



**COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
(CHMP)**

**CONCEPT PAPER ON THE REVISION OF THE GUIDANCE ON SIMILAR BIOLOGICAL
MEDICINAL PRODUCTS CONTAINING RECOMBINANT ERYTHROPOIETINS**

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| AGREED BY THE SIMILAR BIOLOGICAL MEDICINAL PRODUCTS WORKING PARTY (BMWP) | July 2008 |
| ADOPTION BY THE COMMITTEE FOR HUMAN MEDICINAL PRODUCTS (CHMP) FOR RELEASE FOR CONSULTATION | July 2008 |
| END OF CONSULTATION (DEADLINE FOR COMMENTS) | October 2008 |

The proposed guideline will replace guideline EMEA/CHMP/BMWP/94526/2005

Comments should be provided electronically in word format using this [template](#) to BMWP.secretariat@emea.europa.eu

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| KEYWORDS | erythropoietins, recombinant, similar biological medicinal products, indication, extrapolation |
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1. INTRODUCTION

This guideline lays down the non-clinical and clinical requirements for erythropoietin-containing medicinal products claiming to be similar to another one already marketed.

The non-clinical section addresses the pharmaco-toxicological assessment. The clinical section addresses the requirements for pharmacokinetic, pharmacodynamic, efficacy and safety studies as well as the risk management plan. The possibility of extrapolation of clinical data to other indications approved for the reference medicinal product is discussed.

2. PROBLEM STATEMENT

The current guideline has been written based on solid scientific rationale and on theoretical considerations because no experience with marketing authorisation applications (MAAs) for biosimilar erythropoietins was available at that time. In the meanwhile, experience has been gained through Scientific Advice procedures and MAA assessment. Further applications are expected. During the assessments of these biosimilar erythropoietins it was recognised that the guideline needed refinement to take into account several practical considerations relating to the development of biosimilar epoetins.

3. DISCUSSION

The CHMP considers that the following points need to be revisited:

- The recommendation for the clinical data package as stated in the guideline is based on the assumption that both routes of administration (SC and IV) are approved for the reference product and that both routes are applied for by the biosimilar erythropoietin. The current clinical data requirements include phase III studies for both routes of administration because PK profiles and dose requirements usually differ. Based on the experience gained with the recent applications for biosimilar erythropoietins, it should be discussed whether and under which conditions extrapolation of efficacy data from one to the other route of administration via bridging studies (e.g. single dose and multiple dose PK/PD studies) could be an acceptable alternative.
- The possibility of extrapolation of efficacy and safety data to other indications of the reference product should also be reviewed.
- The current guideline recommends a study duration of at least 3 months and ideally 6 months for demonstration of comparable efficacy in both the correction phase and the maintenance phase study. Since stable dosing conditions are often not achieved within 3 months, a longer comparative observation period (e.g. at least 6 months) might be more appropriate.
- The guideline requests at least 12-month comparative immunogenicity data pre-licensing. It should be further highlighted and explained that a comparative phase less than the recommended 12 months might be of concern and under which circumstances this could be acceptable.
- It should be discussed whether immunogenicity evaluation for the SC route only will be sufficient for marketing authorization.
- Other parts of the guideline should be revisited and revised as appropriate.

4. RECOMMENDATION

The BMWP recommends revising the guidance on similar biological medicinal products containing recombinant erythropoietins to reflect the experience gained.

5. PROPOSED TIMETABLE

It is anticipated that a first draft will be available within 3 months after adoption of the concept paper and that the draft revised guideline will be adopted and released for consultation in the last quarter of 2008.

6. RESOURCE REQUIREMENTS FOR PREPARATION

BMWP will be responsible for the revision of the guideline and will seek advice, if needed, from BWP, EWP, SWP and PhVWP.

7. IMPACT ASSESSMENT (ANTICIPATED)

It is important to keep the guidance up-to-date in the currently rapidly moving field of biosimilar medicinal products. The revised guideline will provide improved guidance for both industry and Regulatory Authorities regarding the clinical development and assessment of biosimilar erythropoietin-containing medicinal products.

8. INTERESTED PARTIES

Competent authorities of the member states, and pharmaceutical industry.

9. REFERENCES TO LITERATURE, GUIDELINES

- Directive 2001/83/EC, as amended.
- 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: Non-Clinical and Clinical Issues (CHMP/42832/05)
- Guideline on Immunogenicity Assessment of Biotechnology-derived Therapeutic Proteins (CHMP/BMWP/14327/06)