EMA/444603/2024

European Medicines Agency decision

P/0356/2024

of 25 October 2024

on the acceptance of a modification of an agreed paediatric investigation plan for daunorubicin / cytarabine (Vyxeos), (EMEA-001858-PIP02-16-M04) 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.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
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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/0200/2017 issued on 21 July 2017, the decision P/0299/2017 issued on 4 October 2017, the decision P/0388/2018 issued on 7 December 2018, and the decision P/0292/2019 issued on 14 August 2019,

Having regard to the application submitted by Jazz Pharmaceuticals Ireland Limited on 31 May 2024 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 6 September 2024, 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 and to the deferral.

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

[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 daunorubicin / cytarabine (Vyxeos), powder for concentrate for solution for infusion, intravenous use, including changes to the deferral, 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 Jazz Pharmaceuticals Ireland Limited, Fifth Floor, Waterloo Exchange, Waterloo Road, 4 – Dublin, Ireland.

EMA/PDCO/273597/2024
Amsterdam, 6 September 2024

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

EMEA-001858-PIP02-16-M04

Scope of the application

Active substance(s):

Daunorubicin / cytarabine

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of acute myeloid leukaemia

Pharmaceutical form(s):

Powder for concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Jazz Pharmaceuticals Ireland Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Jazz Pharmaceuticals Ireland Limited submitted to the European Medicines Agency on 31 May 2024 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/0200/2017 issued on 21 July 2017, the decision P/0299/2017 issued on 4 October 2017, the decision P/0388/2018 issued on 7 December 2018, and the decision P/0292/2019 issued on 14 August 2019.

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

The procedure started on 8 July 2024.

Scope of the modification

Some measures and 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 and to the deferral 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 myeloid leukaemia

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- powder for 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

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from 28 days to less than 18 years of age with relapsed/refractory acute myeloid leukaemia or in first relapse and with *de novo* newly diagnosed acute myeloid 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 concentrate for solution for infusion.

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable.
Non-clinical studies	Not applicable.
Clinical studies	**Study 1** Open-label, multiple dose trial to evaluate pharmacokinetics, safety and tolerability of liposomal combination of cytarabine and daunorubicin (CPX-351) in paediatric patients from 28 days to less than 18 years of age (and young adults) with a relapsed/refractory haematologic malignancy (CPX-MA-1201).

	Study 2 Open-label, multiple dose study to evaluate pharmacokinetics, safety, tolerability and anti-tumour activity of liposomal combination of cytarabine and daunorubicin (CPX-351) followed by fludarabine, cytarabine, and G-CSF (FLAG) in paediatric patients from 28 days to less than 18 years of age (and young adults) with relapsed/refractory acute myeloid leukaemia including a dose-finding phase and an expansion phase. (AAML1421). *Study 3 deleted in EMEA-001858-PIP02-16-M02* **Study 4** Open-label, randomised, active-controlled study to evaluate efficacy, safety and tolerability of liposomal combination of cytarabine and daunorubicin (CPX-351) and gemtuzumab ozogomicin (GO, to be used only in patients CD33 positive) compared to standard induction therapy with daunorubicin, cytarabine and GO in paediatric patients from 28 days to less than 18 years of age (and adults) with *de novo* newly-diagnosed acute myeloid leukaemia (AAML1831, Arm A and arm B).
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 June 2024
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 myeloid leukaemia

Authorised indication(s):

- Vyxeos liposomal is indicated for the treatment of adults with newly diagnosed, therapy-related acute myeloid leukaemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC).
  - Invented name(s): Vyxeos liposomal
  - Authorised pharmaceutical form(s): Powder for concentrate for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure