcare professionals in the EU at the same time. Under EU legislation, marketing authorisation holders are also obliged to inform the Agency and relevant national competent authorities of their intention to publish information on the safety of medicines. This exchange and coordination of safety communication in the EU is described in Good Pharmacovigilance Practice (GVP) Module XV.

Annex: Tabulated overview of EMA documents on human medicinal products

Table 1: Applications for centralised marketing authorisation: Medicines under initial evaluation

Type of document	Location	Publication time
List of medicines that are under evaluation	Medicines under evaluation page	Monthly
COMP monthly meeting reports (for orphan medicines)	COMP page	Week following COMP plenary

Table 2: Applications for centralised marketing authorisation: Positive opinions

Type of document		Location	Publication time
Summary of opinion		CHMP meeting highlights and pending EC decisions page (document moved to medicine's EPAR page after EC decision)	Friday following CHMP plenary
Dedicated press release (for selected medicines)		EMA homepage and CHMP meeting highlights	Friday following CHMP plenary
EPAR	EPAR summary	Medicine's EPAR page	2 weeks after EC decision
	Product information	Medicine's EPAR page (under tab 'Product information')	
	List of all authorised presentations	Medicine's EPAR page (under tab 'Product information')	
	Public assessment report	Medicine's EPAR page (under tab 'Assessment history')	
Communication on medication error prevention (if applicable)		Recommendations on medication errors page	2 weeks after EC decision
Summary of the review of orphan designation (for orphan medicines)		Rare disease designations page (under tab 'Review of designation')	2 weeks after EC decision

Table 3: Applications for centralised marketing authorisation: Negative opinions

Type of document	Location	Publication time
Refusal Q&A	CHMP meeting highlights and pending EC decisions page (Q&A moved to medicine's EPAR page after EC decision)	Friday following CHMP plenary
Refusal public assessment report	Medicine's EPAR page (under tab 'Assessment history')	2 weeks after EC decision

Table 4: Applications for centralised marketing authorisation: Re-examination of opinions[§]

Type of document	Location	Publication time
Re-examination Q&A (for both positive and negative outcomes)	CHMP meeting highlights and pending EC decisions page (Q&A moved to medicine's EPAR page after EC decision)	Friday following CHMP plenary
Summary of opinion (for positive outcomes only)	CHMP meeting highlights and pending EC decisions page	Friday following CHMP plenary

[§] After EC decision, depending on the outcome of the re-examination, the same set of documents as for positive and negative opinions will also be published (see tables 2 and 3 above).

Table 5: Applications for centralised marketing authorisation: Withdrawal of applications

Type of document	Location	Publication time
Withdrawal Q&A	CHMP meeting highlights and withdrawn applications page	Friday following upcoming CHMP plenary
Withdrawal letter	Withdrawn applications page (under tab 'All documents')	Friday following upcoming CHMP plenary
Withdrawal public assessment report	Withdrawn applications page (under tab 'All documents')	Within 3 months of receipt of withdrawal letter

Table 6: Changes to centralised marketing authorisations: Extensions of indication

Type of document	Location	Publication time
Positive opinions		
Summary of opinion (excluding generics and biosimilars)	CHMP meeting highlights and pending EC decisions page (document moved to medicine's EPAR page after EC decision)	Friday following CHMP plenary
Dedicated press release (for selected extensions of indication)	EMA homepage and CHMP meeting highlights	Friday following CHMP plenary
Update of EPAR documents (product information, procedural steps document and, if applicable, EPAR summary and list of all authorised presentations)	Medicine's EPAR page	2 weeks after EC decision
Summary of the review of orphan designation (if applicable)	Rare disease designations page (under tab 'Review of designation')	2 weeks days after EC decision
Public assessment report	Medicine's EPAR page (under tab 'Assessment history')	2 weeks days after EC decision
Negative opinions		
Refusal Q&A	CHMP meeting highlights and pending EC decisions page (Q&A moved to medicine's EPAR page after EC decision)	Friday following CHMP plenary
Update of procedural steps document	Medicine's EPAR page (under tab 'Assessment history')	4-5 weeks after CHMP opinion
Refusal public assessment report	Medicine's EPAR page (under tab 'Assessment history')	4-5 weeks after CHMP opinion
Re-examinations[§]		
Re-examination Q&A (for both positive and negative outcomes)	CHMP meeting highlights and pending EC decisions page (Q&A moved to medicine's EPAR page after EC decision)	Friday following CHMP plenary
Summary of opinion (for positive outcomes only)	CHMP meeting highlights and pending EC decisions page	Friday following CHMP plenary
Withdrawal		
Withdrawal Q&A	Withdrawn applications page	Friday following next CHMP plenary
Withdrawal letter	Withdrawn applications page (under tab 'All documents')	Friday following next CHMP plenary

Type of document	Location	Publication time
Withdrawal public assessment report	Withdrawn applications page (under the tab 'All documents')	Within 3 months of receipt of withdrawal letter
Update of procedural steps document	Medicine's EPAR page (under tab 'Assessment history')	Within 3 months of receipt of withdrawal letter
Changes of scope during extension of indication applications		
Q&A for change in scope	Medicine's EPAR page	Friday following CHMP plenary
Update of procedural steps document	Medicine's EPAR page (under tab 'Assessment history')	2 weeks after EC decision
Updated product information	Medicine's EPAR page (under tab 'Product information')	2 weeks after EC decision
Public assessment report	Medicine's EPAR page (under tab 'Assessment history')	2 weeks after EC decision

[§] After EC decision, depending on the outcome of the re-examination, the same set of documents as for positive or negative opinions on extension of indication will be published.

Table 7: Changes to centralised marketing authorisations: Other variations, annual re-assessments, renewals and line extensions

Type of document	Location	Publication time
Summary of opinion for: • changes to contra-indications • changes that significantly alter the medicine's use	CHMP meeting highlights and pending EC decisions page	Friday following CHMP plenary
Public health communication (for selected changes of major public health importance)	CHMP meeting highlights and medicine's EPAR page	Friday following CHMP plenary
Update of EPAR documents (product information, procedural steps document and, if applicable, EPAR summary and list of all authorised presentations)	Medicine's EPAR page	2 weeks after EC decision or 4-5 weeks after CHMP opinion/notification, as applicable
Public assessment reports (for those changes that are of significant clinical relevance)	Medicine's EPAR page (under the tab 'All documents')	2 weeks after EC decision or 4-5 weeks after CHMP opinion/notification, as applicable

Table 8: Withdrawal / expiry of centralised marketing authorisations

Type of document	Location	Publication time
Public statement	Medicine's EPAR page	At time of withdrawal or expiry of marketing authorisation
EPAR documents watermarked	Medicine's EPAR page	At time of withdrawal or expiry of marketing authorisation

Table 9: EU referrals: Article 20, 31 and 107i referrals

Type of document	Location	Publication time
Announcement of start of referral	CHMP meeting highlights or PRAC meeting highlights and referrals page	Friday following PRAC or CHMP plenary where referral is started
Notification Draft list of medicines List of questions Timetable Rationale for Art. 107i procedure	Referrals page (under tab 'All documents')	Friday following PRAC or CHMP plenary where referral is started
PRAC list of questions addressed to stakeholders (for Art. 107i referrals)	Referrals page (under tab 'Data submission')	Friday following PRAC plenary where referral is started
Summary of PRAC recommendation (when PRAC is involved)	PRAC meeting highlights and referrals page	Friday following PRAC plenary where PRAC recommendation is adopted
Public health communication	EMA homepage, CHMP meeting highlights (if applicable) and referrals page	Friday following CHMP or CMDh plenary where CHMP opinion or CMDh position is adopted
Text of the updated product information in English	Referrals page (under tab 'All documents')	Friday following CHMP or CMDh plenary where CHMP opinion or CMDh position is adopted
Timetable for implementation of CMDh consensus position	Referrals page (under tab 'All documents')	Friday following CMDh plenary where CMDh consensus position is adopted
Public assessment report	Referrals page (under tab 'All documents')	1 week after EC decision or CMDh consensus position
Annexes	Referrals page (under tab 'All documents')	4 weeks after EC decision or 8 weeks after CMDh consensus position
Update of EPAR documents (product information, procedural steps document and, if applicable EPAR summary and list of all authorised presentations) if CAPs are involved	Medicine's EPAR page	2 weeks after EC decision

Table 10: EU referrals: Article 13(2), 29(4) and 30 referrals

Type of document	Location	Publication time
Table 'Start of community reviews'	CHMP meeting highlights	Friday following CHMP plenary where referral is started
Announcement of start of referral (for Article 30 referrals only)	CHMP meeting highlights or PRAC meeting highlights and referrals page	Friday following CHMP plenary where referral is started
Notification Draft list of medicines List of questions Timetable (for Article 30 referrals only)	Referrals page (under tab 'All documents')	Friday following CHMP plenary where referral is started
Q&A document	CHMP meeting highlights and referrals page	Friday following CHMP plenary where CHMP opinion is adopted
Text of the updated product information in English (if applicable)	Referrals page (under tab 'All documents')	Friday following CHMP plenary where CHMP opinion is adopted
Public assessment report	Referrals page (under tab 'All documents')	1 week after EC decision
Annexes	Referrals page (under tab 'All documents')	4 weeks after EC decision

Table 11: EU referrals: Article 5(3) opinions

Type of document	Location	Publication time
Table 'Start of community reviews'	CHMP meeting highlights	Friday following CHMP plenary where referral is started
Press release (for selected opinions)	EMA homepage, CHMP meeting highlights	Friday following CHMP plenary where CHMP opinion is adopted
Public assessment report	Article 5(3) opinions page	15 days after CHMP opinion

Table 12: EU referrals: Article 29(Paediatrics) opinions

Type of document	Location	Publication time
Summary of CHMP conclusions	Referrals page	Friday following CHMP plenary where CHMP opinion is adopted
Public assessment report	Referrals page (under tab 'All documents')	15 days after CHMP opinion

Table 13: Orphan designations

Type of document	Location	Publication time
Public summary of opinion on orphan designation	Rare disease designations page	4 weeks after EC decision on orphan designation
Summary of review of orphan designation	Rare disease designations page (under tab 'Review of designation')	2 weeks after EC decision
Summary of the review of orphan designation following Member State request	Rare disease designations page (under tab 'Review of designation')	6-8 weeks after COMP opinion

Table 14: ATPM classification

Type of document	Location	Publication time
Summary of scientific recommendations on classification of advanced-therapy medicinal products	Advanced-therapy classification page	After CAT conclusion

Table 15: Paediatric investigation plans

Type of document	Location	Publication time
Decisions on PIPs and waivers	Paediatrics page	6-8 weeks after EMA decision
Summary of PDCO evaluation	Paediatrics page	6-8 weeks after EMA decision
Compliance check outcome	Paediatrics page	Twice a year
Compliance statement	Medicine's EPAR page	2 weeks after EC decision or 4-5 weeks after CHMP opinion/notification, as applicable

Table 16: Safety signals

Type of document	Location	Publication time
PRAC recommendations on signals	PRAC recommendations on safety signals page	Within a month of PRAC plenary
Recommendations for updates of product information (if applicable)	PRAC recommendations on safety signals page	Within a month of PRAC plenary

Table 17: Medicines under additional monitoring

Type of document	Location	Publication time
List of medicines under additional monitoring	List of medicines under additional monitoring page	Monthly

Table 18: Compassionate use

Type of document	Location	Publication time
Summary of compassionate use	Compassionate use page	After CHMP opinion
Conditions of use, conditions for distribution and patients targeted and conditions for safety monitoring	Compassionate use page	After CHMP opinion
Dedicated press release (for selected opinions)	EMA homepage and CHMP meeting highlights	Friday following CHMP plenary

Table 19: Shortages

Type of document	Location	Publication time
Shortages catalogue	Shortages catalogue page	At time of shortage and when shortage is resolved

Table 20: Periodic safety update reports

Type of document	Location	Publication time
PSUSAs for active substances found only in centrally authorised medicines		
Update of EPAR documents (product information, procedural steps document and, if applicable EPAR summary and list of all authorised presentations)	Medicine's EPAR page	2 weeks after EC decision
Document 'The scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation' (for PSUSAs that lead to changes to product information)	Medicine's EPAR page (under tab 'Assessment history')	2 weeks after EC decision
Public assessment report (for PSUSAs that are of significant clinical relevance)	Medicine's EPAR page (under tab 'Assessment history')	2 weeks after EC decision
PSUSAs for active substances found only in nationally authorised medicines		
List of medicines	Periodic safety update report single assessments page	Within 1 week or 2 months of conclusion of PSUSA (for maintenance or variation, respectively)
Scientific conclusions and grounds for variation to the terms of the marketing authorisations (if applicable)	Periodic safety update report single assessments page	Within 2 months after conclusion of PSUSA
Public assessment report (for PSURs that are of significant clinical relevance)	Periodic safety update report single assessments page	Within 2 months after conclusion of PSUSA

Table 21: Imposed non-interventional post-authorisation safety studies

Type of document	Location	Publication time
PASS for active substances found only in centrally authorised medicines		
Update of EPAR documents (product information, procedural steps document and, if applicable, EPAR summary and list of all authorised presentations)	Medicine's EPAR page	2 weeks after EC decision
Document 'Scientific conclusions, amendments to product information and implementation timetable'	Medicine's EPAR page (under tab 'Assessment history')	2 weeks after EC decision
Public assessment report (for PASS that are of significant clinical relevance)	Medicine's EPAR page (under tab 'Assessment history')	2 weeks after EC decision
PASS for active substances found only in nationally authorised medicines		
List of medicines	Outcomes of imposed non-interventional post-authorisation safety studies page	Within 2 months after conclusion of PASS
Scientific conclusions, amendments to product information and implementation timetable'	Outcomes of imposed non-interventional post-authorisation safety studies page	Within 2 months after conclusion of PASS
Public assessment report (for PASS that are of significant clinical relevance)	Outcomes of imposed non-interventional post-authorisation safety studies page	Within 2 months after conclusion of PASS

Table 22: Medicines for use outside the EU (Article 58)

Type of document	Location	Publication time
Same documents as for centrally authorised medicines (see tables 1 to 7)	Medicines for use outside the EU page	Within 2 months of CHMP opinion

Table 23: Ancillary medicinal substances

Type of document	Location	Publication time
Consultation public assessment report	Ancillary medicinal substances page	2 weeks after notified body confirms issue of CE mark

Table 24: Agendas, minutes and reports of meetings of EMA's scientific committees

Type of document	Location	Publication time
Committees agendas	Committee pages	Before start of Committee plenary
Committees minutes	Committee pages	After Committee plenary where minutes are adopted
CHMP meeting highlights	EMA homepage, and Committee pages	Friday following CHMP plenary
PRAC meeting highlights	EMA homepage, and Committee pages	Friday following PRAC plenary
CAT, COMP and PDCO monthly meeting reports	Committee pages	Week following Committee plenary

Table 25: Medical literature monitoring

Type of document	Location	Publication time
Medical literature monitoring: substance and herbal substance groups	Medical literature monitoring page	Annually

European Medicines Agency

30 Churchill Place
Canary Wharf
London E14 5EU
United Kingdom

Telephone +44 (0)20 3660 6000
Facsimile +44 (0)20 3660 5555
Send a question www.ema.europa.eu/contact

www.ema.europa.eu