EMA/708063/2011

European Medicines Agency decision

P/235/2011

of 30 September 2011

on the acceptance of a modification of an agreed paediatric investigation plan for rituximab (Mabthera) (EMEA-000308-PIP01-08-M01) 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 rituximab (Mabthera) (EMEA-000308-PIP01-08-M01) 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 726/2004[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/128/2009 issued on 14 July 2009,

Having regard to the application submitted by Roche Products Ltd on 30 May 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 12 August 2011, 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 and to the waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan including changes to the 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

Changes to the agreed paediatric investigation plan for rituximab (Mabthera), concentrate for solution for infusion, solution for injection, intravenous use, subcutaneous use, including changes to the waiver, 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 Products Ltd, 6 Falcon Way, Shire Park, AL7 1TW Welwyn Garden City, United Kingdom.

Done at London, 30 September 2011

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

EMA/PDCO/585877/2011

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

EMEA-000308-PIP01-08-M01

Scope of the application

Active substance(s):

Rituximab

Invented name:

Mabthera

Condition(s):

Treatment of diffuse large B-cell lymphoma

Treatment of autoimmune arthritis

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Concentrate for solution for infusion

Solution for injection

Route(s) of administration:

Intravenous use

Subcutaneous use

Name/corporate name of the PIP applicant:

Roche Products Ltd

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Products Ltd submitted to the European Medicines Agency on 30 May 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/128/2009 issued on 14 July 2009.

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

The procedure started on 15 June 2011.

Scope of the modification

Details of the paediatric trial and the timeline was 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 and to the waiver 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, 12 August 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 autoimmune arthritis

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age;
- for concentrate for solution for infusion for intravenous use and for solution for injection for subcutaneous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

1.2. Condition: Treatment of diffuse large B-cell lymphoma

The waiver applies to:

- Children from birth to less than 6 months of age;
- for concentrate for solution for infusion for intravenous use and for solution for injection for subcutaneous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of diffuse large B-cell lymphoma

2.1.1. Indication(s) targeted by the PIP

Treatment of mature B-cell malignancies, that is, diffuse large B-cell lymphoma, Burkitt and Burkitt-like lymphoma/leukaemia.

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. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	1	Study 1: Open-label, randomised, controlled, parallel-group, multicentre trial to evaluate the pharmacokinetics, pharmacodynamics, safety and efficacy of rituximab add-on to standard chemotherapy in children from 6 months to less than 18 years of age with advanced stage with B-cell lymphoma (excluding primary mediastinal B-cell lymphoma), Burkitt and Burkitt-like lymphoma/leukaemia.

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 2019
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 diffuse large B-cell lymphoma

   Authorised indications:

   - MabThera is indicated for the treatment of previously untreated patients with stage III-IV follicular lymphoma in combination with chemotherapy;
   - MabThera maintenance therapy is indicated for the treatment of follicular lymphoma patients responding to induction therapy;
   - MabThera monotherapy is indicated for treatment of patients with stage III-IV follicular lymphoma who are chemoresistant or are in their second or subsequent relapse after chemotherapy;
   - MabThera is indicated for the treatment of patients with CD20 positive diffuse large B cell non-Hodgkin's lymphoma in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy.

2. Treatment of chronic lymphocytic leukaemia

   Authorised indication:

   - MabThera in combination with chemotherapy is indicated for the treatment of patients with previously untreated and relapsed/refractory chronic lymphocytic leukaemia. Only limited data are available on efficacy and safety for patients previously treated with monoclonal antibodies including MabThera or patients refractory to previous MabThera plus chemotherapy.

3. Treatment of autoimmune arthritis

   Authorised indications:

   - MabThera in combination with methotrexate is indicated for the treatment of adult patients with severe active rheumatoid arthritis who have had an inadequate response or intolerance to other disease-modifying anti-rheumatic drugs (DMARD) including one or more tumour necrosis factor (TNF) inhibitor therapies. MabThera has been shown to reduce the rate of progression of joint damage as measured by x-ray and to improve physical function, when given in combination with methotrexate.

EU Number	Invented name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content (concentration)	Package size
EU/1/98/067/001	Mabthera	100 mg	Concentrate for solution for infusion	Intravenous use	vial (glass)	10 ml (10 mg/ml)	2 vials
EU/1/98/067/002	Mabthera	500 mg	Concentrate for solution for infusion	Intravenous use	vial (glass)	50 ml (10 mg/ml)	1 vial