EMA/395845/2021

European Medicines Agency decision

P/0303/2021

of 13 August 2021

on the acceptance of a modification of an agreed paediatric investigation plan for tocilizumab (RoActemra), (EMEA-000309-PIP04-17-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/0217/2017 issued on 9 August 2017, the decision P/0181/2018 issued on 12 June 2018 and the decision P/0253/2019 issued on 16 July 2019,

Having regard to the application submitted by Roche Registration GmbH on 19 March 2021 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 25 June 2021, 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 deferral.

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

[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 tocilizumab (RoActemra), solution for injection, concentrate for solution for infusion, subcutaneous use, intravenous use, including changes to the deferral, 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-Whylen, Germany.

EMA/PDCO/201920/2021
Amsterdam, 25 June 2021

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

EMEA-000309-PIP04-17-M03

Scope of the application

Active substance(s):

Tocilizumab

Invented name:

RoActemra

Condition(s):

Treatment of cytokine release syndrome associated with chimeric antigen receptor (CAR) T cell therapy or T-cell-engaging bispecific antibody therapy

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection

Concentrate for solution for infusion

Route(s) of administration:

Subcutaneous use

Intravenous use

Name/corporate name of the PIP applicant:

Roche Registration GmbH

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 GmbH submitted to the European Medicines Agency on 19 March 2021 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/0217/2017 issued on 9 August 2017, the decision P/0181/2018 issued on 12 June 2018 and the decision P/0253/2019 issued on 16 July 2019.

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

The procedure started on 27 April 2021.

Scope of the modification

Some measures and timelines 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 and to the deferral in the scope set out in the Annex I of this opinion.
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 cytokine release syndrome associated with chimeric antigen receptor (CAR) T cell therapy or T-cell-engaging bispecific antibody therapy

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- solution for injection, subcutaneous use; concentrate for solution for infusion, intravenous use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of cytokine release syndrome associated with chimeric antigen receptor (CAR) T cell therapy or T-cell-engaging bispecific antibody therapy.

2.1.1. Indication(s) targeted by the PIP

Treatment of chimeric antigen receptor (CAR) T cell induced severe or life-threatening cytokine release syndrome (CRS) in paediatric patients 2 years of age and older.

Treatment of T-cell-engaging bispecific antibody-induced severe or life-threatening CRS in paediatric patients 2 years of age or older.

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

From 2 years to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion.

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	0	Not applicable.
Extrapolation, modelling and simulation studies	2	**Study 2** Modelling and simulation study to support the dosing recommendation of RoActemra (tocilizumab) in the

		treatment of T-cell-engaging bispecific antibody-induced CRS in children aged 2 years to less than 18 years old. **Study 3** Analysis of available data on the use of tocilizumab for the treatment of severe or life-threatening CRS induced by T-cell engaging bispecific antibodies in paediatric patients aged 2 years or older.
Other studies	0	Not applicable.
Other measures	1	**Study 1** Review of available data on use of tocilizumab in treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) (in adults and) paediatric patients 2 years of age and older

3. Follow-up, completion and deferral of PIP

Concerns on potential long-term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 2027
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 chronic idiopathic arthritis

Authorised indication(s):

RoActemra, in combination with methotrexate (MTX), is indicated for:

- the treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX.
- the treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more diseasemodifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists.

In these patients, RoActemra can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

RoActemra 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.

RoActemra is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 2 years of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. RoActemra can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate) or in combination with MTX.

RoActemra in combination with methotrexate (MTX) is indicated for the treatment of juvenile idiopathic polyarthritis (pJIA; rheumatoid factor positive or negative and extended oligoarthritis) in patients 2 years of age and older, who have responded inadequately to previous therapy with MTX.

RoActemra can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

2. Treatment of of Giant Cell Arteritis (GCA)

Authorised indication(s):

RoActemra is indicated for the treatment of Giant Cell Arteritis (GCA) in adult patients.

3. Treatment of cytokine release syndrome associated with chimeric antigen receptor (CAR) T cell therapy

Authorised indication(s):

RoActemra is indicated for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in adults and paediatric patients 2 years of age and older.

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Solution for injection

Authorised route(s) of administration:

Intravenous use

Subcutaneous use