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Committee for Human Medicinal Products (CHMP)

Concept paper on an addendum to the note for guidance on evaluation of medicinal products indicated for treatment of bacterial infections (CPMP/EWP/558/95 rev 2) to address indication-specific clinical data requirements

Agreed by Infectious Diseases Working Party	July 2011
Adoption by CHMP for release for consultation	22 September 2011
End of consultation (deadline for comments)	31 December 2011

Comments should be provided using this template. The completed comments form should be sent to IDWPSecretariat@ema.europa.eu

Keywords	Treatment of bacterial infections, guidance, data requirements

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1. Introduction

This Concept Paper proposes the development of an addendum to the Note for Guidance on Evaluation of New Anti-bacterial Medicinal Products (CPMP/EWP/558/95 Rev 2).

During the revision of the previous version of the guideline (CPMP/EWP/558/95 Rev 1) consideration was given to the need to develop guidance on clinical data requirements to support the approval of specific indications for use. During the consultation period several requests were made for the CHMP to provide more detailed guidance on issues such as patient selection criteria and primary endpoints, including efficacy variables and the timing of the assessment of outcomes. It was proposed that CHMP should give further consideration to, and provide additional clarification regarding, indications for which superiority or non-inferiority study designs could be accepted. In the case of superiority studies, it was requested that further consideration should be given to the feasibility of conducting comparisons between test agents and either placebo or active comparators. In the case of non-inferiority studies there were requests for further consideration of appropriate values of delta. More guidance was considered to be needed regarding clinical development programmes for new antibacterial agents with potential for clinical activity against rare and/or multidrug-resistant pathogens and the accumulation of data to support indications for which there is currently no established regulatory pathway.

In order to gain further insight into the issues raised during consultation a 2-day Workshop was held in February 2011 at which representatives from the pharmaceutical industry and academia met with EU Regulators to discuss several of these matters (for further details see here). Taking into account the written comments received during the consultation period and the discussions during this Workshop it appeared to be appropriate to provide additional guidance along the lines requested. It is proposed that following adoption of the revision of the main guidance document an addendum should be developed to provide indication-specific guidance. The issues that have been identified for inclusion or further consideration in the addendum are detailed below.

2. Problem statement

The content of CPMP/EWP/558/95 Rev 2 covers the general approach to the development of antibacterial agents. This guideline (as with its predecessors) does not provide detailed indication-specific guidance. It is now apparent that such guidance is needed in order to describe and clarify the CHMP's position on various matters.

3. Discussion (on the problem statement)

In the case of indications that are commonly sought by sponsors the CHMP has established a position on several matters that to some extent may be discerned from the outcomes of recent procedures. However, the position of CHMP is not adequately reflected in current guidance and the main guideline does not give detailed consideration of issues that are of importance when designing studies to support specific indications for use. For some indications there is no established position regarding clinical data requirements either because such types of use are rarely studied or because the existing guidance does not cover the particular problems posed by individual new agents. To some extent, the guidance that can be provided must be regarded as provisional or at least open to adaptation as experience is accumulated with very novel agents and to fit specific circumstances. Therefore it will be important to acknowledge that not all the guidance that may be included in the addendum could or should be regarded as definitive.

4. Recommendation

The Working Party/Committee recommends that an addendum to the Note for Guidance on Evaluation of New Anti-bacterial Medicinal Products (CPMP/EWP/558/95 Rev 2 should be developed to incorporate guidance on the following matters:

Major and commonly sought indications for severe infections

(e.g. community- and hospital-acquired pneumonia, complicated urinary tract, skin and soft tissue and intra-abdominal infections)

- Further clarification on patient selection criteria, primary efficacy variables, timing of the primary assessment of outcomes and suggested non-inferiority margins.

Indications for which placebo arms could be envisaged

(e.g. acute bacterial sinusitis, exacerbations of obstructive airway disease and otitis media)

- Consideration of indications and specific patient populations for which non-inferiority study designs might be acceptable and suggestions for non-inferiority margins.
- Consideration of indications and specific patient populations for which non-inferiority study designs are not currently acceptable and suggestions for possible regulatory pathways.

Other indications for use that might be sought

(e.g. specific endorsements for use in bacteraemic patients, in neutropenic patients suspected to have bacterial infections and for the eradication of carriage)

- Discussion of expectations regarding the extent of the data to be collected.
- Consideration of possible specific study designs.
- Consideration of reflection of the clinical evidence in the SmPC.

Novel antibacterial agents with specific properties

(e.g. agents for which the usual approach to clinical development is not appropriate/feasible, including agents that may have clinical utility against rare and/or multidrug-resistant pathogens)

- Consideration of the minimum data requirements and study design.
- Consideration of the possible adaptations of clinical development programmes to support specific indications for use and how the clinical evidence might be reflected in the SmPC.

5. Proposed timetable

- Adoption of Concept Paper by IDWP/CHMP September 2011.
- First draft revision agreed by IDWP during 2Q2012.
- Release for consultation 2Q2012 for a period of 6 months.
- Finalisation during 4Q2012 – 1Q2013.

6. Resources required for preparation

The resources needed for this addendum relate to IDWP members who will develop the draft addendum and proceed to develop a final version after the consultation period.

It may be considered appropriate at a later stage (e.g. during or immediately following the consultation period) to convene a Workshop to facilitate finalisation of the addendum.

7. Impact Assessment (Anticipated)

The most important impact is expected to be on:

- clinical development in the most sought indications related to severe infections for which a clearer definition of the EU regulatory requirements would be beneficial in the streamlining of the programmes.
- Global clinical development programmes to support indications for use for which regulatory requirements may differ and may have important implications for study designs and analyses.
- The development of antibacterial agents for use in indications for which there are no well-established clinical data requirements and/or for which there are potential problems surrounding the feasibility of some types of study designs.
- The development of novel antibacterial agents for which the more usual approaches to clinical development are unsuitable because of their specific properties (e.g. very limited spectra of antibacterial activity).
- The content of CHMP scientific advice to sponsors on the abovementioned matters will need to take into account the content of the addendum.

8. Interested Parties

As listed previously for the development of CHMP/EWP/558/95/Rev 1.

9. References to literature, guidelines etc