European Medicines Agency
Pre-Authorisation Evaluation of Medicines for Human Use

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

CONCEPT PAPER ON THE HARMONISATION AND UPDATE OF THE CLINICAL ASPECTS IN THE AUTHORISED CONDITIONS OF USE FOR RADIOPHARMACEUTICALS AND OTHER DIAGNOSTIC MEDICINAL PRODUCTS

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Comments should be provided using this template to EWPSecretariat@emea.europa.eu

Fax +44 20 74 18 86 13

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7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20)
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

1. INTRODUCTION

The clinical aspects of the conditions of use for radiopharmaceuticals were established and harmonised in Europe by means of core SmPCs formulated by an *ad hoc* group of the CHMP. However, this *ad hoc* group ceased to meet and core SmPCs have not been updated in the recent past.

2. PROBLEM STATEMENT

Nuclear Medicine and, in general, Diagnostic Imaging are medical fields employing state-of-the-art techniques which are evolving rapidly. Continuous technical advances in equipment (e.g. hybrid PET/CT cameras, functional MRI, 3 Tesla MRI, gated-SPECT, gamma probe, non-lineal ultrasound imaging, spiral CT and so on) and in software for imaging acquisition and processing mean that imaging techniques are constantly changing in clinical practice. New radiopharmaceuticals and diagnostic medicinal products are developed, new therapeutic indications are proven for those already registered, and some of these products or their indications may become obsolete. However, the summaries of product characteristics for radiopharmaceuticals have neither been updated since early 90's nor formally harmonised.

The clinical specifications for use of a single radiopharmaceutical or diagnostic medicinal product often vary significantly from one country to the other in the European market. That makes no sense, especially if this product is unique in its family. The authorisation of a generic product can lead to confusion since Health Authorities have to ask the Applicant to keep the specifications for use of the generic product similar to that of the innovator in their own country. The content of the SmPC is the most important issue from a clinical point of view, since by nature the generic application is not based on any new clinical trial and the clinical expert report is exclusively based on bibliographic references.

For radiopharmaceuticals and other diagnostic medicinal products, the clinical specifications for use of an active substance may differ in a single country or different countries. This might confuse prescribers and users becoming a potential risk for public health.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

Harmonisation and update of the clinical aspects in the authorised conditions of use for radiopharmaceuticals and other diagnostic medicinal products in the European market, by the formulation of a core SmPC for their active substance, would provide a useful document to assure consistency of their authorisation and use. This procedure would be necessary for widely used radiopharmaceuticals and certain other relevant diagnostic medicinal products registered in Europe and registered PET radiopharmaceuticals.

Update is mandatory for existing core SmPCs from a scientific point of view as well as for ensuring compliance with the Points to Consider on the Evaluation of the diagnostic agents (CPMP/EWP/1119/98), the guideline of the SmPC (October 2005) and the QRD templates for the documents of information of medicinal products. Indeed, indications for these medicinal products should be reviewed for their use with state-of-the-art techniques and to describe the population and the clinical context in which they have been studied and have actually proven to be effective and safe, as CPMP/EWP/1119/98 states, and not just the type of scintigraphic procedure. Posology, precautions of use, interaction with other medicines, adverse reactions and dosimetry should also be reviewed.

Importantly, here is also a need to implement the Euratom Directive in the core SmPCs of radiopharmaceuticals, as some of the core SmPCs contain information that is obsolete in mentioning old-fashioned indications that have little chance to be considered as a relevant justification for medical irradiation.

4. RECOMMENDATION

It is proposed to initiate a harmonisation procedure for radiopharmaceuticals and diagnostic medicinal products in order to achieve:

- An update of the relevant existing core SmPCs for:

- Those radiopharmaceuticals involved in the Coordinated Procedure taking place at the early 90's at EMEA.
- Fludeoxyglucose (^{18}F).

- A formulation of a core SmPC for:
  - Widely used radiopharmaceuticals authorised when the Coordinated Procedure concluded and in the European market (such as sestamibi, tetrofosmine, etc.).
  - Relevant registered PET radiopharmaceuticals.
  - Other relevant well-established diagnostic medicinal products commonly used in clinical practice in Europe.

This procedure could be performed by constitution of a small *ad hoc* discussion group in which the assessors of the national Medicines Agencies with expertise in the clinical evaluation of radiopharmaceuticals and diagnostic medicinal products should become part.

5. PROPOSED TIMETABLE

As soon as the Concept Paper is adopted, it is anticipated that this *ad hoc* group could begin to define which existing core SmPCs should be updated and which radiopharmaceuticals, or other diagnostic medicinal products, require a core SmPC to be formulated. Update and formulation of core SmPCs will be optimal by taking into account the existing core SmPC and any updates already performed by any Member State, or by declaring the SPCs from some recent and some ongoing marketing authorisation procedures as core SPC.

The group will initially formulate or update core SPCs for products such as fludeoxyglucose (^{18}F), flurodopa (^{18}F), radiopharmaceuticals for myocardial perfusion imaging (technetium (^{99m}Tc) sestamibi), technetium (^{99m}Tc) mertiatide/betiaitide, technetium (^{99m}Tc) macrosalb, gadolinium contrast agents, technetium (^{99m}Tc) diphosphonates, and technetium (^{99m}Tc) nanocolloids. The group will also consider current core SmPCs in order to select relevant candidates SmPC requiring update.

6. RESOURCE REQUIREMENTS FOR PREPARATION

It is anticipated that a small *ad hoc* discussion group should be constituted, and that expert assessors in the clinical evaluation of radiopharmaceuticals and diagnostic medicinal products of those national Medicines Agency actively working in this medical field should at least become part of the group.

7. IMPACT ASSESSMENT (ANTICIPATED)

It is anticipated a positive impact on a number of expectations. This procedure would contribute to harmonising the clinical conditions of use for a radiopharmaceutical and other diagnostic medicinal product within the EU, and for all of these products composed of the same active substance, preventing confusion of health professionals and avoiding differences in the healthcare of patients.

For the regulatory authorities and the industry, new therapeutic indications or clinical conditions of use of an active substance might be potentially considered for inclusion on the core SmPC as soon as it safety and efficacy can be proven. If included, they might be applied to those similar registered products. The same applies to obsolete conditions of use.

8. INTERESTED PARTIES

Regulatory authorities
Interested external parties include patients, health professionals of Nuclear Medicine and other diagnostic medical fields, pharmaceutical industry and other regulatory bodies.