EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Patient Health Protection

Procedure for review of information on medicinal products by patients' and consumers' organisations

1. Introduction

The European Medicines Agency (EMA) is responsible for providing information about medicines authorised via the centralised procedure which includes information directed to the patient and the public. During the preparation of this information, the Agency interacts with patients' and consumers' organisations to ensure that it is adequately formulated and comprehensible to the target audience.

The package leaflet (PL) is supplied to the patient in the package in which the medicinal product is contained, and provides information related to the use of the medicine.

The EPAR summary is a lay-language document, available on the EMA website, which contains general information about the medicine. It also provides a summary of the grounds on which the EMA based its recommendation for the medicine to receive a marketing authorisation.

These documents are initially prepared during the course of the procedure for evaluating the marketing-authorisation application for a medicine; they follow specific deadlines and are confidential during the evaluation. The review procedure described herein also includes the review of PLs at the time of their renewal.

Safety communications refer to documents which are specifically addressed to the public once a medicinal product has been authorised and which conveys an important (emerging) message relating to the product. For example, informing patients when a product is withdrawn or suspended from the market for safety reasons, has a new contraindication or warning, or where there is a product defect or supply shortage.

As expressed in the 'Framework on the Interaction between the EMA and Patients' and Consumers' Organisations' (EMEA/354515/2005) the EMA should ensure adequate consultation with patients' and consumers' organisations (PCOs) so that the information provided by the Agency fulfils patients' and the general public's expectations.

This document describes the procedures for involving PCOs during the EMA review of PLs and EPAR summaries and in the preparation and dissemination of Agency safety communications. These

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procedures are managed by the EMA Medical Information Sector (MIS) as part of its responsibilities for interacting with PCOs.

2. Background

Articles 78(1) and 78(2) of Council Regulation (EC) No 726/2004 provide a mandate for the EMA to develop interaction with PCOs:

1. *"The Management Board shall, in agreement with the Commission, develop appropriate contacts between the Agency and the representatives of the industry, consumers and patients and the health professions. These contacts may include the participation of observers in certain aspects of the Agency's work, under conditions determined beforehand by the Management Board, in agreement with the Commission."*

2. *"The committees referred to in Article 56(1) and any working parties and scientific advisory groups established in accordance with that Article, shall in general matters establish contacts, on an advisory basis, with parties concerned with the use of medicinal products, in particular patient organisations and health-care professionals' associations. Rapporteurs appointed by these committees may, on an advisory basis, establish contacts with representatives of patient organisations and health-care professionals' associations relevant to the indication of the medicinal product concerned."*

The EMA/CHMP Working Group with Patients Organisations (forerunner of the Patients' and Consumers' Working Party) recommended that feedback be sought from patients on the readability of information contained in package leaflets, public statements and similar materials intended for the public.

3. Proposed scope of interaction

The purpose of the consultation between the EMA and PCOs on these documents is not to rewrite them but to ensure that the information is clear and understandable by the target audience, and that it fulfils their needs in terms of information content.

The consultation of PCOs on safety communications includes several different types of important material to be addressed to the public, such as question-and-answer documents relating to emerging safety information, withdrawal or suspension of a product from the market for safety reasons, shortage in supply or new contraindications or warnings. PCOs will also systematically be involved in the preparation of communications when they have previously been involved in the benefit/risk evaluation of the product.

4. Procedural principles for the interaction

Organisations and experts to be involved

- Any organisation that is consulted must fulfil the 'Criteria to be fulfilled by Patients' and Consumers' Organisations' (EMA/14610/04/Final) and be listed in the EMA's approved list of eligible organisations (See: http://www.ema.europa.eu/Patients/organisations.htm).

- The 'Rules of involvement of member(s) of Patients' and/or Consumers' Organisations in Committees related activities' (EMA/161660/2005) will apply. Since patients will act as experts in these procedures, they will have to adhere to the same rules as all other experts participating in EMA activities, especially with regard to confidentiality undertaking and the EMA Code of Conduct.
- Since the documents to be reviewed are in English, experts should be fluent in English. In addition, they should have access to appropriate information-technology equipment and to the Internet.
- With regards to the participation in the preparation and dissemination of safety communications, the experts involved should also have a good understanding of the specific therapeutic area in question.

Identification of a list of experts

- Every organisation fulfilling the criteria for involvement in EMA activities will be invited to designate experts for participation. After consideration, the EMA can nominate them as EMA experts and they will be included in the Agency's European expert database. Thereafter additional experts may be proposed and nominated whenever necessary.
- As far as possible, for consistency and efficiency reasons, each organisation should nominate one of their members as a coordinator. This coordinator will be the initial reference contact point between the EMA and the organisation and will have the responsibility of ensuring that experts from their organisation adhere to the above-mentioned rules, in particular with regard to confidentiality undertakings and declarations of interests.
- The EMA will prepare a list of nominated PCO experts, identifying the coordinator for each organisation, as well as the area of expertise of each expert, if relevant.
- This list will be updated according to organisations' proposals, as necessary.

Consultation process

- For each document to be produced, the EMA will consult an organisation(s) that specialises in the therapeutic area of the product, from the above-mentioned list. If there is no specialised organisation available, a general organisation will be consulted. If there is more than one organisation having expertise in the field, the EMA will select which organisation(s) to consult. Experts who have participated in specific training organised by the EMA will have preference.
- The EMA will send the request for review to the coordinator.
- When providing comments to the EMA, the coordinator should identify the expert(s) having participated to the review.
- The EMA will organise only one round of consultation and will ensure processing of the comments as part of EMA procedures. The final version will be circulated for information to the organisation having participated.
- The EMA will monitor the PCOs' input in these reviews and will provide regular feedback to the Patients' and Consumers' Organisations Working Party (PCWP).

Training

- All nominated experts will be invited to attend training sessions at the EMA, currently held on an annual basis, to introduce the procedure. Preference for attending the training sessions will be given to those recently added to the list of experts. Outside of the training sessions, all training material will be provided to new experts.

Confidentiality

- All documents subject for review and covered in this procedure are confidential (i.e. PLs, EPAR summaries and safety communication material) until they are made public. All experts must have signed confidentiality undertaking at the time of being involved in the review.

5. Implementation

The specific procedures for each type of review mentioned above are annexed hereafter.

Annex I

Procedure for review of PL

1. Package Leaflet

The Package Leaflet (PL) is part of the product information that is approved at the time of marketing authorisation by the regulatory authority. It is initially prepared by the applicant (pharmaceutical company), when requesting a marketing authorisation. The PL is prepared in accordance with legal requirements, as well as with EMA templates and guidance.

For centrally authorised medicines, the EMA reviews the PL proposed by the company at the time of initial evaluation for marketing authorisation and after the commercialisation of the product. During EMA reviews, scientific and linguistic amendments are proposed by assessors, and the quality and content of the PL are deeply scrutinised prior to finalisation of the product information by the EMA's relevant scientific committee; the Committee for Medicinal Products for Human Use (CHMP).

2. Initial marketing-authorisation procedure

The EMA is responsible for the centralised procedure. This procedure results in a single marketing authorisation that is valid across the European Union, as well as in Iceland, Liechtenstein and Norway. The marketing-authorisation applicant (pharmaceutical company) will submit a consolidated dossier on the medicine to be authorised, including a proposal for the English version of the PL. This dossier is evaluated by the Agency's relevant scientific committee (CHMP) within 210 days, at the end of which the committee adopts an opinion on whether the medicine should be marketed or not. This opinion is then transmitted to the European Commission, which issues a formal decision on the authorisation of the product.

In parallel to the scientific assessment, the EMA and its Quality Review of Documents (QRD) group perform a linguistic review of the English version of the PL between Days 121-165 of the assessment procedure (before the CHMP gives a final opinion).

Upon receipt from the company of an EN PL at Day 121, the EMA forwards it to all QRD members for comments (via written procedure) within 15 days. The consolidated comments are sent to the company by Day 157 for implementation. The procedure foresees the possibility of a meeting at the EMA around Day 165 (EMA QRD sub-group meeting) with EMA, QRD representatives, with the participation of company representatives, if necessary.

3. Renewal procedure

A Community marketing authorisation is initially valid for five years and may be renewed after this period on the basis of a re-evaluation of the risk-benefit balance by the CHMP. To this end, the marketing-authorisation holder (pharmaceutical company) will submit a consolidated dossier on the medicine, including a revised proposal for PL. This dossier must be assessed within 90 to 120 days by the CHMP before the marketing authorisation expires. This procedure is called the 'renewal procedure'.

In parallel to the scientific assessment, the EMA and its QRD group perform a linguistic review of the English version of the product information. Linguistic comments are consolidated and sent to the pharmaceutical company by Day 75 of the procedure.

4. PCO experts review

The purpose of the consultation and interaction between the EMA and PCOs is not to rewrite the document, but to confirm that the information is clear and understandable by the target audience, and that it fulfils the public's needs in terms of information content. It is acknowledged that the PL of every medicine undergoes a readability testing by target patient groups during the evaluation procedure (Articles 59(3) and 61(1) of Council Directive 2001/83/EC, as amended by Directive 2004/27/EC). The current procedure does not intend to be a repetition of it. Specific comments are recommended rather than general ones.

Review of PLs at the time of initial evaluation for marketing authorisation

PCOs experts perform the review in parallel to QRD members; thereafter the comments will be compiled for both groups (QRD members and PCO experts) simultaneously and sent to the company.

At the request of the EMA, and depending on the comments received and the issues to be discussed, PCO experts may be invited to participate in an EMA QRD sub-group meeting.

The documentation will be exchanged by e-mail (via a secure system called Eudralink), and comments should be made clear by using track changes mode (without modifying the original text).

The procedure for evaluating new PLs is as follows:

- Start of the evaluation procedure.
- EMA Medical Information Sector (MIS) will contact the coordinator(s) of the selected organisation(s) requesting availability for the review of a specific PL giving a response deadline of 5 days.
- Once an organisation has responded, MIS will provide the PL for review.
- The coordinator will organise the review and send back comments to MIS within 10 days after receipt of the document.
- QRD will validate comments and transmit them to the applicant, without naming the organisation.
- PCO experts will be informed if their participation is requested at an EMA QRD sub-group meeting.
- The CHMP will adopt the PL as part of its opinion.
- The final PL will be sent to the coordinator of the reviewing organisation for information.

Review of PLs at the time of the renewal of a marketing authorisation

The procedure for evaluating renewal PLs is the same as for new applications (above), apart from the overall application timeline (days) which are shorter, but which does not affect the review time for the PL.

Annex II

Procedure for review of EPAR summary

1. EPAR summary

When a marketing authorisation is granted for a medicine, the EMA publishes a European public assessment report (EPAR). The EPAR provides a comprehensive summary of available data on the quality, safety and efficacy of the product, justifying its marketing authorisation. The EPAR also includes a summary written in a manner that is understandable to the public.

The EPAR and the EPAR summary have to be prepared within 70 days of a CHMP positive opinion being adopted, to be available at the time of the marketing authorisation.

The first draft of the EPAR summary is prepared by the EMA, within the Medical Information Sector (MIS), immediately after the CHMP opinion. According to the internal procedure for the preparation of EPAR summaries, the first draft prepared by the Medical Information Sector is sent for consultation first to CHMP and EMA project managers (10 days), and then to the applicant (5 days). The EPAR summary is finalised within about one month, and has to be adopted by the CHMP as part of the full EPAR. Finally, the EPAR summary has to be translated into all official EU languages before publication.

2. PCO experts review

The purpose of the consultation and interaction between EMA and PCOs is not to rewrite the document, but to ensure that the information is clear and understandable by the target audience, and that it fulfils their needs in terms of information content.

PCOs will be consulted at the same time as the CHMP Rapporteur/Co-Rapporteur and EMA project managers, i.e. the 10-day consultation that takes place following the CHMP opinion.

The documentation will be exchanged by e-mail (via a secure system called Eudralink), and comments should be made clear by using track changes mode (without modifying the original text).

The procedure is as follows:

- Following an adopted opinion, the MIS will prepare a draft EPAR summary.
- The MIS will provide the draft EPAR Summary to be reviewed to the coordinator of the selected organisation.
- The coordinator will organise the review and send back comments within 10 days after receipt of the document.
- The MIS will implement the comments together with those received from other parties.
- The final EPAR summary, together with some general feedback, will be sent to the coordinator of the reviewing organisation for information.

Annex III

Procedure for review of safety communications

1. Communication tools

The Agency uses several different tools to communicate with the public, such as European Public Assessments Reports, press releases, question-and-answer documents (Q&A), summaries of opinion, monthly reports and public statements. For "safety announcements" the methods used tend to be Q&As and press releases.

Press releases are stand-alone documents which are essentially prepared by the Agency's press office and are intended for the media to help them prepare news stories.

Q&As are prepared by the Medical Information Sector (MIS), in collaboration with internal and external expertise and are written for the general public, including patients. They concern authorised medicinal products and tend to relate to major safety issues: withdrawal or suspension of a product from the market, shortage in supply or new contraindications or warnings, restriction of use or product defect for safety reasons.

Preparation of these communications (especially risk-based) implies short timelines with limited predictability but at the same time need to take into account views of many stakeholders. The procedure involves multiple stages of review and input from internal and external experts and once finalised they are published on the Agency website (as PDF files). The final version may differ substantially from the initial draft reviewed.

The selected expert(s) may discuss the document with other experts within their organisation, however all experts consulted must have signed the confidentiality undertaking in advance.

It is not initially proposed to include the review of withdrawals or refusals of applications unless patients or consumers have been involved within the medicine's benefit/risk evaluation (during evaluation).

2. PCO experts review

The purpose of the consultation and interaction between EMA and PCOs on safety communications is to ensure that the message to be conveyed is clear and comprehensible to its targeted audience and fulfils its needs in terms of information content.

PCOs will be consulted at the same time as the CHMP Rapporteur/Co-Rapporteur and EMA experts, the documentation will be exchanged by e-mail (secure system - Eudralink), and comments should be clearly defined using track changes mode (without modifying the original text).

The procedure is as follows:

- As soon as MIS is aware of an upcoming safety communication, they will contact the coordinator(s) of the selected organisation(s) requesting availability for the review of the document, indicating the nature of the communication and, when possible, the expected timelines.
- As soon as a draft document is available it will be forwarded to the selected expert(s), usually giving 12-24 hours to provide comments on the text, however in some urgent cases only 3-4 hours may be available for consultation.

- The expert(s) are welcome to contact the EMA MIS for further discussion or clarification on the specific issues and in some cases, particularly when timelines are tight, comments may be given via telephone.
- The coordinator of the relevant organisation(s) will receive a link to the final document at the time of publication and is responsible for disseminating it within the organisation and to any other interested parties - no confidentiality applies at this stage, as the document is published on the EMA website.