EMA/429693/2023

European Medicines Agency decision

P/0408/2023

of 27 October 2023

on the acceptance of a modification of an agreed paediatric investigation plan for carfilzomib (Kyprolis), (EMEA-001806-PIP04-19-M02) 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/0016/2021 issued on 27 January 2021 and the decision P/0107/2023 issued on 14 April 2023,

Having regard to the application submitted by Amgen Europe BV on 25 May 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 8 September 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 carfilzomib (Kyprolis), powder for solution for infusion, intravenous 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 is addressed to Amgen Europe B.V, 7061 Minervum, 4817 ZK – Breda, The Netherlands.

EMA/PDCO/261388/2023
Amsterdam, 8 September 2023

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

EMEA-001806-PIP04-19-M02

Scope of the application

Active substance(s):

Carfilzomib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of acute lymphoblastic leukaemia

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Amgen Europe BV

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Amgen Europe BV submitted to the European Medicines Agency on 25 May 2023 an application for modification of the agreed paediatric investigation plan with a waiver as set out in the European Medicines Agency's decision P/0016/2021 issued on 27 January 2021 and the decision P/0107/2023 issued on 14 April 2023.

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

The procedure started on 10 July 2023.

Scope of the modification

Some timelines 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 acute lymphoblastic leukaemia

The waiver applies to:

- the paediatric population from birth to less than 1 month of age;
- powder for solution for infusion, intravenous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

2. Paediatric investigation plan

2.1. Condition:

Treatment of acute lymphoblastic leukaemia

2.1.1. Indication(s) targeted by the PIP

Treatment for paediatric patients with relapsed or refractory T-cell acute lymphoblastic leukaemia or paediatric patients with relapsed or refractory B-cell acute lymphoblastic leukaemia who received prior targeted immune therapy

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

From 1 month to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder for solution for infusion

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**Study 1 (20140106):** Part 1 (phase 1b): uncontrolled, dose-escalation study in patients from 1 year to less than 18 years of age (and adults), with relapsed or refractory T-cell or B-cell acute lymphoblastic leukaemia with or without extramedullary disease, to assess the safety and tolerability of carfilzomib, alone and in combination with induction chemotherapy, and to determine the optimal dose for the subsequent part 2 study of carfilzomib (CFZ) in combination with induction chemotherapy.

	Part 2 (phase 2): externally-controlled, single arm study of carfilzomib (CFZ) in combination with VXLD induction chemotherapy (vincristine, dexamethasone, PEG-asparaginase, and daunorubicin) from 1 month to less than 18 years (diagnosis must be prior to 18 years) of age (and adults) with relapsed or refractory T-cell ALL or B-cell acute lymphoblastic leukaemia, who must have a bone marrow relapse with or without extramedullary disease after receiving a targeted B-cell immune therapy as treatment for a prior relapse, to compare the rate of complete remission (CR) at the end of induction therapy to an external control.
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/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By October 2024
Deferral for one or more measures contained in the paediatric investigation plan:	No

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of multiple myeloma in adults

Authorised indication(s):

- Kyprolis in combination with daratumumab and dexamethasone, with lenalidomide and dexamethasone, or with dexamethasone alone is indicated for the treatment of adult patients with multiple myeloma who have received at least one prior therapy
  - Invented name(s): Kyprolis
  - Authorised pharmaceutical form(s): Powder for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure