EMA/722479/2013

European Medicines Agency decision

P/0311/2013

of 19 December 2013

on the acceptance of a modification of an agreed paediatric investigation plan for gadobutrol (Gadovist) (EMEA-000994-PIP01-10-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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on the acceptance of a modification of an agreed paediatric investigation plan for gadobutrol (Gadovist) (EMEA-000994-PIP01-10-M01) 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/176/2011 issued on 8 July 2011,

Having regard to the application submitted by Bayer Pharma AG on 16 August 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 8 November 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 gadobutrol (Gadovist), solution for injection, 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 Bayer Pharma AG, Muellerstrasse 178, D-13342 – Berlin, Germany

Done at London, 19 December 2013

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

EMA/PDCO/516837/2013

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

EMEA-000994-PIP01-10-M01

Scope of the application

Active substance(s):

Gadobutrol

Invented name:

Gadovist

Condition(s):

Diagnostic evaluation of tissue pathologies with contrast-enhanced magnetic resonance imaging (MRI)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Bayer Pharma AG

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, Bayer Pharma AG submitted to the European Medicines Agency on 16 August 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/176/2011 issued on 8 July 2011.

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

The procedure started on 12 September 2013.

Scope of the modification

A measure of the Paediatric Investigation Plan has 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, 8 November 2013

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

1. Waiver

1.1. Condition: Diagnostic evaluation of tissue pathologies with contrast-enhanced magnetic resonance imaging (MRI)

The waiver applies to:

- The paediatric population of preterm newborn infants and from 7 to less than 18 years of age;
- for solution for injection for intravenous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in preterm newborn infants;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered in children from 7 to less than 18 years of age.

2. Paediatric Investigation Plan

2.1. Condition: Diagnostic evaluation of tissue pathologies with contrast-enhanced magnetic resonance imaging (MRI)

2.1.1. Indication(s) targeted by the PIP

Contrast-enhanced magnetic resonance imaging (MRI) of CNS.

Contrast-enhanced MRI in liver and kidneys.

Contrast-enhanced magnetic resonance angiography.

Contrast-enhanced whole body MRI.

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

From birth to less than 7 years of age.

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	Number of studies	Description
Quality		Not applicable.
Non-clinical	2	Study 1 Repeated dose toxicity study in juvenile rats after intravenous administration with a following recovery period up to 8 weeks. Study 2 Extended single dose toxicity study in juvenile rats after intravenous

Area	Number of studies	Description
		administration with a following recovery period up to day 28.
Clinical	2	Study 3 Open-label, multicentre trial to evaluate pharmacokinetic and safety of gadobutrol in children from birth to less than 2 years of age. Study 4 Open-label, multi-center trial to evaluate pharmacokinetics, safety and tolerability gadobutrol in children from 2 to less than 18 years of age.

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 April 2014
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. Diagnosis of tissue pathologies

Authorised indications:

Gadovist 1.0 mmol/ml solution for injection is for diagnostic use only. Gadovist is indicated in adults, adolescents, and children aged 7 years and older for:

- Contrast enhancement in cranial and spinal magnetic resonance imaging (MRI).
- Contrast enhanced MRI of liver or kidneys in patients with high suspicion or evidence of having focal lesions to classify these lesions as benign or malignant.
- Contrast enhancement in magnetic resonance angiography (CE-MRA).

Authorised pharmaceutical form(s):

Solution for injection

Authorised route(s) of administration:

Intravenous use