EMA/134107/2023

European Medicines Agency decision

P/0123/2023

of 14 April 2023

on the acceptance of a modification of an agreed paediatric investigation plan for denosumab (Prolia, Xgeva), (EMEA-000145-PIP02-12-M05) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to 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[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0086/2013 issued on 29 April 2013, the decision P/0058/2016 issued on 18 March 2016, the decision P/0102/2020 issued on 20 March 2020, the decision P/0001/2021 issued on 5 January 2021 and the decision P/0213/2021 issued on 21 May 2021,

Having regard to the application submitted by Amgen Europe B.V. on 15 November 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 February 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for denosumab (Prolia, Xgeva), solution for injection, subcutaneous use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/89/2008 issued on 14/10/2008, including subsequent modifications thereof.

Article 3

This decision is addressed to Amgen Europe B.V., 7061 Minervum, 4817-ZK – Breda, The Netherlands.

EMA/PDCO/904598/2022
Amsterdam, 24 February 2023

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-000145-PIP02-12-M05

Scope of the application

Active substance(s):

Denosumab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of osteoporosis

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Amgen Europe B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Amgen Europe B.V. submitted to the European Medicines Agency on 15 November 2022 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0086/2013 issued on 29 April 2013, the decision P/0058/2016 issued on 18 March 2016, the decision P/0102/2020 issued on 20 March 2020, the decision P/0001/2021 issued on 5 January 2021 and the decision P/0213/2021 issued on 21 May 2021.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 3 January 2023.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of osteoporosis

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- solution for injection, subcutaneous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of osteoporosis

2.1.1. Indication(s) targeted by the PIP

Treatment of glucocorticoid-induced osteoporosis in paediatric patients who had previously experienced an osteoporotic fracture

Treatment of osteogenesis imperfecta

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	**Description**
Quality	Not applicable
Non-clinical	Not applicable
Clinical	**Study 1** Open-label single-arm, historically controlled study to evaluate safety, efficacy and pharmacokinetics of denosumab in children from 2 years to less than 18 years of age with osteogenesis imperfecta. **Study 2** Double-blind, placebo-controlled randomised study to evaluate safety and efficacy of denosumab in children from 5 years to less than 18 years of age with glucocorticoid-induced osteoporosis.

Extrapolation, modelling and simulation studies	Not applicable
Other studies	Not applicable
Other measures	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s):

1. Treatment of bone loss associated with sex hormone ablative therapy

Authorised indication(s):

- Treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures. In men with prostate cancer receiving hormone ablation, Prolia significantly reduces the risk of vertebral fractures.
  - Invented name(s): Prolia, Xgeva
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure

2. Prevention of skeletal related events in patients with bone metastases

Authorised indication(s):

- Prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumours.
  - Invented name(s): Prolia, Xgeva
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure

3. Treatment of giant cell tumour of bone

Authorised indication(s):

- Treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity.
  - Invented name(s): Prolia, Xgeva
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure

4. Treatment of osteoporosis *(Condition covered by EMEA-000145-PIP02-12 and subsequent modifications thereof)*

Authorised indication(s):

- Treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures. In postmenopausal women Prolia significantly reduces the risk of vertebral, non-vertebral and hip fractures.
  - Invented name(s): Prolia, Xgeva
  - Authorised pharmaceutical form(s): Solution for injection

  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure
- Treatment of bone loss associated with long-term systemic glucocorticoid therapy in adult patients at increased risk of fracture.
  - Invented name(s): Prolia, Xgeva
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure