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European Commission
Health and Consumers Directorate-General
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Att.: sanco-pharmaceuticals-D5@ec.europa.eu

Date 2013-02-18

Our ref POUM_18022013
Your ref -

Subject: PCPAES/12/01 – Public Consultation on PAES
Position from H. Lundbeck A/S on a delegated act on post-authorisation efficacy studies – Ref. Ares(2012)1405774 – 28/11/2012

Dear Sir/Madam,

H. Lundbeck A/S welcomes this reflection paper and appreciates the possibility to provide comments.

We support the response submitted by the European Federation of Pharmaceutical Industries and Associations (EFPIA).

We would like to stress that the study methodology (investigational/non-investigational) should be defined according to the purpose of the PAES.

As described in the legislation, a PAES aims to respond to specific efficacy question(s) raised by the competent authorities (e.g. CHMP/PRAC) and the design should subsequently be adapted to PAES objectives. Therefore the most suitable PAES design could either be investigational (i.e. RCT) or non-investigational (e.g. observational study) and should be envisaged on a case-by-case basis with the regulators.

In addition, benefit aspects of a medicinal product collected during life-cycle management should be considered in real-life settings as well as in classical settings, especially where RCTs would lack appropriate/sensitive efficacy measures to detect the effect in real-life or if the study is not comparative. In this respect it is important to consider the need for external validity where further evaluation in the post-approval setting may be needed to satisfy both regulatory and payer requirements. As stated in the reflection document for a Delegated Act, this external validity will not be achieved with a RCT design per definition, and needs real-life conditions.

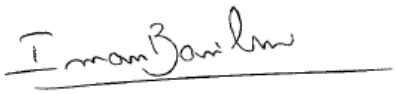
The current legislation provides support for this interpretation:

- Art. 9(4)(cc) of Regulation 726/2004/EC as amended and Art. 21a of Directive 2001/83/EC as amended: PAES may be required after an initial marketing authorisation where '*concerns relating to some aspects of the efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed'*.
- Recital 16 of Regulation 1235/2010/EU: *'such studies* (PASS and PAES) *may be aimed at collecting data to enable the assessment of safety or efficacy of medicinal products for human use in everyday medical practice'*.

We acknowledge the Commission's view that the real-life methodologies '*have limitations'*, including '*issues concerning data quality and completeness'*. However, such concerns should not limit the use of observational studies as they, although yielding a different level of evidence and addressing different populations and designs, can be performed with suitable quality, appropriate design and valid statistical analyses.

Finally, while PAES results aim at supplying the benefit aspect of the balance, PASS data, which are mainly collected in real-life conditions, aim at supplying the risk aspect. It would be beneficial that the benefit-risk balance is also assessed (as complementary to potential investigational study) under real-life conditions during life-cycle of the products. This was already highlighted in the EMA reflection paper on benefit-risk assessment methods (EMEA/CHMP/15404/2007, where the EMA recommends expanding the benefit-risk methodology to incorporate post approval safety/effectiveness data into the risk/benefit analysis (lifetime approach).

Yours faithfully,



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