EMA/181812/2017

European Medicines Agency decision

P/0091/2017

of 11 April 2017

on the acceptance of a modification of an agreed paediatric investigation plan for regorafenib (Stivarga), (EMEA-001178-PIP01-11-M03) 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 European Medicines Agency's decision P/0258/2012 issued on 31 October 2012, the decision P/0270/2014 issued on 27 October 2014 and the decision P/0190/2016 issued on 15 July 2016,

Having regard to the application submitted by Bayer Pharma AG on 12 December 2016 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 24 February 2017, 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 regorafenib (Stivarga), film-coated tablet, granules, oral 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 Bayer Pharma, Muellerstrasse 178, 13353 - Berlin, Germany.

EMA/PDCO/857549/2016 Corr
London, 24 February 2017

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

EMEA-001178-PIP01-11-M03

Scope of the application

Active substance(s):

Regorafenib

Invented name:

Stivarga

Condition(s):

Treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Granules

Route(s) of administration:

Oral 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 12 December 2016 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/0258/2012 issued on 31 October 2012, the decision P/0270/2014 issued on 27 October 2014 and the decision P/0190/2016 issued on 15 July 2016.

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

The procedure started on 3 January 2017.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have 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 and to the deferral 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.

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 (PIP)

1. Waiver

1.1. Condition

Treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue)

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 all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue)

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. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of granules for oral use as age-appropriate formulation
Non-clinical studies	2	**Study 2** Juvenile toxicity study **Study 3** Pharmacology testing of regorafenib in paediatric tumour models including biomarker exploration and combination testing

Clinical studies	3	**Study 4** Physiologically-based pharmacokinetic model to predict pharmacokinetics in the paediatric population 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 the paediatric population with a solid malignant tumour refractory to standard therapy **Study 6** Deleted in procedure EMEA-001178-PIP01-11-M03. **Study 7** Multi-centre, randomised, controlled, open label trial to evaluate the activity, safety and efficacy of regorafenib in combination with vincristine and irinotecan (VI) compared to VI alone in the paediatric population from 6 months to less than 18 years with a first and subsequent relapses of rhabdomyosarcoma.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety / efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 2024
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. Treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue)

   Authorised indication(s):

- Stivarga is indicated for the treatment of adult patients with metastatic colorectal cancer (CRC) who have been previously treated with, or are not considered candidates for, available therapies. These include fluoropyrimidine-based chemotherapy, an anti-VEGF therapy and an anti-EGFR therapy.

2. Treatment of colon carcinoma

Authorised indication(s):

- Stivarga is indicated for the treatment of adult patients with unresectable or metastatic gastrointestinal stromal tumors (GIST) who progressed on or are intolerant to prior treatment with imatinib and sunitinib.

Authorised pharmaceutical form(s)

Film-coated tablet

Authorised route(s) of administration

Oral use