EMA/540970/2012

European Medicines Agency decision

P/0192/2012

of 24 August 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-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy) [1,1'- biphenyl]-3-carboxamide diphosphate (LDE225) (EMEA-000880-PIP02-11) 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 726/2004[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 application submitted by Novartis Europharm Limited on 2 December 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 6 July 2012, 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-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy) [1,1'- biphenyl]-3-carboxamide diphosphate (LDE225), capsule, hard, film-coated tablet, powder and solvent 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-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy) [1,1'- biphenyl]-3-carboxamide diphosphate (LDE225), capsule, hard, film-coated tablet, powder and solvent 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-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy) [1,1'-biphenyl]-3-carboxamide diphosphate (LDE225), capsule, hard, film-coated tablet, powder and solvent 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 Novartis Europharm Limited, Wimblehurst Road, Horsham RH12 5AB, United Kingdom.

Done at London, 24 August 2012

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

EMA/PDCO/325632/2012

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

EMEA-000880-PIP02-11

Scope of the application

Active substance(s):

N-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy) [1,1'- biphenyl]-3-carboxamide diphosphate (LDE225)

Condition(s):

Treatment of medulloblastoma

Pharmaceutical form(s):

Capsule, hard

Film-coated tablet

Powder and solvent for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted for agreement to the European Medicines Agency on 2 December 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.

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The procedure started on 12 January 2012.

Supplementary information was provided by the applicant on 23 April 2012. 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 occurs only in adult populations.

   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.

Langen, Germany, 6 July 2012

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 medulloblastoma

The waiver applies to:

- The paediatric population from birth to less than 4 months of age;
- for capsule, hard, film-coated tablet and powder and solvent for oral suspension 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 subset(s).

2. Paediatric Investigation Plan

2.1. Condition: Treatment of medulloblastoma

2.1.1. Indication(s) targeted by the PIP

- Treatment of paediatric and adult patients with hedgehog pathway-activated medulloblastoma who relapse following standard of care therapy (including children younger than 3 years of age and children not eligible for radiation therapy).
- Treatment of paediatric patients with high-risk hedgehog pathway-activated medulloblastoma in combination with standard chemotherapy following primary surgical resection with or without radiotherapy (including children younger than 3 years of age).

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

From 4 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

- Capsule, hard.
- Film-coated tablet.
- Powder and solvent for oral suspension.

2.1.4. Studies

Area	Number of studies	Description
Quality	1	Study 1: Development of a powder and solvent for oral suspension.
Non-clinical	0	Not applicable.
Clinical	4	Study 2: Open-label, single-arm, non-controlled, dose-escalating, cohort-expanding trial to evaluate pharmacokinetics, tolerability and activity of LDE225 in children from 1 to less than 18 years of age (and in adults) with a refractory or recurrent solid malignant tumour which is potentially driven by hedgehog pathway. Study 3: Randomised, active-controlled, open-label multi-centre trial to evaluate the safety and activity of LDE225 compared to temozolomide in children from 4 months to less than 18 years of age (and adults) with a relapse of medulloblastoma with hedgehog pathway-activation after radiation therapy, with an open-label non-controlled arm in children who could not receive radiation therapy. Study 4: Randomised, double-blind, multi-centre, placebo-controlled trial to evaluate the efficacy and safety of LDE225 as add-on to standard frontline chemotherapy and, where appropriate, radiation therapy in children from 12 months to less than 18 years with medulloblastoma with high-risk features and with hedgehog activation, with a safety run-in phase. Study 5: Population pharmacokinetic model using data from paediatric and adult patients.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety 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