EMA/112081/2019

European Medicines Agency decision

P/0064/2019

of 22 March 2019

on the acceptance of a modification of an agreed paediatric investigation plan for rituximab (MabThera), (EMEA-000308-PIP01-08-M04) 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/128/2009 issued on 14 July 2009, the decision P/235/2011 issued on 30 September 2011, the decision P/0017/2013 issued on 18 January 2013 and the decision P/0113/2017 issued on 11 April 2017,

Having regard to the application submitted by Roche Registration GmbH on 26 October 2018 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 1 February 2019, 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 rituximab (MabThera), concentrate for solution for infusion, solution for injection, intravenous use, subcutaneous 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 GmbH, Emil-Barell-Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/782084/2018
London, 1 February 2019

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

EMEA-000308-PIP01-08-M04

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 Registration GmbH

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 Registration GmbH submitted to the European Medicines Agency on 26 October 2018 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/128/2009 issued on 14 July 2009, the decision P/235/2011 issued on 30 September 2011, the decision P/0017/2013 issued on 18 January 2013 and the decision P/0113/2017 issued on 11 April 2017.

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

The procedure started on 4 December 2018.

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 in the scope set out in the Annex I of this opinion.

   The Norwegian Paediatric Committee member agrees 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.

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 (PIP)

1. Waiver

1.1. Condition: treatment of diffuse large B-cell lymphoma

The waiver applies to:

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

1.2. Condition: treatment of autoimmune arthritis

The waiver applies to:

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

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. Measures

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.

Clinical	1	**Study 1 (Intergroup B-NHL-2010)** 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 June 2019
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

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.

4. Treatment of granulomatosis with polyangiitis (Wegener's)

   Authorised indication(s):

   - MabThera, in combination with glucocorticoids, is indicated for the induction of remission in adult patients with severe, active granulomatosis with polyangiitis (Wegener's) and microscopic polyangiitis.

5. Treatment of microscopic polyangiitis

   Authorised indication(s):

   - MabThera, in combination with glucocorticoids, is indicated for the induction of remission in adult patients with severe, active granulomatosis with polyangiitis (Wegener's) and microscopic polyangiitis.

Authorised pharmaceutical formulation(s):

Concentrate for solution for infusion

Solution for injection

Authorised route(s) of administration:

Intravenous use

Subcutaneous use