EMA/121752/2014

European Medicines Agency decision

P/0078/2014

of 2 April 2014

on the acceptance of a modification of an agreed paediatric investigation plan for trametinib (dimethyl sulfoxide) (EMEA-001177-PIP01-11-M01) 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/0044/2012 issued on 28 February 2012,

Having regard to the application submitted by Glaxo Group Limited on 20 November 2013 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 February 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.

(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 trametinib (dimethyl sulfoxide), film-coated tablet, powder for oral solution, 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 Glaxo Group Limited, 980 Great West Road, TW8 9GS – Brentford, United Kingdom.

Done at London, 2 April 2014

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

EMA/PDCO/731225/2013

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

EMEA-001177-PIP01-11-M01

Scope of the application

Active substance(s):

Trametinib (dimethyl sulfoxide)

Condition(s):

Treatment of melanoma

Treatment of all conditions included in the category of malignant neoplasms (except melanoma, nervous system, haematopoietic and lymphoid tissue)

Pharmaceutical form(s):

Film-coated tablet

Powder for oral solution

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Glaxo Group Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Glaxo Group Limited submitted to the European Medicines Agency on 20 November 2013 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/0044/2012 issued on 28 February 2012.

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

The procedure started on 18 December 2013.

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Scope of the modification

Some measures of the Paediatric Investigation Plan were 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 annex and appendix.

London, 14 February 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman

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 all conditions included in the category of malignant neoplasms (except melanoma, nervous system, haematopoietic and lymphoid tissue)

The waiver applies to:

- Preterm and term newborn infants from birth to less than 28 days;
- for film-coated tablets, for oral use, and for powder for oral solution, for oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur 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)

Film-coated tablet.

Powder for oral solution.

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	1	**Study 1:** Development of an age-appropriate powder for oral solution formulation of trametinib.
Non-clinical studies	1	**Study 2:** Juvenile rat toxicity study to evaluate toxicokinetics, clinical observations, laboratory parameters and histopathology of trametinib.
Clinical studies	3	**Study 3:** Open-label, single agent, dose escalation trial to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of trametinib in children from 1 month to less than 18 years of age with relapsed or refractory solid malignant tumours. **Study 4:** Double-blind, randomised, controlled, parallel-group trial to evaluate the safety and efficacy of trametinib in children from 1 month to less than 18 years of age with solid malignant tumours with known or expected RAS, RAF or MEK pathway activation. **Study 5:** Relative bioavailability study in adults.

Extrapolation, modelling and simulation studies	1	**Study 6:** Study to demonstrate that pharmacokinetics, pharmacodynamics and efficacy of trametinib 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 of efficacy.
Other studies	0	Not applicable.

2.2. Condition: treatment of all conditions included in the category of malignant neoplasms (except melanoma, nervous system, haematopoietic and lymphoid tissue)

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with a solid malignant tumour with known or expected RAS, RAF or MEK pathway activation.

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

From 1 month to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Film-coated tablet.

Powder for oral solution.

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1:** Same as for condition treatment of melanoma.
Non-clinical studies	1	**Study 2:** Same as for condition treatment of melanoma.
Clinical studies	3	**Study 3:** Same as for condition treatment of melanoma. **Study 4:** Same as for condition treatment of melanoma. **Study 5:** Same as for condition treatment of melanoma.
Extrapolation, modelling and simulation studies	1	**Study 6:** Same as for condition treatment of melanoma.
Other studies	0	Not applicable.

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 October 2019
Deferral for one or more measures contained in the paediatric investigation plan:	Yes