



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Concept paper on the revision of the guideline on non-clinical and clinical development of similar biological medicinal products containing low-molecular-weight heparins

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| Agreed by Biosimilar Medicinal Products Working Party (BMWP) | June 2011 |
| Adoption by CHMP for release for consultation | 21 July 2011 |
| End of consultation (deadline for comments) | 30 September 2011 |

The proposed guideline will replace Guideline on Non-clinical and Clinical Development of Similar Biological Medicinal Products containing Low-Molecular-Weight Heparins, EMEA/CHMP/BMWP/118264/2007.

Comments should be provided using this [template](#). The completed comments form should be sent to BMWP.Secretariat@ema.europa.eu

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| Keywords | Low molecular weight heparins, similar biological medicinal products, non-clinical studies, clinical studies |
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1. Introduction

The Guideline on Similar Medicinal Products containing Low-Molecular-Weight Heparins (LMWH) lays down the non-clinical and clinical requirements for the development of LMWH claimed to be similar to a reference product already authorised in the EU. This guideline came into effect in October 2009. So far, no biosimilar LMWH has been licensed in the EU.

2. Problem statement

LMWHs are complex sugar molecules and difficult to characterise. Structure-activity relationship is not fully elucidated and other mechanisms of action beyond Anti-Xa and Anti-IIa activity may be important for the pharmacological activity.

The current CHMP guidance requires a comparative clinical trial demonstrating similar efficacy and safety of the biosimilar versus the reference LMWH in the prevention of venous thromboembolism (VTE) in patients undergoing major orthopaedic surgery.

Based on scientific and analytical progress, e.g. in the field of physicochemical characterisation, it can be discussed if in exceptional cases convincing analytical data can substitute for clinical data, at least for clinical efficacy.

3. Discussion (on the problem statement)

The BMWP suggests discussing the inclusion of considerations about the possibility to modify clinical data requirements in the guideline taking into account the extent and quality of characterisation and the possibility to convincingly ensure similar efficacy and safety (including immunogenicity) of the biosimilar and the reference LMWH by other means. It should be discussed if a reduction in clinical data requirements could, in exceptional cases, be possible.

4. Recommendation

The Working Party recommends revising the *Guideline on Non-clinical and Clinical Development of Similar Biological Medicinal Products containing Low-Molecular-Weight Heparins* (EMA/CHMP/BMWP/118264/2007).

As part of this revision, the Working Party recommends a discussion about including the possibility of a modification in clinical data requirements, providing similarity of physicochemical characteristics of the biosimilar and the reference LMWH has been convincingly shown and similar efficacy and safety can be ensured by other means.

At the same time there should be a discussion if for the non-clinical part a risk-based approach should be introduced as currently discussed for other biosimilar products.

5. Proposed timetable

It is anticipated that the draft revised guideline will be released for consultation in the first semester of 2012.

6. Resource requirements for preparation

The BMWP experts will develop the guideline. At least one formal meeting of the drafting group will be required in the margins of the working party meetings.

7. Impact assessment (anticipated)

Anticipated benefit for industry (potentially reduced requirements) and assessors of biosimilar low-molecular-weight heparin containing products.

8. Interested parties

- Pharmaceutical industry and competent authorities of the Member States.
- CHMP and its working parties, especially BWP and SAWP.

9. References to literature, guidelines, etc.

- Part II of the Annex I of Directive 2001/83/EC, as amended
- Guideline on similar biological medicinal products (CHMP/437/04)
- Guideline on Similar Biological Medicinal Products containing Biotechnology-Derived Proteins as Active Substance: Quality Issues (EMA/CHMP/BWP/49348/2005)
- Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues (EMA/CHMP/BMWP/42832/2005)
- ICH topic S6 - Note for guidance on Pre-clinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals (CPMP/ICH/302/95)