



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/738884/2013

European Medicines Agency decision

P/0004/2014

of 22 January 2014

on the acceptance of a modification of an agreed paediatric investigation plan for bevacizumab (Avastin), (EMEA-000056-PIP01-07-M02) 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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on the acceptance of a modification of an agreed paediatric investigation plan for bevacizumab (Avastin), (EMA-000056-PIP01-07-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 European Medicines Agency's decision P/82/2008 issued on 1 October 2008, and the decision P/0019/2012 issued on 27 January 2012,

Having regard to the application submitted by Roche Registration Ltd. on 12 September 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 6 December 2013, 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 bevacizumab (Avastin), concentrate for solution for infusion, intravenous 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 Roche Registration Ltd., 6 Falcon Way, Shire Park, AL7 1TW – Welwyn Garden City, United Kingdom.

Done at London, 22 January 2014

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



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/580326/2013

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

EMA-000056-PIP01-07-M02

Scope of the application

Active substance(s):

Bevacizumab

Invented name:

Avastin

Condition(s):

Treatment of rhabdomyosarcoma

Treatment of non-rhabdomyosarcoma soft tissue sarcoma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name / corporate name of the PIP applicant:

Roche Registration Ltd.

Information about the authorised medicinal product:

See Annex II



Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Registration Ltd. submitted to the European Medicines Agency on 12 September 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/82/2008 issued on 1 October 2008, and the decision P/0019/2012 issued on 27 January 2012.

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

The procedure started on 10 October 2013.

Scope of the modification

A measure of the Paediatric Investigation Plan has 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 in the scope set out in the Annex I of this opinion.

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 annexes and appendix.

London, 6 December 2013

On behalf of the Paediatric Committee
Dr Dirk Mentzer, 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 rhabdomyosarcoma

The waiver applies to:

- preterm newborn infants, term newborn infants (from birth to less than 28 days) and infants (from 28 days to less than 6 months);
- for the concentrate for solution for infusion for intravenous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

1.2. Condition: treatment of non-rhabdomyosarcoma soft tissue sarcoma

The waiver applies to:

- preterm newborn infants, term newborn infants (from birth to less than 28 days) and infants (from 28 days to less than 6 months);
- for the concentrate for solution for infusion for intravenous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition: treatment of rhabdomyosarcoma

2.1.1. Indication(s) targeted by the PIP

Treatment of newly-diagnosed metastatic rhabdomyosarcoma or newly-diagnosed metastatic non-rhabdomyosarcoma soft tissue sarcoma

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

From 6 months to less than 18 years.

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion for intravenous use.

2.1.4. Measures

Area	Number of measures	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	1	Study 1: Randomised, open-label, multi-centre, comparative trial to evaluate pharmacokinetics, pharmacodynamics, safety and efficacy of bevacizumab as add-on to combination chemotherapy in children with newly-diagnosed metastatic rhabdomyosarcoma or non-

Area	Number of measures	Description
		rhabdomyosarcoma soft tissue tumour.

2.2. Condition: treatment of non-rhabdomyosarcoma soft tissue sarcoma

2.2.1. Indication(s) targeted by the PIP

Treatment of newly-diagnosed metastatic rhabdomyosarcoma or newly-diagnosed metastatic non-rhabdomyosarcoma soft tissue sarcoma.

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

Same as for condition treatment of rhabdomyosarcoma.

2.2.3. Pharmaceutical form(s)

Same as for condition treatment of rhabdomyosarcoma.

2.2.4. Measures

Area	Number of measures	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	1	Same as for condition treatment of rhabdomyosarcoma.

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 September 2016
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 colon carcinoma

Authorised indications:

- Bevacizumab in combination with fluoropyrimidine-based chemotherapy is indicated for treatment of adult patients with metastatic carcinoma of the colon or rectum.

2. Treatment of breast carcinoma

Authorised indications:

- Bevacizumab in combination with paclitaxel is indicated for first-line treatment of adult patients with metastatic breast cancer. For further information as to human epidermal growth factor receptor 2 (HER2) status, please refer to section 5.1.
- Bevacizumab in combination with capecitabine is indicated for first-line treatment of adult patients with metastatic breast cancer in whom treatment with other chemotherapy options including taxanes or anthracyclines is not considered appropriate. Patients who have received taxane and anthracycline containing regimens in the adjuvant setting within the last 12 months should be excluded from treatment with Avastin in combination with capecitabine. For further information as to HER2 status, please refer to section 5.1.

3. Treatment of non-small cell lung carcinoma

Authorised indications:

- Bevacizumab, in addition to platinum-based chemotherapy, is indicated for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer other than predominantly squamous cell histology.

4. Treatment of renal cell carcinoma

Authorised indications:

- Bevacizumab in combination with interferon alfa-2a is indicated for first line treatment of adult patients with advanced and/or metastatic renal cell cancer.

5. Treatment of ovarian carcinoma, Treatment of fallopian tube carcinoma, Treatment of peritoneal carcinoma

Authorised indications:

- Bevacizumab, in combination with carboplatin and paclitaxel is indicated for the front-line treatment of adult patients with advanced (International Federation of Gynecology and Obstetrics (FIGO) stages III B, III C and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer.
- Bevacizumab, in combination with carboplatin and gemcitabine, is indicated for treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor-targeted agents

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use