EMA/58042/2012

European Medicines Agency decision

P/0028/2012

of 27 January 2012

on the acceptance of a modification of an agreed paediatric investigation plan for imatinib mesilate (Glivec) (EMEA-000463-PIP01-08-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 726/2004[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/243/2009 issued on 2 December 2009, the decision P/2/2011 issued on 3 January 2011 and the decision P/131/2011 issued on 8 June 2011,

Having regard to the application submitted by Novartis Europharm Limited on 21 October 2011 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 January 2012, 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 imatinib mesilate (Glivec), hard capsule, film-coated tablet, 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, Wimblehurst Road, West Sussex, RH12 5AB Horsham, United Kingdom.

Done at London, 27 January 2012

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

EMA/PDCO/856750/2011

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

EMEA-000463-PIP01-08-M03

Scope of the application

Active substance(s):

Imatinib mesilate

Invented name:

Glivec

Condition(s):

Treatment of Philadelphia chromosome (BCR-ABL translocation)-positive chronic myeloid leukaemia

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

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

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

Treatment of kit (CD 117)-positive gastrointestinal stromal tumours

Treatment of dermatofibrosarcoma protuberans

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Hard capsule

Film-coated tablet

Route(s) of administration:

Oral use

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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 21 October 2011 an application for modification of the agreed paediatric investigation plan with a waiver as set out in the European Medicines Agency's decision P/243/2009 issued on 2 December 2009, the decision P/2/2011 issued on 3 January 2011, and the decision P/131/2011 issued on 8 June 2011.

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

The procedure started on 16 November 2011.

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.

   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 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, 13 January 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 Philadelphia chromosome (BCR-ABL translocation) - positive chronic myeloid leukaemia

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- for hard capsule and film-coated tablet for oral use;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit as the needs are already covered.

1.2. Condition: Treatment of Philadelphia chromosome (BCR-ABL translocation) - positive acute lymphoblastic leukaemia

The waiver applies to:

- children from birth to less than 1 year of age;
- for hard capsule and film-coated tablet 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.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of Philadelphia chromosome (BCR-ABL translocation) - positive acute lymphoblastic leukaemia

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with newly diagnosed Philadelphia chromosome (BCR-ABL translocation)-positive acute lymphoblastic leukaemia integrated with chemotherapy after induction therapy.

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

From 1 year to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Hard capsule for oral use

Film-coated tablet for oral use

2.1.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	3	Study 1: Open-label, multi-centre, non-randomised, dose-escalation trial to evaluate safety and efficacy of chemotherapy, haematopoietic stem cell transplantation and imatinib in children from 1 year to less than 18 years (and young adults) with acute lymphoblastic leukaemia. Study 2: Open-label, multi-centre, randomised trial to evaluate safety, activity and efficacy of imatinib on top of chemotherapy and in combination with haematopoietic stem cell transplantation in children from 1 year to less than 18 years with acute lymphoblastic leukaemia. Study 3: Development and validation of an integrated physiology-based pharmacokinetic (PBPK) and population pharmacokinetics model.

2.2. Conditions:

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

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

Treatment of kit (CD 117)-positive gastrointestinal stromal tumours

Treatment of dermatofibrosarcoma protuberans

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with myelodysplastic / myeloproliferative diseases associated with platelet-derived growth factor receptor gene re-arrangements; hypereosinophilic syndrome and/or chronic eosinophilic leukaemia with FIP1L1-platelet-derived growth factor receptor alpha gene re-arrangement; kit (CD 117)-positive gastrointestinal stromal tumours; dermatofibrosarcoma protuberans.

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

From birth to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Hard capsule for oral use

Film-coated tablet for oral use

2.2.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	2	Study 3: same as for condition treatment of Philadelphia chromosome (BCR-ABL translocation)-positive acute lymphoblastic leukaemia. Study 4: Measure to extrapolate efficacy to the paediatric population.

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 June 2011
Deferral for one or more studies contained in the paediatric investigation plan:	No

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