Clinical type II variations in the national procedure "out of scope comments"

2.2

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Scope

During the evaluation of clinical type II variations in the national procedure, the assessors or the medicines commission can have comments on SPC sections that are not affected by the variation application.

This document discusses the strategy to deal with those comments.

Discussion

- The assessment of a clinical type II variation should focus on the scope of the variation.

  When the company proposes to amend specific sections of the SPC (and leaflet), the proposed wording of those sections and the supporting scientific data should be assessed.

  The changes that the applicant proposes in specific SPC sections can also have consequences for other SPC sections. Where the assessor has comments on SPC sections that are indirectly affected by the proposed changes, those comments are considered to be within the scope of the variation. For example, when the use of the product below a specific age is introduced as a contraindication in section 4.3 there should not remain a posology for children below that age in section 4.2.

  Due to the strong link between the non-clinical data in sections 4.6 (fertility, pregnancy and lactation) and 5.3 (preclinical safety data) both sections are considered to be in the scope of the variation when changes are proposed to one of them.

- On the other hand, the assessor can note that other SPC sections (i.e. not within the scope of the variation) are not up to date, incomplete or not completely accurate.

  It is considered useful to transfer the assessor's recommendations to the company. They can, for example, to be taken into consideration in the preparation of future dossiers regarding the product (e.g. PSURs, future variations, renewals where relevant). However, those recommendations should not block or delay the ongoing variation procedure.

  The possibility to give recommendations out of the scope of the variation should not lead to full review of the SPC (or leaflet) during each variation procedure, which would lead to an inacceptable increase in workload.

  The agency does not have the intention to systematically monitor the follow-up of the recommendations. They are mainly intended as advice to the company. However, to assure a consistent treatment of the product during the lifecycle, those recommendations should also be archived in an appropriate way at the agency. This can, for example, be done in MeSeA at the medicinal product level.

It is noted that there are at least two other procedures in the agency where a distinction is made between issues to be cleared during the procedure and recommendations between future procedures, namely:

- ✓ the clinical trial applications
- ✓ the national type II variations to module 3 of the MA dossier.

- When the assessor indentifies potential major health risks that are not related to the scope of the variation it is not appropriate to communicate them as questions or recommendations in the variation procedure.

  When there is a renewal procedure ongoing, those issues can be raised during that procedure.

  If this is not the case, another procedure should be initiated to deal with those major issues, independent of the variation procedure:

  - ✓ the marketing authorisation holder can be asked for data to demonstrate that the benefit risk balance for the product remains positive, as foreseen in Article 6 §1quarter of the Medicines Law (24/03/1964), or

  - ✓ the intention to suspend, withdraw or change the marketing authorisation can be communicated to the holder who has then the possibility of an hearing, as foreseen in Article 8bis of the Medicines Law (24/03/1964)

  Those issues should in first instance be discussed between the assessor and the file manager and where necessary with the scientific coordinators and/or division heads.

Procedure

For SPC and leaflet related issues, in national clinical type II variations, a distinction will be made between:

- Questions:
  - ✓ Related to SPC (and leaflet) sections that are directly or indirectly affected by the variation application
  - ✓ A response is required during the variation procedure
- Recommendations:
  - ✓ Related to SPC (and leaflet) sections that are not affected by variation application
  - ✓ A response is not required during the variation procedure.

    The applicant can voluntary make the recommended amendments during the procedure.

For transparency reasons it is important that the assessor makes in his/her report a clear distinction between the questions and recommendations.

The FAMHP does not organise a systematic follow-up of the recommendations. However, they are appropriately archived so that they can be consulted during subsequent procedures related to the dossier.

When the assessor indentifies potential major health risks that are not related to the scope of the variation, they should be handled in an independent procedure (ongoing renewal procedure or according to article 6 §1quater or 8bis of the Medicines Law).