EMA/50728/2014

European Medicines Agency decision

P/0031/2014

of 21 February 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for azacitidine (Vidaza) (EMEA-001272-PIP02-13) 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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

European Medicines Agency decision

P/0031/2014

of 21 February 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for azacitidine (Vidaza) (EMEA-001272-PIP02-13) 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 726/2004[1],

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 Agency[2],

Having regard to the application submitted by Celgene Europe Ltd on 15 February 2013 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 13 February 2014, in accordance with Article 18 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) of Regulation (EC) No 1901/2006, 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 azacitidine (Vidaza), powder for suspension for injection, powder for solution for infusion, subcutaneous use, 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 azacitidine (Vidaza), powder for suspension for injection, powder for solution for infusion, subcutaneous use, 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 azacitidine (Vidaza), powder for suspension for injection, powder for solution for infusion, subcutaneous use, 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 Celgene Europe Ltd, 1 Longwalk Road, Stockley Park, UB11 1DB – Uxbridge, United Kingdom.

Done at London, 21 February 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/23669/2014

Final Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation plan and a deferral and a waiver (after re-examination)

EMEA-001272-PIP02-13

Scope of the application

Active substance(s):

Azacitidine

Invented name:

Vidaza

Condition(s):

Treatment of acute myeloid leukaemia

Treatment of myelodysplastic syndrome (including juvenile myelomonocytic leukaemia)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder for suspension for injection

Powder for solution for infusion

Route(s) of administration:

Subcutaneous use

Intravenous use

Name/corporate name of the PIP applicant:

Celgene Europe Ltd

Information about the authorised medicinal product:

See Annex II

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Celgene Europe Ltd submitted for agreement to the European Medicines Agency on 15 February 2013 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.

An Opinion was adopted by the Paediatric Committee on 6 December 2013 for the above mentioned product. Celgene Europe Ltd received the Paediatric Committee Opinion on 16 December 2013.

On 14 January 2014 Celgene Europe Ltd submitted to the European Medicines Agency a written request, including detailed grounds for re-examination of the Opinion.

The re-examination procedure started on 15 January 2014.

A meeting with the Paediatric Committee took place on 12 February 2014.

Final Opinion

1. The Paediatric Committee, having assessed the detailed grounds for re-examination, in accordance with Article 25(3) of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   1.1. to revise its opinion and

   - to agree the paediatric investigation plan in accordance with Article 18 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)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population and 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 annexes and appendix.

London, 13 February 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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

Waiver

1.1. Condition: treatment of acute myeloid leukaemia

The waiver applies to:

- The paediatric population from birth to less than 3 months;
- for powder for suspension for injection for subcutaneous use and for powder for solution for infusion for 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).

1.2. Condition: treatment of myelodysplastic syndrome (including juvenile myelomonocytic leukaemia)

The waiver applies to:

- The paediatric population from birth to less than 1 month;
- for powder for suspension for injection for subcutaneous use and for powder for solution for infusion for intravenous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in 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 children with molecular relapse of acute myeloid leukaemia in first complete remission.

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

From 3 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder for suspension for injection for subcutaneous use.

Powder for solution for infusion for intravenous use.

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 1:** Multicentre, randomized, open-label trial to evaluate the safety, pharmacodynamics and efficacy of azacitidine compared to no anti-cancer treatment in children from 3 months to less than 18 years of age (and young adults) in first complete remission after treatment for acute myeloid leukaemia who have increasing molecular signals of aberrations associated with acute myeloid leukaemia
Extrapolation, modelling & simulation studies	0	Not applicable.
Other studies	0	Not applicable.

2.2. Condition: treatment of myelodysplastic syndrome (including juvenile myelomonocytic leukaemia)

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with newly diagnosed advanced myelodysplastic syndrome, or juvenile myelomonocytic leukaemia prior to stem cell transplantation.

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

From 1 month to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Powder for suspension for injection for subcutaneous use.

Powder for solution for infusion for intravenous use.

2.2.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 2:** Multicentre, open-label trial to evaluate the pharmacokinetics, pharmacodynamics, safety and activity of azacitidine in paediatric patients from 1 month to less than 18 years of age with newly-diagnosed advanced myelodysplastic syndrome or a newly-diagnosed juvenile myelomonocytic leukaemia, including a comparison to historical data
Extrapolation, modelling & simulation studies	0	Not applicable.
Other studies	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By May 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of myelodysplastic syndrome

Authorised indication(s):

Vidaza is indicated for the treatment of adult patients who are not eligible for haematopoietic stem cell transplantation with:

- intermediate-2 and high-risk myelodysplastic syndromes (MDS) according to the International Prognostic Scoring System (IPSS),
- chronic myelomonocytic leukaemia (CMML) with 10-29 % marrow blasts without myeloproliferative disorder,

2. Treatment of acute myeloid leukaemia

Authorised indication(s):

Vidaza is indicated for the treatment of adult patients who are not eligible for haematopoietic stem cell transplantation with:

- acute myeloid leukaemia (AML) with 20-30 % blasts and multi-lineage dysplasia, according to World Health Organisation (WHO) classification.

Authorised pharmaceutical form(s):

Powder for suspension for injection

Authorised route(s) of administration:

Subcutaneous use