EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human use (CHMP)

Concept paper on the need for revision of the guideline on the evaluation of medicinal products in the treatment of primary osteoporosis

Agreed by Rheumatology/Immunology Working Party	August 2012
Adopted by CHMP for release for consultation	08 October 2012
Start of public consultation	01 November 2012
End of consultation (deadline for comments)	31 January 2013

The proposed guideline will replace guideline on the evaluation of medicinal products in the treatment of primary osteoporosis (CPMP/EWP/552/95 Rev. 2)

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

Keywords	Glucocorticoid induced osteoporosis, Paediatric GIOP, Bone mineral density, Post-menopausal osteoporosis

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1. Introduction

Oral glucocorticoid therapy is widely used for the treatment of a variety of diseases. Approximately 1% of the population is prescribed oral glucocorticoids, and in the elderly this prevalence rises to 2.5%[1]. The association between glucocorticoid therapy and osteoporosis is well documented[2]. Bone loss is particularly rapid in the first few months after initiation of therapy, with a slower rate of loss subsequently[3]. Fracture risk also increases rapidly during the early months of therapy and declines after its cessation[4,5]. Although the severity of glucocorticoid induced osteoporosis (GIOP) is related to the dose and duration of glucocorticoid therapy, some increase in fracture risk is seen even at daily doses of ≤7.5 mg daily for 3–6 months. In addition the effect of glucocorticoids on bone fragility is, to some extent, independent of bone mineral density, fractures occurring at a higher bone mineral density (BMD) threshold than in postmenopausal osteoporosis (PMO)[6,7,8].

2. Problem statement

Currently, the only guidelines dealing with osteoporosis are intended to provide guidance for the evaluation of new medicinal products in the treatment of primary osteoporosis, principally in postmenopausal women but also in men. They specifically mention that secondary osteoporosis, especially glucocorticoid therapy are not covered by this guideline9. There are several agents available for PMO and there is a clinical need for therapies with proven efficacy in GIOP. In addition GIOP in children needs to be addressed.

3. Discussion (on the problem statement)

The design and endpoints of clinical studies required for demonstration of efficacy in GIOP for different populations including children and pre-menopausal women will be addressed. Particular problems relating to the diagnosis of GIOP in children will be discussed.

4. Recommendation

The RIWP recommends updates to the "Guideline on the evaluation of medicinal products in the treatment of primary osteoporosis" (CPMP/EWP/552/95 Rev. 2).

Points to be addressed in the addendum include:

- the need to differentiate the indications "prevention" and "treatment" of GIOP (i.e., intervention at the start of glucocorticoid therapy and intervention after at least 3 months of glucocorticoid therapy);
- the need to separate estimation of efficacy in females and males;
- the need to separate estimation of efficacy in premenopausal and postmenopausal females;
- the need to use placebo-controlled studies with fracture as a primary endpoint or to use bone mineral density, or even other biochemical endpoints, as an acceptable surrogate endpoint;
- the expected duration of the studies;
- specific approaches for the definition of GIOP in children;
- BMD estimation in children

It is proposed to update the CHMP Guideline addressing the clinical investigation of medicinal products for the treatment of GIOP in order to achieve a European common position on the above-mentioned issues.

5. Proposed timetable

It is anticipated that the updated draft CHMP Guideline will be available within 6 months after adoption of the concept paper. The draft CHMP guideline will then be released for 6 months for external consultation and following receipt of comments it will be finalised in approximately 3 months.

6. Resource requirements for preparation

The preparation of this Guideline will involve the RIWP and close cooperation with PDCO is envisioned.

7. Impact assessment (anticipated)

It is expected that the number of products developed with the intention to treat GIOP will increase in the near future. Therefore it is expected that such guidance document would improve quality and comparability of submitted studies by pharmaceutical industries.

8. Interested parties

International Osteoporosis Foundation;

International clinical densitometry society

The Group for the Respect of Ethics and Excellence in Science;

European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis.

9. References to literature, guidelines, etc.

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