National Institute for Health and Clinical Excellence

PCPEAS/12/01

Public consultation on PAES

Response from The Centre for Health Technology Evaluation

National Institute for Health and Clinical Excellence

Question 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?

1. We welcome the opportunity to comment on the proposals and support the greater involvement of HTA agencies in ENCEPP.

2. The consultation document does not specify the potential implications of the provision of a delegated act or the details of what will be included. It is therefore difficult for us to comment in detail on the proposals.

3. It would seem prudent to allow for greater clarity and enforcement, than currently provided, for the EMA to require companies to produce the necessary data. Additionally, re-assessments of the benefit risk balance of medicines would also seem pertinent in circumstances where efficacy may alter over time, for example in the case of antimicrobials or when the risk-benefit balance alters in the light of new information generated by more widespread use in populations beyond those included in the initial registration RCTs.

4. There is a balance to be made between guidance that provides clarity and precision and that which is overly restrictive and prevents action in circumstances that could not be anticipated at the time of drafting.

5. The potential impact on healthcare systems and, therefore, overall public health should be considered when drafting legislation. If the legislation becomes more permissive towards allowing use of medicines alongside the collection of follow-up data, healthcare systems may become more cautious in their willingness to recommend newly licensed medicines for routine use. This may particularly be the case if those healthcare systems are required to support the data collection either financially or in terms of infrastructure. To avoid a negative impact across the innovation and healthcare system, there must be a direct relationship between the indications permitted in the initial marketing authorisation and the specification of further data collection on efficacy for potential future indications. This will strike the appropriate balance between permitted use within the marketing authorisation and the generation of the necessary data.

6. The legislation should not introduce perverse incentives for companies not to provide the data to answer relevant questions before initial licensing application, for example not collecting data in known sub-groups where efficacy is anticipated to be different from the overall population.

Question 2: (PAES should generally focus on the collection of efficacy data as opposed to “real-life” data’)

7. As the consultation document notes, there is a need for clarity and consistency over terminology. The document also notes the trade-offs between internal validity and generalizability, which arise due to the different decision-making paradigms that are used by regulatory and reimbursement/HTA bodies.

8. The call for additional post-authorisation efficacy data may appear to unduly increase the data-burden and additional costs on companies. It would therefore seem sensible to develop a mechanism for providing the necessary data that specifies the minimum data set needed to

address the uncertainty together with the least burdensome approach to generating the data, whilst still ensuring rigour in methodology. Guidance should explore the use of other relevant study designs for generating the data, for example, adaptive trial designs or cluster randomisation.

9. The new requirements should not be used as an alternative to the generation of appropriate clinical data during product development. Early joint scientific advice between regulators and HTA bodies can ensure that the best data is generated before the point of authorisation and reimbursement.

Question 3 (whether the types of PAES studies are appropriate)

10. The seven scenarios outlined in the consultation document all seem to be appropriate. Data generation requirements for additional combinations with other medicinal products should reflect those likely to occur in everyday clinical practice.

11. An additional useful scenario is the impact of withdrawal of treatment where these are given on a long-term basis (for example ‘rebound’ effects in rheumatoid arthritis).

12. As noted previously some of the scenarios requiring long term efficacy or clinical endpoints might be challenging and costly if a strict ‘efficacy data generating framework’ is used. The use of other clinical study methodologies should be considered, depending on the nature of the clinical uncertainty.

Question 4 (comments on study design)

13. Review of guidance should be planned in the light of advances in the methodology of clinical trial design and the use and novel approaches to the generation of clinical data and analysis of health outcomes generated in ‘real life’ should be encouraged.

Question 5 (any other issues)

14. The document refers to ‘European standard of care’. This concept is not implementable. In particular, it is impossible to identify a single standard of care at a European level. A process that considers the clinical patterns of member states before determining appropriate study designs and protocols should be developed.