EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, European Medicines Agency

PHARM 655

PHARMACEUTICAL COMMITTEE
26 March 2014

Subject: **Study on off-label use**

Agenda item 1b

1. Background: context of the study

The European Parliament adopted on 22 October 2013 a resolution[1] on the report from the Commission to the Council, on the basis of Member States' reports, on the implementation of the Council Recommendation (2009/C 151/01) on patient safety including the prevention and control of healthcare associated infections.

The resolution calls for specific action regarding the off-label use of medicines:
"Calls on the European Medicines Agency (EMA) to draw up a list of off-label medicines which are used in spite of there being an approved alternative" (paragraph 13); *"Calls on the European Medicines Agency to develop guidelines on the off-label use of medicines, on the basis of medical need and taking account of patient protection";* (paragraph 53)

The Commission reply sent to the European Parliament on 5 March 2014 states that:
"*The issue of off-label use of medicinal products is complex and deserves consideration. EMA could be an important player in that context; however, possible actions of EMA should be seen in an overall context and within the remit of its competences. Calling on EMA to draft a list of medicines used off label in spite of approved alternative may not be representative, as not all Member States have the same approved medicinal products on their market (national marketing authorisation through decentralised procedures). In addition, in some Member States recommendations and guidelines have been developed regarding off-label use. Although EU legislation regulates marketing authorisations of medicinal products, it does not specifically regulate the off-label use of medicinal products, and* ***the Commission plans to commission a study in 2014 in order to understand the ramification of the issue of off-label use of medicinal products****. In view*

[1] EP reference : A7-0320/2013 / P7_TA(2013)0435;

of this, the call for action by the European Medicines Agency would be premature" [emphasis added].[2]

The Commission services are currently drafting the terms of reference for this study and are sharing the on-going reflections with the members of the Pharmaceutical Committee in order to receive comments from Member States, in particular in view of their experience on this issue.

2. Drafting of the terms of reference:

a. Scope of the study

The study intends to cover two aspects:

- a scientific one regarding the public health aspects related to the off-label use of medicinal products and in particular patient safety;
- a legal one regarding the regulatory framework for the off-label use of medicines.

The study would gather information in order to identify if there is a need for coordination at EU level and, if so, possibly, to what extend.

To note: We do not intend to be conclusive at this stage regarding the definition of off-label use. Notwithstanding the lack of a uniform definition of off-label use of medicinal products at the EU level, it would be mostly understood as any use of an authorised product not covered by the terms of its marketing authorisation and therefore not in accordance with the summary of the product characteristics (SmPC). This usually implies that the pharmaceutical product is used:

- For a different indication,
- At a different posology or method of administration,
- For a different patient group.

The consultant would focus on above understanding, but should be able to extend- or specify the working definition as appropriate.

The possible specific and operational objectives of the study are listed below. The information and the analysis may be different depending on the interlocutors, it is therefore important for the study to systematically consult the Members States authorities and stakeholders (patients, healthcare professionals and industry) for each of these objectives as necessary.

1. **To gather comprehensive information from Member States authorities and stakeholders (patients, healthcare professionals and industry) on:**

    a. Uses/practices regarding the off-label use, including comprehensive information on the national regulatory framework;

    b. Drivers for off-label use;

[2] Commission reply will be available at the following address: http://www.europarl.europa.eu/oeil/popups/ficheprocedure.do?reference=2013/2022(INI)&l=en#tab-0

The following drivers which are already identified should be further substantiated and complemented by the contractor: availability of medicinal products due to, in particular, lack of therapeutic indications authorisation; shortage of medicinal products; cost of authorised medicinal products.

c. Measures in place and needs identified to ensure patient safety for off-label use.

2. To analyse the gathered information in particular from the point of view of:

a. The EU legal stand point, in particular in view of recent Court cases

The current Commission services position is that EU legislation on medicinal products does not regulate the so-called "off-label" use of medicinal products. It is the marketing authorisation which defines the approved indications and any departure from those terms will remain, in most Member States, the responsibility of the prescribing physician.

b. Possible specificities for particular areas (i.e. orphan, paediatric) and/or therapeutic use.

The study is a stock taking exercise with analytical elements. The conclusions of the study will be further assessed by Commission services and discussed with the Member States. It is expected that the conclusions of the study would also allow addressing the EP concerns on off-label use.

b. Methodology aspects

The study should:

- Be a comprehensive review of available documents including 'grey literature'[3] on off label use of medicinal products as well as non-official documentation;
- Include interviews /surveys with key actors from Member States authorities and stakeholders (patients, healthcare professionals and industry).

The possibility of using, inter alia, the EMA network for the information gathering and analysis is one of the options that can be discussed and explored.

3. Conclusion

We kindly invite all Member States to reflect and suggest any other issues that need to be addressed in the study or methodology approaches to be used.

[3] Publication outside the realm of commercial publishers

In particular we would appreciate if Member States would:

- Provide feedback on-going reflections at Union and national level;
- Share with Commission services (at time of drafting the terms of reference) and/or the consultant (at time of the study) internal and publicly available information/documents on the matter;
- Indicate if they would volunteer for more extended consultation during the study.