EMA/689054/2012

European Medicines Agency decision

P/0258/2012

of 31 October 2012

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for regorafenib (EMEA-001178-PIP01-11) 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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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 Pharma AG on 8 August 2011 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 5 October 2012, 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 regorafenib, film-coated tablet, granules, oral 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 regorafenib, film-coated tablet, granules, oral 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 regorafenib, film-coated tablet, granules, oral 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 Pharma AG, Muellerstrasse 178, 13353 Berlin, Germany.

Done at London, 31 October 2012

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

EMA/PDCO/582002/2012

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

EMEA-001178-PIP01-11

Scope of the application

Active substance(s):

Regorafenib

Condition(s):

Treatment of solid malignant tumours

Pharmaceutical form(s):

Film-coated tablet

Granules

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bayer Pharma AG

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Bayer Pharma AG submitted for agreement to the European Medicines Agency on 8 August 2011 an application for a 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 14 September 2011.

Supplementary information was provided by the applicant on 13 July 2012. The applicant proposed modifications to the paediatric investigation plan.

A meeting with the Paediatric Committee took place on 3 October 2012.

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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 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 Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   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, 5 October 2012

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 solid malignant tumours

The waiver applies to:

- the paediatric population from birth to less than 6 months of age
- for film-coated tablet and granules for oral use
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of solid malignant tumours

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with a solid malignant tumour(s) integrated with anti-cancer therapy

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

From 6 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Granules

2.1.4. Studies

Area	Number of studies	Description
Quality	1	Study 1: Development of granules for oral use as age-appropriate formulation
Non-clinical	2	Study 2: Juvenile toxicity study Study 3: Pharmacology testing of regorafenib in paediatric tumour models including biomarker exploration and combination testing
Clinical	5	Study 4: Physiologically-based pharmacokinetic model to predict pharmacokinetics in children from 6 months to less than 18 years of age Study 5: Multi-centre, open-label, dose-escalating, cohort-expanding trial to evaluate pharmacokinetics, pharmacodynamics, tolerability, safety and tumour activity of regorafenib in children with a solid malignant tumour refractory to standard therapy Study 6: Multi-centre trial to evaluate the tolerability, safety and activity of regorafenib in children with a solid malignant tumour refractory to standard therapy

Area	Number of studies	Description
		Study 7: Multi-centre, randomised, controlled, blinded trial to evaluate the activity, safety and efficacy of regorafenib in combination with anti-cancer therapy compared to anti-cancer therapy in children from 6 months to less than 18 years with a high-risk solid malignant tumour

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 December 2020
Deferral for one or more studies contained in the paediatric investigation plan:	Yes