MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
E IGUALDAD

agencia española de
medicamentos y
productos sanitarios

DEPARTAMENTO DE
MEDICAMENTOS
DE USO HUMANO

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

Comments from the Spanish Agency of Medicines and Medical Devices

14 February, 2013

Consultation item No 1: Do you think that a delegated act on the situations in which a post-authorisation efficacy study may be required will be of added value and that the Commission should consider bringing forward a draft delegated act? Please provide reasons for your opinion.

A delegated act is needed, if this is interpreted as a pre-requisite for requesting post-authorisation efficacy studies as a condition of the marketing authorisation, either at the time of authorisation or at any time after authorisation.

Consultation item No 2: Do you have any comments on the above? Do you agree that generally speaking post-authorisation efficacy studies should focus on generating efficacy data?

We agree that generally speaking post-authorisation efficacy studies should focus (but not strictly) on generating efficacy data, including (relative) efficacy in real life conditions, as stated in the new pharmacovigilance legislation.

However, we do not share the Commission statement about pragmatic and observational studies. Pragmatic clinical trials are by design experimental studies and are not considered observational studies. In other words, they assign treatments by protocol and therefore, are considered clinical trials. The main difference between a pre-authorization clinical trial and a pragmatic trial is that inclusion and exclusion criteria are broader, with the purpose of capturing data in conditions closer to real life. Regarding observational studies (study design or nature), they are not necessarily based only on the collection and analysis of patient registries (a type of information source).

Post-authorization efficacy studies related to the new pharmacovigilance legislation and imposed by regulatory authorities should help regulatory decision making, beyond the general objective of increasing knowledge about the medicine. It is clear that if the medicinal product is not able to show any efficacy in the population taking the drug once marketed, this has a mayor impact in the benefit-risk, as shown in recent examples. Obviously, the methodology of the study should be the appropriate to give answer to the study objectives.

,. Efficacy, comparative/relative efficacy, effectiveness, and comparative/relative effectiveness are all related to properties in different situations of a single medicine and

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should be part of a complete and comprehensive evaluation process. In particular, the evaluation of a medicine is a continuum throughout its entire life cycle, and should consider treatment options available (comparators with therapeutic value) in clinical and community practice. Regulation must be flexible enough to incorporate the knowledge about a medicine derived from different types of data sources and/or study designs, taking into account their reliability, consistency and reproducibility.. Separation between those dealing with efficacy (usually regulators) and those dealing with relative/comparative effectiveness (usually payers) is somewhat artificial, since, as stated above, a lack of demonstration of efficacy/effectiveness in real users should lead to regulatory actions, as has been the case in recent examples. Thus, it should be the medicine (the useful knowledge on a given medicine), and not the methodology, the core of the system.

Regulator must incorporate all relevant information about medicines irrespective of the source of this information.

Consultation item No 3: Please comment on the seven different situations described above. Do you agree that in these situations, a competent authority may ask for a post-authorisation efficacy study? Are there any other situations not covered by points 5.1 to 5.7 in which it would also be justified to oblige a marketing authorisation holder to conduct an efficacy study? If this is the case, could you please elaborate on these situations and, if possible, give specific examples to underpin the need?

Yes, we do agree that in the seven different situations stated in the document, a post-authorization efficacy study can be requested. However, the delegated act should not be restrictive to these situations, since other justified circumstances in which a post-authorisation efficacy study is necessary may be envisaged in the future.

Regarding the first situation (5.1, studies aimed at determining clinical outcome following initial assessment based on surrogate endpoints), it should not be restricted to the area of oncology. There are many other areas in which surrogate endpoints are being used and results in the clinical outcome are needed (e.g. clinical cardiology). Recent drug withdrawals of drugs used for very prevalent conditions have been based on the failure to demonstrate efficacy in clinical outcomes, despite beneficial effects on surrogate endpoints.

Consultation item No 4: Do you have any comments on the above?

See above.

Consultation item No 5: Please feel free to raise any other issues or make any comments which have not been addressed in the consultation items above.

No further comments

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