

EMA/436080/2020

European Medicines Agency decision

P/0331/2020

of 24 August 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for (4S,7aR,9aR,10S,11E,14S,15R)-6'-chloro-10-methoxy-14,15-dimethyl-3',4',7a,8,9,9a,10,13,14,15-decahydro-2'H,7H-spiro[1,19-ethenocyclobuta[i][1,4]oxazepino[3,4-f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide (AMG 176) (EMEA-002631-PIP01-19) 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.

European Medicines Agency decision

P/0331/2020

of 24 August 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for (4S,7aR,9aR,10S,11E,14S,15R)-6'-chloro-10-methoxy-14,15-dimethyl-3',4',7a,8,9,9a,10,13,14,15-decahydro-2'H,7H-spiro[1,19-ethenocyclobuta[i][1,4]oxazepino[3,4-f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide (AMG 176) (EMA-002631-PIP01-19) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 726/2004¹,

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency²,

Having regard to the application submitted by Amgen Europe BV on 15 July 2019 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 24 July 2020, 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.

² OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for (4S,7aR,9aR,10S,11E,14S,15R)-6'-chloro-10-methoxy-14,15-dimethyl-3',4',7a,8,9,9a,10,13,14,15-decahydro-2'H,7H-spiro[1,19-ethenocyclobuta[i][1,4]oxazepino[3,4-f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide (AMG 176), concentrate for solution for infusion, intravenous 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 (4S,7aR,9aR,10S,11E,14S,15R)-6'-chloro-10-methoxy-14,15-dimethyl-3',4',7a,8,9,9a,10,13,14,15-decahydro-2'H,7H-spiro[1,19-ethenocyclobuta[i][1,4]oxazepino[3,4-f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide (AMG 176), concentrate for solution for infusion, intravenous 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 for (4S,7aR,9aR,10S,11E,14S,15R)-6'-chloro-10-methoxy-14,15-dimethyl-3',4',7a,8,9,9a,10,13,14,15-decahydro-2'H,7H-spiro[1,19-ethenocyclobuta[i][1,4]oxazepino[3,4-f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide (AMG 176), concentrate for solution for infusion, intravenous 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 is addressed to Amgen Europe BV, Minervum 7061, 4817 ZK – Breda, The Netherlands.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/254440/2020
Amsterdam, 24 July 2020

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

EMA-002631-PIP01-19

Scope of the application

Active substance(s):

(4S,7aR,9aR,10S,11E,14S,15R)-6'-chloro-10-methoxy-14,15-dimethyl-3',4',7a,8,9,9a,10,13,14,15-decahydro-2'H,7H-spiro[1,19-ethenocyclobuta[i][1,4]oxazepino[3,4-f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide (AMG 176)

Condition(s):

Treatment of acute myeloid leukaemia

Pharmaceutical form(s):

Concentrate 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 16(1) of Regulation (EC) No 1901/2006 as amended, Amgen Europe BV submitted for agreement to the European Medicines Agency on 15 July 2019 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 20 August 2019.

Supplementary information was provided by the applicant on 16 April 2020. The applicant proposed modifications to the paediatric investigation plan.



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 Norwegian Paediatric Committee member 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 annex 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 myeloid leukaemia

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- concentrate for solution for infusion, intravenous 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 acute myeloid leukaemia (AML)

2.1.1. Indication(s) targeted by the PIP

The treatment of first relapse and refractory AML in paediatric patients

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)

Concentrate for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	2	Study 1 Dose range-finding juvenile toxicity study Study 2 Definitive juvenile toxicity study

Area	Number of measures	Description
Clinical studies	1	Study 3 Open-label, two part study to evaluate safety, tolerability, pharmacokinetics (PK) and establish a recommended Phase 2 combination dose (RP2CD) (Part 1) followed by a randomised (3:1), active controlled part 2, to evaluate safety and efficacy of AMG 176 as add-on to re-induction chemotherapy (fludarabine, cytarabine plus optional G-CSF [FLA(G)]) compared to re-induction chemotherapy alone in children from 28 days to less than 18 years of age with relapsed or refractory AML.
Extrapolation, modelling and simulation studies	1	Study 4 Use of Population (Pop)/PKPD to inform initial paediatric dosing in clinical studies.
Other studies	0	Not applicable.
Other measures	0	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 April 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes