EMA/117801/2013

# European Medicines Agency decision

P/0042/2013

of 1 March 2013

on the acceptance of a modification of an agreed paediatric investigation plan for cilengitide (EMEA-000550-PIP02-10-M01) 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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# European Medicines Agency decision

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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 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/201/2011 issued on 30 August 2011,

Having regard to the application submitted by Merck KGaA on 16 October 2012 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 January 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 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

***Article 1***

Changes to the agreed paediatric investigation plan for cilengitide, 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 Merck KGaA, Frankfurter Strasse 250, 64293 Darmstadt, Germany.

Done at London, 1 March 2013

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

EMA/PDCO/749083/2012

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

EMEA-000550-PIP02-10-M01

## Scope of the application

**Active substance(s):**

Cilengitide

**Condition(s):**

Treatment of high-grade glioma

**Pharmaceutical form(s):**

Solution for infusion

**Route(s) of administration:**

Intravenous use

**Name/corporate name of the PIP applicant:**

Merck KGaA

## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merck KGaA submitted to the European Medicines Agency on 16 October 2012 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/201/2011 issued on 30 August 2011.

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

The procedure started on 14 November 2012.

## Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

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## 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 Icelandic and the Norwegian Paediatric Committee members agree 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 annex and appendix.

London, 11 January 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

Not applicable.

# 2. Paediatric Investigation Plan

## *2.1. Condition: Treatment of high-grade glioma*

### 2.1.1. Indication(s) targeted by the PIP

Treatment of newly diagnosed and relapsed/progressive high-grade glioma.

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

From birth to less than 18 years of age.

### 2.1.3. Pharmaceutical form(s)

Solution for infusion for intravenous use.

### 2.1.4. Measures

| Area | Number of studies | Description |
|---|---|---|
| Quality | 0 | Not applicable. |
| Non-clinical | 1 | **Study 1**<br>Repeat-dose toxicity study in juvenile rats to support the development in children below 3 years of age. |
| Clinical | 4 | **Study 2**<br>Open-label, non-randomized, non-controlled, multicentre study in children below 18 years of age and young adults to evaluate safety and tolerability of cilengitide monotherapy in children and adolescents with refractory primary brain tumors (PBTC-012).<br>**Study 3**<br>Open-label, non-randomized, non-controlled, multicentre study in children below 18 years of age and young adults to evaluate the activity of cilengitide monotherapy in recurrent or progressive and refractory high grade gliomas of childhood (COG-ACNS0621).<br>**Study 4**<br>Open-label, randomized, add-on, controlled, multicenter study evaluating the safety and efficacy of cilengitide in combination with temozolomide (TMZ) with concomitant radiationtherapy (RT) and TMZ maintenance treatment versus TMZ plus RT treatment followed by TMZ maintenance treatment alone in children from 3 years to less than 18 years of age with newly diagnosed |

| Area | Number of studies | Description |
|---|---|---|
| | | high-grade glioma including diffuse intrinsic pontine glioma, (CiTRIC).<br>**Study 5**<br>Open-label, randomized, controlled, multicenter study with a safety run-in, evaluating the safety and efficacy of cilengitide add-on to temozolomide (TMZ) and cisplatin (CP) versus TMZ and CP alone in children below 18 years of age with recurrent/progressive high-grade glioma (HGG) including diffuse intrinsic pontine glioma (DIPG) or newly diagnosed HGG (including DIPG) patients not scheduled for radiationtherapy, (CiTCIP). |

# 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 November 2018 |
| Deferral for one or more measures contained in the paediatric investigation plan: | Yes |