EMA/375098/2013

European Medicines Agency decision

P/0176/2013

of 30 July 2013

on the agreement of a paediatric investigation plan and on the granting of a waiver for glucarpidase (EMEA-001391-PIP01-12) 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 agreement of a paediatric investigation plan and on the granting of a waiver for glucarpidase (EMEA-001391-PIP01-12) 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 BTG International Ltd on 10 December 2012 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 14 June 2013, in accordance with Article 18 of Regulation (EC) No 1901/2006, 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 has given an opinion on the agreement of a paediatric investigation plan 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 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 glucarpidase, powder for solution for infusion, 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 waiver for glucarpidase, powder for solution for infusion, intravenous usethe 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

This decision is addressed to BTG International Ltd, 5 Fleet Place, EC4M 7R – London, United Kingdom.

Done at London, 30 July 2013

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

EMA/375098/2013

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a waiver

EMEA-001391-PIP01-12

Scope of the application

Active substance(s):

Glucarpidase

Condition(s):

Treatment of methotrexate toxicity

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

BTG International Ltd

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, BTG International Ltd submitted for agreement to the European Medicines Agency on 10 December 2012 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 15 April 2013.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 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)(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 annex and appendix.

London, 14 June 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 methotrexate toxicity

The waiver applies to:

- The paediatric population from birth to less than 28 days of age;
- 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.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of methotrexate toxicity

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with moderately or severely impaired renal function and with elevated plasma methotrexate concentrations likely associated with methotrexate toxicity (at least 1 µmol/l)

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 solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality	0	Not applicable
Non-clinical	1	Measure 1: Animal model study to evaluate glucarpidase and leucovorin for reducing methotrexate-induced toxicity
Clinical	4	Measure 2: Open-label, non-controlled, multi-centre study to evaluate the safety of glucarpidase in children from 1 month to less than 18 years of age (and adults) who received at least 1 g/m² methotrexate and in whom methotrexate clearance was delayed Measure 3: Open-label, non-controlled, multi-centre study to evaluate the methotrexate-lowering activity and safety of glucarpidase in combination with thymidine in children from 1 month to less than 18 years of age (and adults) who received high-dose methotrexate and in whom methotrexate clearance was delayed Measure 4: Open-label, non-controlled, multi-centre study to evaluate the efficacy and safety of glucarpidase in children from 1 month to less than 18

Area	Number of measures	Description
		years of age (and adults) who received methotrexate and in whom methotrexate clearance was delayed Measure 5: Open-label, multi-centre study to evaluate the effect of glucarpidase on the pharmacokinetics of leucovorin and 5-methyl tetrahydrofolate in children from 2 years to less than 18 years of age (and adults) with delayed elimination of methotrexate

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 June 2012
Deferral for one or more measures contained in the paediatric investigation plan:	No