



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/986418/2011

European Medicines Agency decision P/0024/2012

of 27 January 2012

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for N-{3-[5-(2-Amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzene sulfonamide, methanesulfonate salt (GSK2118436) (EMA-001147-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 726/2004¹,

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 application submitted by GlaxoSmithKline Trading Service Limited on 8 April 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 9 December 2011, 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 N-{3-[5-(2-Amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzene sulfonamide, methanesulfonate salt (GSK2118436), capsule, hard, powder for oral suspension, 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 N-{3-[5-(2-Amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzene sulfonamide, methanesulfonate salt (GSK2118436), capsule, hard, powder for oral suspension, 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 N-{3-[5-(2-Amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzene sulfonamide, methanesulfonate salt (GSK2118436), capsule, hard, powder for oral suspension, 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 GlaxoSmithKline Trading Service Limited, 6900 Cork Airport Business Park, Kinsale Road, County Cork, Ireland.

Done at London, 27 January 2012

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



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/866329/2011

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

EMA-001147-PIP01-11

Scope of the application

Active substance(s):

N-{3-[5-(2-Amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzene sulfonamide, methanesulfonate salt (GSK2118436)

Condition(s):

Treatment of melanoma

Treatment of solid malignant tumours (excluding melanoma)

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

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, GlaxoSmithKline Trading Service Limited submitted for agreement to the European Medicines Agency on 8 April 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 18 May 2011.



Supplementary information was provided by the applicant on 30 September 2011. The applicant proposed modifications to the paediatric investigation plan.

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)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) 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, 9 December 2011

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 melanoma

A class waiver applies to:

- All paediatric patients from birth to less than 12 years of age;
- for capsules, hard, for oral use, and for powder for oral suspension, for oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not normally occur in the specified paediatric subsets.

1.2. Condition: Treatment of solid malignant tumours (excluding melanoma)

The waiver applies to:

- Preterm and term newborn infants from birth to less than 28 days;
- for capsules, hard, for oral use, and for powder for oral suspension, for oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not normally 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)

Capsule, hard.

Powder for oral suspension.

2.1.4. Studies

Area	Number of studies	Description
Quality	1	Measure 1 Development of an age-appropriate powder for oral suspension formulation.
Non-clinical	2	Study 2 Dose range/tolerability juvenile rat toxicity study to evaluate toxicokinetics and clinical observations in rats given GSK2118436 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 GSK2118436 (at doses determined in study 2) or vehicle control.
Clinical	4	Study 4 Open-label, single agent, uncontrolled dose escalation trial to determine the safety, tolerability, pharmacokinetics and maximum tolerated dose of GSK2118436 in children from 1 month to less than 18 years of age with advanced BRAF V600-mutant solid tumours. Study 5 Open-label, randomised controlled parallel-group trial to determine the safety and efficacy of GSK2118436 in children from 1 month 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 Study 4). Study 6 Open-label, randomised, single dose, 3 way cross-over study to evaluate the relative bioavailability of GSK2118436 capsules, the initial GSK2118436 industry-verified powder for oral suspension, and the intended final commercial paediatric powder for oral suspension formulation following administration to adult patients with BRAF V600-mutant solid tumours. Study 7 Measure to demonstrate that the pharmacokinetics, pharmacodynamics and efficacy of GSK 2118436 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.

Condition: Treatment of solid malignant tumours (excluding melanoma)

2.1.5. Indication(s) targeted by the PIP

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

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

From 1 month to less than 18 years of age.

2.1.7. Pharmaceutical form(s)

Capsule, hard.

Powder for oral suspension.

2.1.8. Studies

Area	Number of studies	Description
Quality	1	Measure 1 Development of an age-appropriate powder for oral suspension formulation.
Non-clinical	2	Study 2 Dose range/tolerability juvenile rat toxicity study to evaluate toxicokinetics and clinical observations in rats given GSK2118436 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 GSK2118436 (at doses determined in study 2) or vehicle control.
Clinical	3	Study 4 Open-label, single agent, uncontrolled dose escalation trial to determine the safety, tolerability, pharmacokinetics and maximum tolerated dose of GSK2118436 in children from 1 month to less than 18 years of age with advanced BRAF V600-mutant solid tumours. Study 5 Open-label, randomised controlled parallel-group trial to determine the safety and efficacy of GSK2118436 in children from 1 month 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 Study 4). Study 6 Open-label, randomised, single dose, 3 way cross-over study to evaluate the

Area	Number of studies	Description
		relative bioavailability of GSK2118436 capsules, the initial GSK2118436 industry-verified powder for oral suspension, and the intended final commercial paediatric powder for oral suspension formulation following administration to adult patients with BRAF V600-mutant solid tumours.

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 2018
Deferral for one or more studies contained in the paediatric investigation plan:	Yes