EMA/562590/2013

European Medicines Agency decision

P/0225/2013

of 23 September 2013

on the acceptance of a modification of an agreed paediatric investigation plan for decitabine (Dacogen), (EMEA-000555-PIP01-09-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.

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on the acceptance of a modification of an agreed paediatric investigation plan for decitabine (Dacogen), (EMEA-000555-PIP01-09-M04) 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 European Medicines Agency's decision P/53/2010 issued on 7 April 2010, the decision P/52/2011 issued on 4 March 2011, the decision P/0063/2012 issued on 28 March 2012 and the decision P/0100/2013 issued on 30 April 2013,

Having regard to the application submitted by Janssen-Cilag International NV on 20 May 2013 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 9 August 2013, 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.

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

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for decitabine (Dacogen), powder for solution for infusion, intravenous use, 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 Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 – Beerse, Belgium.

Done at London, 23 September 2013

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

EMA/PDCO/330302/2013

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

EMEA-000555-PIP01-09-M04

Scope of the application

Active substance(s):

Decitabine

Invented name:

Dacogen

Condition(s):

Treatment of acute myeloid leukaemia

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Janssen-Cilag International NV

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International NV submitted to the European Medicines Agency on 20 May 2013 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/53/2010 issued on 7 April 2010, the decision P/52/2011 issued on 4 March 2011, the decision P/0063/2012 issued on 28 March 2012 and the decision P/0100/2013 issued on 30 April 2013.

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

The procedure started on 12 June 2013.

Scope of the modification

Some measures 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 in the scope set out in the Annex I of this opinion.

   The Norwegian Paediatric Committee member 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.

London, 9 August 2013

On behalf of the Paediatric Committee
Dr Daniel Brasseur, 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

1. Waiver

1.1. Condition: treatment of acute myeloid leukaemia

The waiver applies to:

- Term newborn infants (from birth to less than 28 days);
- for powder for solution for infusion, intravenous use;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

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 with acute myeloid leukaemia who have high-risk cytogenetics, or are refractory to, or have a relapse after first-line treatment.

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

From 1 month to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder for solution for infusion, intravenous use.

Measures

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	4	**Measure 1:** Repeated (intermittent) dose toxicity study in juvenile rats. **Measure 2:** In vitro study of primary cultures of AML explants from paediatric patients using decitabine and decitabine in combination with standard chemotherapeutic drugs. **Measure 3:** In vitro study of AML cell lines to evaluate sensitivity and resistance to combinations of cytarabine and decitabine.

Area	Number of studies	Description
		Measure 4: In vivo xenograft studies of primary paediatric AML explants using decitabine and decitabine treatment in combination with standard chemotherapy.
Clinical	2	**Measure 5:** Open-label, multi-centre, multiple dose trial to evaluate pharmacokinetics, safety and activity of decitabine in sequential combination with cytarabine in children from 1 month to less than 18 years of age with acute myeloid leukaemia. **Measure 6:** Open-label, multi-centre, randomised, controlled trial to evaluate safety and efficacy of decitabine in sequential combination with cytarabine compared with standard of care induction therapy in children from 1 month to less than 18 years of age with acute myeloid leukaemia.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes.
Date of completion of the paediatric investigation plan:	By July 2021.
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 acute myeloid leukaemia (AML)

   Authorised indications:

   - Treatment of adult patients aged 65 years and above with newly diagnosed de novo or secondary acute myeloid leukaemia (AML), according to the World Health Organization (WHO) classification, who are not candidates for standard induction chemotherapy.

Authorised pharmaceutical formulation(s):

Powder for concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use