EMA/254705/2011

European Medicines Agency decision

P/85/2011

of 8 April 2011

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for imatinib (mesilate) (Glivec) (EMEA-000463-PIP02-10) 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 30 April 2010 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 18 February 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 imatinib (mesilate) (Glivec), film-coated tablet, capsule, hard, age-appropriate formulation, 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 imatinib (mesilate) (Glivec), film-coated tablet, capsule, hard, age-appropriate formulation, 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 imatinib (mesilate) (Glivec), film-coated tablet, capsule, hard, age-appropriate formulation, 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, West Sussex, RH12 5AB Horsham, United Kingdom.

Done at London, 8 April 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)

EMA/PDCO/46036/2011

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

EMEA-000463-PIP02-10

Scope of the application

Active substance(s):

Imatinib (mesilate)

Invented name:

Glivec

Condition(s):

Treatment of pulmonary arterial hypertension

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Capsule, hard

Age-appropriate formulation

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

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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 30 April 2010 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 10 June 2010.

Supplementary information was provided by the applicant on 06 December 2010. The applicant proposed modifications to the paediatric investigation plan.

A meeting with the Paediatric Committee took place on 16 February 2011.

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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   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 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, 18 February 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 pulmonary arterial hypertension

The waiver applies to:

- Children from birth to less than 6 months of age (including children with persistent pulmonary hypertension of the newborn)
- for film-coated tablet; capsule, hard; age-appropriate formulation; oral use
- on the grounds that the specific medicinal product is likely to be ineffective.

2. Paediatric Investigation Plan

Condition: Treatment of pulmonary arterial hypertension

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with pulmonary arterial hypertension (PAH) who remain symptomatic despite treatment with PAH-specific therapy, including combination therapy with a vasodilator and a prostacyclin analogue.

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

From 6 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Capsule, hard

Age-appropriate formulation

2.1.4. Studies

Area	Number of studies	Description
Quality	1	Study 1: Age-appropriate formulation(s) to support either fixed dose bands or normalised dosing
Non-clinical	1	Study 2: Juvenile toxicity study
Clinical	1	Study 3: Double-blind, randomised, multicentre, placebo-controlled trial to evaluate pharmacokinetics, pharmacodynamics, safety and efficacy of imatinib in children from 6 months to less than 18 years of age with pulmonary arterial hypertension

3. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By September 2013
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 Philadelphia chromosome (BCR-ABL translocation)-positive chronic myeloid leukaemia

   Authorised indication(s):

- Glivec is indicated for the treatment of adult and paediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML) for whom bone marrow transplantation is not considered as the first line of treatment.
- Glivec is indicated for the treatment of adult and paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis.

2. Treatment of Philadelphia chromosome (BCR-ABL translocation)-positive acute lymphoblastic leukaemia

   Authorised indication(s):

- Glivec is indicated for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) integrated with chemotherapy.
- Glivec is indicated for the treatment of adult patients with relapsed or refractory Ph+ ALL as monotherapy.

3. Treatment of myelodysplastic / myeloproliferative diseases associated with platelet-derived growth factor receptor gene re-arrangements

   Authorised indication(s):

- Glivec is indicated for the treatment of adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements.

4. Treatment of hypereosinophilic syndrome and/or chronic eosinophilic leukaemia with FIP1L1-platelet-derived growth factor receptor alpha gene re-arrangement

   Authorised indication(s):

- Glivec is indicated for the treatment of adult patients with advanced hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukaemia (CEL) with FIP1L1-PDGFRα rearrangement.

5. Treatment of Kit (CD 117)-positive gastrointestinal stromal tumours

   Authorised indication(s):

- Glivec is indicated for the treatment of adult patients with Kit (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST)
- Glivec is indicated for the adjuvant treatment of adult patients who are at significant risk of relapse following resection of Kit (CD117)-positive GIST

6. Treatment of dermatofibrosarcoma protuberans

   Authorised indication(s):

- Glivec is indicated for the treatment of adult patients with unresectable dermatofibrosarcoma protuberans (DFSP) and adult patients with recurrent and/or metastatic DFSP who are not eligible for surgery

EU Number	(Invented) name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content (concentration)	Package size
EU/1/01/198/001	Glivec	50 mg	Capsule, hard	Oral use	blister (PVC/alu)		30 capsules
EU/1/01/198/002	Glivec	100 mg	Capsule, hard	Oral use	blister (PVC/alu)		24 capsules
EU/1/01/198/003	Glivec	100 mg	Capsule, hard	Oral use	blister (PVC/alu)		48 capsules
EU/1/01/198/004	Glivec	100 mg	Capsule, hard	Oral use	blister (PVC/alu)		96 capsules
EU/1/01/198/005	Glivec	100 mg	Capsule, hard	Oral use	blister (PVC/alu)		120 capsules
EU/1/01/198/006	Glivec	100 mg	Capsule, hard	Oral use	blister (PVC/alu)		180 capsules
EU/1/01/198/007	Glivec	100 mg	Film-coated tablet	Oral use	blister (PVC/alu)		20 film-coated tablets
EU/1/01/198/008	Glivec	100 mg	Film-coated tablet	Oral use	blister (PVC/alu)		60 film-coated tablets
EU/1/01/198/009	Glivec	400 mg	Film-coated tablet	Oral use	blister (PVDC/alu)		10 film-coated tablets
EU/1/01/198/010	Glivec	400 mg	Film-coated tablet	Oral use	blister (PVDC/alu)		30 film-coated tablets
EU/1/01/198/011	Glivec	100 mg	Film-coated tablet	Oral use	blister (PVC/alu)		120 film-coated tablets
EU/1/01/198/012	Glivec	100 mg	Film-coated tablet	Oral use	blister (PVC/alu)		180 film-coated tablets
EU/1/01/198/013	Glivec	400 mg	Film-coated tablet	Oral use	blister (PVDC/alu)		90 film-coated tablets