

EMA/23029/2016

European Medicines Agency decision

P/0022/2016

of 29 January 2016

on the acceptance of a modification of an agreed paediatric investigation plan for dabrafenib (Tafinlar), (EMA-001147-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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/0332/2014 issued on 22 December 2014, the decision P/0239/2013 issued on 24 September 2013, and the decision P/0024/2012 issued on 27 January 2012,

Having regard to the application submitted by Novartis Europharm Limited on 18 September 2015 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 11 December 2015, 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 dabrafenib (Tafinlar), capsule, hard, powder for oral suspension, oral 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 Novartis Europharm Limited, Frimley Business Park, Frimley, GU16 7SR - Camberley, United Kingdom.

Done at London, 29 January 2016

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



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/631864/2015
London, 11 December 2015

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-001147-PIP01-11-M03

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:

Novartis Europharm Limited

Information about the authorised medicinal product:

See Annex II



Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted to the European Medicines Agency on 18 September 2015 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/0332/2014 issued on 22 December 2014, the decision P/0239/2013 issued on 24 September 2013 and the decision P/0024/2012 issued on 27 January 2012.

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

The procedure started on 13 October 2015.

Scope of the modification

Some measures 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 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 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-related studies	1	Study 1 Development of an age-appropriate powder for oral suspension formulation.
Non-clinical studies	2	Study 2 Dose range / tolerability juvenile rat toxicity study to evaluate toxicokinetics and clinical observations in rats given dabrafenib or vehicle control. Study 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. Study 8 Juvenile rat renal toxicity study.
Clinical studies	4	Study 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. Study 6 Trial to evaluate the relative bioavailability of dabrafenib pharmaceutical forms in adults. Study 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	Study 1 As for condition "Treatment of melanoma".

Non-clinical studies	2	Study 2 As for condition "Treatment of melanoma". Study 3 As for condition "Treatment of melanoma". Study 8 As for condition "Treatment of melanoma".
Clinical studies	3	Study 4 As for condition "Treatment of melanoma". Study 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). Study 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