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TER BEOORDELING VAN
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C B G
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MEDICINES
EVALUATION
BOARD

Directorate-General for Health and Consumers
Unit SANCO/D/5
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Your letter	Your reference	Utrecht,
--	11	18 February 2013
Casenumber	Our reference	
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Re:
PCPAES/12/01 — Public Consultation on PAES

L.S.

Please find below the response of the Medicines Evaluation Board (MEB) of the Netherlands on the consultation paper:

DELEGATED ACT ON POST-AUTHORISATION EFFICACY STUDIES (ARTICLE 10B OF REGULATION (EC) NO 726/2004 AND ARTICLE 22B OF DIRECTIVE 2001/83/EC)

The scope of the document is to start discussion on those situations in which post-authorisation efficacy studies (PAES) may be required. This in order to complement the data available at the time of authorisation with additional data about the efficacy of a medicinal product.

Position statement/Discussion/recommendations

The life-cycle of a pharmaceutical product is a continuous process of which a successful application is a part. The information based on the pre-registration dossiers is limited for both efficacy and safety. Hence as the development of a drug has not ended the need for post-authorisation studies for both efficacy and safety is foreseeable.

However, new developments are often unpredictable and it is questioned whether this can be regulated in detail as this assumes a level of predictability.

In principle a request for Post-Authorisation-Marketing-Efficacy-Studies can be made either in the context of a RMP, conditional approval, approval under exceptional circumstances, referrals,

suspension, but also on an ad hoc basis when during a life cycle of a pharmaceutical product relevant issue emerges. It is questioned whether this should be further formalised in detail in the context of a delegated act. An evaluation of the effectiveness of the existing options is recommended.

It is emphasised that post authorisation efficacy studies should not be used to compromise the initial level of evidence that is required to grant a marketing authorisation for the specific product.
An increased possibility of post authorisation efficacy studies should therefore not be used as an instrument for premature approval i.e. a benefit/risk assessment is difficult. Which data are needed pre-approval are reflected in the guidelines and subject of Scientific Advices.
In the document a limited number of situations are described as justification for requesting post-authorisation efficacy. Indeed these situations all have been used as justification for asking additional efficacy studies. However, the same situations have also been used as justification for labelling dossiers premature. Hence the situations described are mainly examples, not criteria. They should neither be used as a 'tick box' instrument, nor seen as a limiting list, but should be considered together in context where it is applied too i.e. on a case by case basis.
The importance for effectiveness studies, relative efficacy studies, pragmatic trials, real-life information is acknowledged and supported. However study designs should be dictated by the question the study tries to address. Conclusion of efficacy is based on causal inference for which randomised controlled studies are the better options.

The principle of an obligation to conduct post authorisation efficacy studies when requested as part of the marketing condition and that the results may have a direct impact on maintenance, revision or withdrawal of the marketing authorisation is agreed. However, this also should oblige regulatory authorities to justify the request, to reflect on the relevance of the study requested and to anticipate on the likelihood different outcome scenarios of the study and their consequences for marketing authorisation. The anticipated feasibility to perform this study may be part of the decision making as well. The proposal in the document does in the opinion of the Medicines Evaluation Board not address this sufficiently.

A.A.W. Kalis
Executive Director of the Medicines Evaluation Board in the Netherlands