EMA/383650/2015

European Medicines Agency decision

P/0134/2015

of 15 June 2015

on the acceptance of a modification of an agreed paediatric investigation plan for tocilizumab (RoActemra), (EMEA-000309-PIP01-08-M06) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

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on the acceptance of a modification of an agreed paediatric investigation plan for tocilizumab (RoActemra), (EMEA-000309-PIP01-08-M06) 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/57/2009 issued on 25 March 2009, the decision P/129/2009 issued on 14 July 2009, the decision P/71/2010 issued on 5 May 2010, the decision P/277/2011 issued on 28 November 2011, the decision P/0179/2012 issued on 20 August 2012, and the decision P/0185/2013 issued on 30 July 2013,

Having regard to the application submitted by Roche Registration Limited on 2 March 2015 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 22 May 2015, 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), concentrate for solution for infusion, solution for injection (in pre-filled syringe), intravenous use, subcutaneous 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 Limited, 6 Falcon Way, Shire Park, AL7 1TW - Welwyn Garden City, United Kingdom.

Done at London, 15 June 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/157163/2015
London, 22 May 2015

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

EMEA-000309-PIP01-08-M06

Scope of the application

Active substance(s):

Tocilizumab

Invented name:

RoActemra

Condition(s):

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Concentrate for solution for infusion

Solution for injection (in pre-filled syringe)

Route(s) of administration:

Intravenous use

Subcutaneous use

Name/corporate name of the PIP applicant:

Roche Registration Limited

Information about the authorised medicinal product:

See Annex II

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Registration Limited submitted to the European Medicines Agency on 2 March 2015 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/57/2009 issued on 25 March 2009, the decision P/129/2009 issued on 14 July 2009, the decision P/71/2010 issued on 5 May 2010, the decision P/277/2011 issued on 28 November 2011, the decision P/0179/2012 issued on 20 August 2012, and the decision P/0185/2013 issued on 30 July 2013.

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

The procedure started on 24 March 2015.

Scope of the modification

Some measures andtimelines 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.

   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 chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis)

The waiver applies to:

- children from birth to less than 2 years;
- for concentrate for solution for infusion for intravenous use;
- on the grounds that measures would not be justified by expected therapeutic benefit as clinical trials are not feasible.

The waiver applies to:

- children from birth to less than 1 year;
- for solution for injection (in pre-filled syringe) 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 chronic idiopathic arthritis (including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis)

2.1.1. Indication(s) targeted by the PIP

Treatment of juvenile idiopathic arthritis.

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

From 1 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion.

Solution for injection (in pre-filled syringe).

2.1.4. Measures

Area	Number of measures	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	4	**Measure 1** Randomised, double-blind, placebo-controlled, parallel-group, 2-arm 12-week study to evaluate the efficacy and safety of tocilizumab in patients aged from 2 years to less than 18 years with active systemic juvenile idiopathic arthritis with 92-week single-arm open-label extension. **Measure 2** Open-label, multi-centre withdrawal study to evaluate the efficacy and safety of tocilizumab in patients aged from 2 years to less than 18 years with active polyarticular-course juvenile idiopathic arthritis, with open-label extension. **Measure 3** Open label multi-centre study to investigate pharmacokinetics, pharmacodynamics, efficacy and safety of tocilizumab following subcutaneous administration in patients aged from 1 to less than 18 years old with systemic juvenile idiopathic arthritis. **Measure 4** Open label multi-centre study to investigate pharmacokinetics, pharmacodynamics, efficacy and safety of tocilizumab following subcutaneous administration in patients with polyarticular juvenile idiopathic arthritis.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By November 2017
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 rheumatoid 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..

2. Treatment of juvenile idiopathic arthritis

   Authorised indication(s):

   - 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.

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Solution for injection in pre-filled syringe

Authorised route(s) of administration:

Intravenous use