EMA/740214/2014

European Medicines Agency decision

P/0332/2014

of 22 December 2014

on the acceptance of a modification of an agreed paediatric investigation plan for dabrafenib (Tafinlar), (EMEA-001147-PIP01-11-M02) 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/0024/2012 issued on 27 January 2012, and the decision P/0239/2013 issued on 24 September 2013,

Having regard to the application submitted by GlaxoSmithKline Trading Service Limited on 26 August 2014 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 14 November 2014, 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 waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the 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

Changes to the agreed paediatric investigation plan for dabrafenib (Tafinlar), capsule, hard, powder for oral suspension, oral use, including changes to the waiver, 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 GlaxoSmithKline Trading Service Limited, Currabinny, Carrigaline, Ireland.

Done at London, 22 December 2014

For the European Medicines Agency
Zaide Frias
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/538638/2014

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

EMEA-001147-PIP01-11-M02

Scope of the application

Active substance(s):

Dabrafenib

Invented name:

Tafinlar

Condition(s):

Treatment of melanoma

Treatment of solid malignant tumours (excluding melanoma)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsule, hard

Powder for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

GlaxoSmithKline Trading Service Limited

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, GlaxoSmithKline Trading Service Limited submitted to the European Medicines Agency on 26 August 2014 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/0024/2012 issued on 27 January 2012, and the decision P/0239/2013 issued on 24 September 2013.

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

The procedure started on 16 September 2014.

Scope of the modification

Some timelines of the Paediatric Investigation Plan have been modified. A waiver for a new paediatric subset has been added for safety reasons.

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 waiver in the scope set out in the Annex I of this opinion.

   The Icelandic and the Norwegian Paediatric Committee members agree 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, 14 November 2014

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 (PIP)

1. Waiver

1.1. Condition:

Treatment of solid malignant tumours (excluding melanoma)

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- for capsules, hard, for oral use, and for powder for oral suspension, for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe in the specified paediatric subsets.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of melanoma

2.1.1. Indication(s) targeted by the PIP

Treatment of adolescent patients with melanoma containing BRAF V600 activating mutations.

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

From 12 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Capsule, hard.

Powder for oral suspension.

2.1.4. Measures

Area	Number of studies	Description
Quality	1	**Measure 1** Development of an age-appropriate powder for oral suspension formulation.
Non-clinical	2	**Measure 2** Dose range / tolerability juvenile rat toxicity study to evaluate toxicokinetics and clinical observations in rats given dabrafenib or vehicle control. **Measure 3** Definitive juvenile rat toxicity study to evaluate toxicokinetics, clinical observations, laboratory parameters and histopathology of major organs in rats given dabrafenib (at doses determined in

		measure 2) or vehicle control. **Measure 8** Juvenile rat renal toxicity study.
Clinical	4	**Measure 4** Open-label, single agent, uncontrolled dose escalation trial to determine the safety, tolerability, pharmacokinetics and maximum tolerated dose of dabrafenib in children from 1 year to less than 18 years of age with advanced BRAF V600-mutant solid tumours. **Measure 6** Trial to evaluate the relative bioavailability of dabrafenib pharmaceutical forms in adults. **Measure 7** Measure to demonstrate that the pharmacokinetics, pharmacodynamics and efficacy of dabrafenib in adolescent patients (aged from 12 to less than 18 years of age) with BRAF V600-mutant melanoma are similar to that in adults with BRAF V600-mutant melanoma, using a modelling and simulation approach for the purpose of extrapolation.

2.2. Condition:

Treatment of solid malignant tumours (excluding melanoma)

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with solid malignant tumours containing BRAF V600 activating mutations.

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

From 1 year to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Capsule, hard

Powder for oral suspension

2.2.4. Measures

Area	Number of studies	Description
Quality-related studies	1	**Studies 1** As for condition "Treatment of melanoma".

Non-clinical studies	2	**Studies 2** As for condition "Treatment of melanoma". **Studies 3** As for condition "Treatment of melanoma". **Studies 8** As for condition "Treatment of melanoma".
Clinical studies	3	**Studies 4** As for condition "Treatment of melanoma". **Studies 5** Open-label, randomised controlled parallel-group trial to determine the safety and efficacy of dabrafenib in children from 1 year to less than 18 years of age with advanced BRAF V600-mutant solid tumours excluding melanoma (specific tumour type to be decided based on the results of measure 4). **Studies 6** As for condition "Treatment of melanoma".

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 July 2019
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 melanoma

Authorised indication(s):

- Dabrafenib is indicated in monotherapy for the treatment of adult patients with unresectable or metastatic melanoma with a *BRAF V600* mutation

Authorised pharmaceutical form(s):

Capsules, hard

Authorised route(s) of administration:

Oral use