MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan (MHRA-100485-PIP01-22-M01) and to the deferral

MHRA-100485-PIP01-22-M02

Scope of the Application

Active Substance(s)

AMG 176 (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[3,4f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide

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 Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Amgen Limited submitted to the licensing authority on 26/07/2023 16:00 BST an application for a Modification

The procedure started on 15/11/2023 09:17 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100485-PIP01-22-M02

Of 18/12/2023 09:27 GMT

On the adopted decision for AMG 176 (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[3,4f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide (MHRA-100485-PIP01-22-M02) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for AMG 176 (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[3,4f][1,2,7]thiadiazacyclohexadecine-4,1'-naphthalen]-18(17H)-one 16,16-dioxide, Concentrate for solution for infusion , INTRAVENOUS USE .

This decision is addressed to Amgen Limited, 216 Cambridge Science Park, Cambridge, UNITED KINGDOM, CB4 0WA

ANNEX I

1. Waiver

1.1 Condition:

Treatment of acute myeloid leukaemia The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 28 days of age Pharmaceutical form(s): Concentrate for solution for infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: 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(s):

Treatment of acute myeloid leukaemia (AML)

2.2 Indication(s) targeted by the PIP:

Treatment of first relapse and refractory AML in paediatric patients

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 28 days to less than 18 years of age

2.4 Pharmaceutical Form(s):

Concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	2	Study 1 Dose range-finding juvenile toxicity study. Study 2 Definitive juvenile toxicity study.
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, Modeling & 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 a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	30/09/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes