EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Paediatric Investigation Plans for treatment of osteoporosis

Presentation to EMA expert meeting 2 June 2014

Presented by: Richard Veselý
Scientific officer

The European Medicines Agency (EMA)

7, Westferry Circus
Canary Wharf
London E14 4HB
United Kingdom

www.ema.europa.eu

The European Medicines Agency (EMA)

30 Churchill Place
Canary Wharf

The EMA Mission…

is to foster scientific excellence, for the benefit of public and animal health.

Guiding principles

We are strongly committed to public and animal health.

We support research and innovation to stimulate the development of better medicines.

Gatekeeper and Enabler

The European Medicines Agency (EMA)

EMA is an interface for co-operation and co-ordination of Member States' activities with respect to medicinal products

EMA scientific work is carried out through its scientific committees

- CHMP (Committee for Human Medicinal Products)
- CVMP (Committee for Veterinary Medicinal Products)
- HMPC (Committee for Herbal Medicinal Products)
- COMP (Committee for Orphan Medicinal Products)
- CAT (Committee for Advanced Therapy Medicinal Products)
- PDCO (Paediatric Committee)
- PRAC (Pharmacovigilance & Risk assessment Committee)

Agency activities

- Management of the Centralised Procedure
- Human and veterinary, chemical and biological products
- Evaluation of new products, generics, OTCs
- Scientific advice and protocol assistance to companies
- Orphan drugs designation
- Review of Paediatric Investigation Plans (PIP)
- Regulatory & scientific guidance (guidelines) to companies
- Support to Small and Medium Sized companies (SMEs)
- Arbitration and referral procedures for national medicines
- Coordination of EU pharmacovigilance activities
- Coordination of Member States' inspections *(GMP, GCP, GLP)*

EU Paediatric Regulation

Entry into force 26 January 2007

REGULATION (EC) No 1901/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004

Objectives:

Improve the health of children

- Increase high quality, ethical research into medicines for children
- Increase availability of authorised medicines for children
- Increase information on medicines

Achieve the above

- Without unnecessary studies in children
- Without delaying authorisation for adults

General authorisation requirements

Article 7

• (a) the results of all studies performed and details of all information collected in compliance with an agreed **paediatric investigation plan**;

(b) a decision of the Agency granting a product-specific **waiver**;

(c) a decision of the Agency granting a class waiver pursuant to Article 11;

(d) a decision of the Agency granting a deferral.

• The documents submitted pursuant to paragraph 1 shall, cumulatively, cover all subsets of the paediatric population.

Paediatric investigation plan

Article 15

The paediatric investigation plan shall specify

• the **timing** and the **measures** proposed to assess the *quality, safety and efficacy* of the medicinal product

• in **all subsets of the paediatric population** that may be concerned.

In addition, it shall describe any measures

• to adapt the **formulation** of the medicinal product so as to make its use *more acceptable, easier, safer or more effective* for different subsets of the paediatric population.

Waiver

Article 11

Grounds for waiver:

(a) that the specific medicinal product or class of medicinal products is likely to be **ineffective or unsafe** in part or all of the paediatric population;

(b) that the disease or condition for which the specific medicinal product or class is intended **occurs only in adult** populations;

(c) that the specific medicinal product does not represent a **significant therapeutic benefit** over existing treatments for paediatric patients.

EMA = A Networking Agency

- National competent authorities in 28 Member States
- Agency is an interface of co-operation and co-ordination of Member States' activities with respect to medicinal products
- European **experts' network** underpins the work of the Agencies' Committees (6) and working parties
- Expert list of 4,900 nominated experts
- European Commission, European Parliament, other EU agencies (ECDC, EFSA), European Pharmacopoeia ...

Clinical and regulatory guidelines –different universes?

Need to overcome discrepancies

- Not identical scope
- Potentially different approach

- Collaboration
- Mutual learning, exchange of expertise

Condition vs. indication

CHMP opinion is on the **indication**, consequently indication is authorised.

PDCO opinion is on the **condition**

30 July 2012
EMA/272931/2011
Human Medicines Development and Evaluation

Policy on the determination of the condition(s) for a Paediatric Investigation Plan/Waiver (scope of the PIP/waiver)

Background

Experience with the evaluation of Paediatric Investigation Plans (PIP) has shown that a systematic and consistent approach is needed to determine the condition(s) of a PIP in relation to the proposed indication(s) as determined by the applicant. An approach based on the characteristics of the product and a hierarchical classification of diseases and conditions should provide a framework for both the applicants and the PDCO evaluating the PIPs.

Regulation (EC) No 1901/2006 on medicinal products for paediatric use (hereinafter the Paediatric Regulation) [1] requires that an application for marketing authorisation includes the elements

How the PIP condition is identified?

1. Proposed indication in adults
2. Properties of the product (mechanism of action)
3. Unmet paediatric needs
4. Hierarchical classification of diseases
5. Treatment, prevention or diagnosis of the disease

Condition: Treatment of osteoporosis

Proposed indications in adults:

Treatment of postmenopausal osteoporosis (class waiver revoked in April 2009)

Treatment of male osteoporosis

Treatment of primary osteoporosis

Treatment of secondary osteoporosis (e.g. GIOP…)

Indications in children:

Treatment of glucocorticoid induced osteoporosis

Treatment of osteogenesis imperfecta

Agreed PIPs and waivers in treatment of osteoporosis

PIPs:

Zoledronic acid

Odanacatib

Denosumab

Waivers:

Lasofoxifene

Arzoxifene

Strontium

Bazedoxifene/Conjugated estrogens

Teriparatide

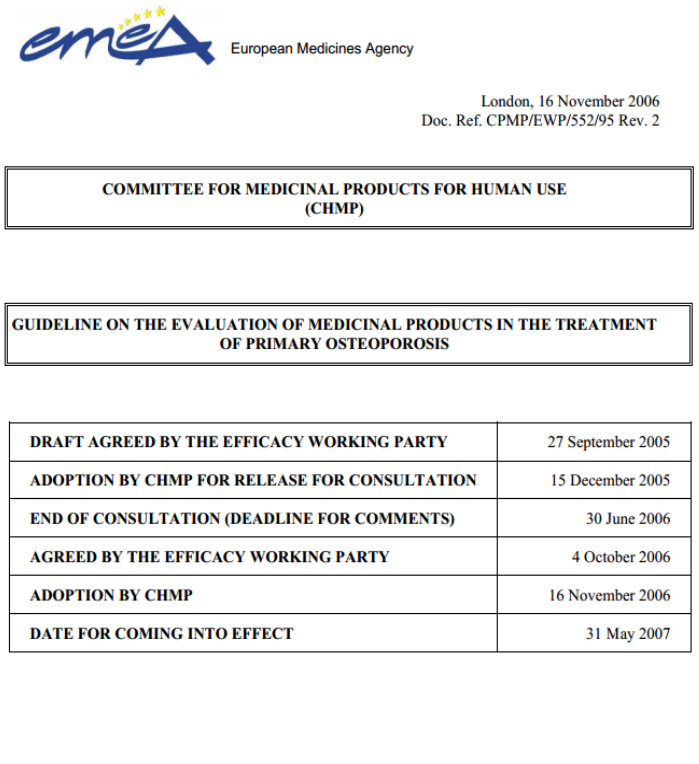
Calcitonin

Alendronic acid/colecalciferol

Feasility issues identified

1. Decrease in the use of corticosteroid treatment in paediatric patients with IBD and chronic rheumatologic conditions
2. Difficulties related to recruitment of paediatric patients with osteoporotic fractures
3. Refusal to enter the study due to the placebo treatment arm

Guidelines



European Medicines Agency

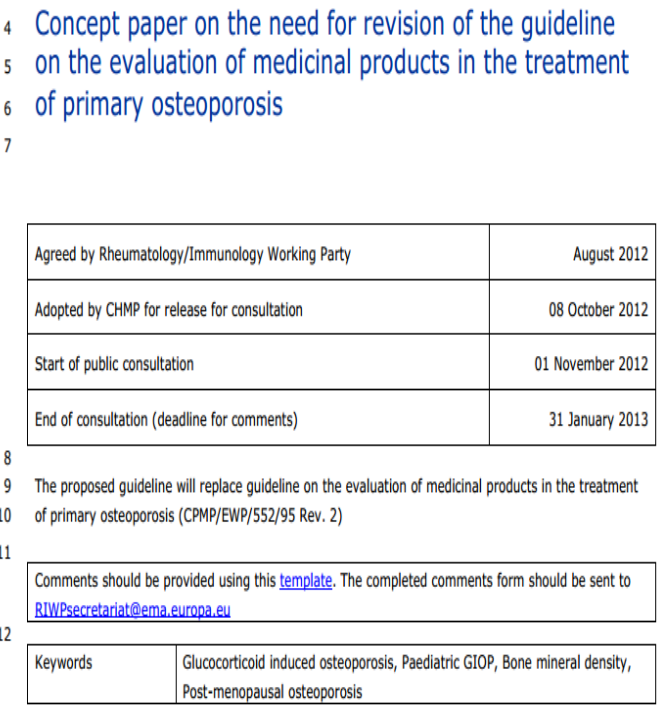
London, 16 November 2006
Doc. Ref. CPMP/EWP/552/95 Rev. 2

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

GUIDELINE ON THE EVALUATION OF MEDICINAL PRODUCTS IN THE TREATMENT OF PRIMARY OSTEOPOROSIS

DRAFT AGREED BY THE EFFICACY WORKING PARTY	27 September 2005
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	15 December 2005
END OF CONSULTATION (DEADLINE FOR COMMENTS)	30 June 2006
AGREED BY THE EFFICACY WORKING PARTY	4 October 2006
ADOPTION BY CHMP	16 November 2006
DATE FOR COMING INTO EFFECT	31 May 2007

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003405.pdf



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

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/10/WC500134467.pdf