EMA/47058/2024

European Medicines Agency decision

P/0040/2024

of 7 February 2024

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for blinatumomab, (Blincyto) (EMEA-000574-PIP03-23) 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 application submitted by Amgen Europe B.V. on 17 March 2023 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 19 January 2024, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[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

A paediatric investigation plan for blinatumomab, (Blincyto), powder for solution for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for blinatumomab, (Blincyto), powder for solution for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver blinatumomab, (Blincyto), powder for solution for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0145/2014 issued on 13 June 2014, including subsequent modifications thereof.

Article 5

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

EMA/PDCO/482495/2023 Corr[1]
Amsterdam, 19 January 2024

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-000574-PIP03-23

Scope of the application

Active substance(s):

Blinatumomab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of B-lymphoblastic leukaemia/lymphoma

Pharmaceutical form(s):

Powder for 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 16(1) of Regulation (EC) No 1901/2006 as amended, Amgen Europe B.V. submitted for agreement to the European Medicines Agency on 17 March 2023 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 24 April 2023.

Supplementary information was provided by the applicant on 12 October 2023. The applicant proposed modifications to the paediatric investigation plan.

[1] 31 January 2024

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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

2. The measures and timelines of the agreed 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 B-lymphoblastic leukaemia/lymphoma

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- powder for solution for injection, subcutaneous use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of B-lymphoblastic leukaemia/lymphoma

2.1.1. Indication(s) targeted by the PIP

Treatment of relapsed/refractory B cell precursor acute lymphoblastic leukaemia

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

From 28 days to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder for solution for injection

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	Study 1 Open-label, uncontrolled, single arm study to evaluate safety, activity and pharmacokinetic (PK) parameters following subcutaneous (SC) administration of blinatumomab in adolescent patients from 12 years to less than 18 years of age (and adults) with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (R/R B-ALL). (20180257) Study 2 Open label, uncontrolled, single arm trial to evaluate safety and tolerability and determine the recommended Phase 2 dose (Phase 1)

	and evaluate the activity (Phase 2) of SC blinatumomab in patients from 28 days to less than 18 years of age with R/R B-ALL. (20220107)
Modelling and simulation studies	Study 3 Modelling and simulation population pharmacokinetic (Pop-PK) study to predict the initial paediatric doses to be used in further clinical studies in children from 28 days to less than 18 years of age with R/R B-ALL. Study 4 Modelling and simulation Pop-PK/PD study to confirm or modify the paediatric posology compared to the regimen used in clinical trials in children from 28 days to less than 18 years of age with R/R B-ALL.
Other studies	Not applicable
Extrapolation plan	Study 1 (Study 20180257), Study 2 (Study 20220107) and Study 4 are part of an extrapolation plan covering the paediatric population from 28 days to less than 18 years of age, as agreed by the PDCO.

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 March 2029
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 acute lymphoblastic leukaemia

Authorised indication(s):

- BLINCYTO is indicated as monotherapy for the treatment of adults with CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL). Patients with Philadelphia chromosome positive B-precursor ALL should have failed treatment with at least 2 tyrosine kinase inhibitors (TKIs) and have no alternative treatment option.
  - Invented name(s): BLINCYTO
  - Authorised pharmaceutical form(s): Powder for concentrate and solution for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure
- BLINCYTO is indicated as monotherapy for the treatment of adults with Philadelphia chromosome negative CD19 positive B-precursor ALL in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%.
  - Invented name(s): BLINCYTO
  - Authorised pharmaceutical form(s): Powder for concentrate and solution for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure
- BLINCYTO is indicated as monotherapy for the treatment of paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic haematopoietic stem cell transplantation.
  - Invented name(s): BLINCYTO
  - Authorised pharmaceutical form(s): Powder for concentrate and solution for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure
- BLINCYTO is indicated as monotherapy for the treatment of paediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor ALL as part of the consolidation therapy.
  - Invented name(s): BLINCYTO
  - Authorised pharmaceutical form(s): Powder for concentrate and solution for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure