EMA/513777/2011

# European Medicines Agency decision

P/176/2011

of 8 July 2011

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for gadobutrol (Gadovist) (EMEA-000994-PIP01-10) 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 application submitted by Bayer Schering Pharma AG on 2 July 2010 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 17 June 2011, 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 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 gadobutrol (Gadovist), solution for injection, 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 gadobutrol (Gadovist), solution for injection, 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 gadobutrol (Gadovist), solution for injection, 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 Bayer Schering Pharma AG, Muellerstrasse 178, D-13342, Berlin, Germany.

Done at London, 8 July 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)

EMA/PDCO/377108/2011

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

EMEA-000994-PIP01-10

## 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 Schering Pharma AG

**Information about the authorised medicinal product:**

See Annex II

## Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Bayer Schering Pharma AG submitted for agreement to the European Medicines Agency on 2 July 2010 an application for a

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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.

The procedure started on 13 October 2010.

Supplementary information was provided by the applicant on 4 April 2011.

## 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 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 Articles 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 annex(es) and appendix.

London, 17 June 2011

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: 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. Studies

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

| Area | Number of studies | Description |
|---|---|---|
| | | Extended single dose toxicity study in juvenile rats after intravenous administration with a following recovery period up to day 28. |
| Clinical | 2 | Study 3<br>Open-label, multicentre trial to evaluate pharmacokinetic and safety of gadobutrol in children from birth to less than 2 years of age.<br>Study 4<br>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

| | |
|---|---|
| Measures to address long term follow-up of potential safety issues in relation to paediatric use: | Yes |
| Date of completion of the paediatric investigation plan: | By April 2014 |
| Deferral for one or more studies 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).

| **Invented name** | **Strength** | **Pharmaceutical form** | **Route of administration** |
|---|---|---|---|
| Gadovist | 1.0 mmol/ml | Solution for injection | Intravenous use |
| Gadograf | 1.0 mmol/ml | Solution for injection | Intravenous use |