European Medicines Agency

Doc. Ref. EMEA/759533/2009
P/242/2009

EUROPEAN MEDICINES AGENCY DECISION

of 2 December 2009

on the acceptance of a modification of an agreed Paediatric Investigation Plan for Recombinant human monoclonal antibody of the IgG1 class to insulin-like growth factor-1 receptor (RO4858696) (EMEA-000281-PIP01-08-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

DISCLAIMER: This Decision does not entitle to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006, as amended.

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THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

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 as amended 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 decision P/70/2009 of the European Medicines Agency on 20 April 2009,

Having regard to the application submitted by Roche Registration Limited on 3 August 2009 under Article 22 of Regulation (EC) No 1901/2006 as amended proposing changes to the agreed Paediatric Investigation Plan,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 October 2009, in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended,

Having regard to Article 25 of Regulation (EC) No 1901/2006 as amended,

WHEREAS:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to an agreed Paediatric Investigation Plan,

(2) It is therefore appropriate to adopt a Decision on the acceptance of changes to an 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 Recombinant human monoclonal antibody of the IgG1 class to insulin-like growth factor-1 receptor (RO4858696), powder for concentrate for solution for infusion, intravenous use, the details of which are set out in the Opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, are hereby accepted.

Article 2

This decision, that supersedes previous decision of the European Medicines Agency P/70/2009, as far as the agreed changes to the PIP for Recombinant human monoclonal antibody of the IgG1 class to insulin-like growth factor-1 receptor (RO4858696) are concerned, is addressed to Roche Registration Limited, 6 Falcon Way, Shire Park, AL7 1TW, Welwyn Garden City, United Kingdom.

Done at London, 2 December 2009

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Doc. Ref. EMEA/PDCO/653794/2009
EMEA-000281-PIP01-08-M02

OPINION OF THE PAEDIATRIC COMMITTEE ON THE ACCEPTANCE OF A MODIFICATION OF AN AGREED PAEDIATRIC INVESTIGATION PLAN

Scope of the application

Active substance(s):
Recombinant human monoclonal antibody of the IgG1 class to insulin-like growth factor-1 receptor (RO4858696)

Condition(s):
Ewing sarcoma family of tumours (including Ewing sarcoma of bone, peripheral primitive neuroectodermal tumour, extraskeletal Ewing sarcoma, and Askin tumour)

Pharmaceutical form(s):
Powder for concentrate for solution for infusion

Route(s) of administration:
Intravenous use

Name/corporate name of the PIP applicant:
Roche Registration Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Registration Limited submitted to the EMEA on 3 August 2009 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the EMEA decision P/70/2009 of 20 April 2009. The application for modification proposed changes.

The procedure started on 20 August 2009.

Scope of the modification

The modification concerns timelines and design aspects of some of the clinical studies.

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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 the changes proposed by the applicant regarding the timelines of the paediatric investigation plan.

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 Agency, together with its annex(es) and appendix.

London, 16 October 2009

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

ANNEX I

THE MEASURES AND TIMELINES OF THE AGREED PAEDIATRIC INVESTIGATION PLAN AND THE SUBSET(S) OF THE PAEDIATRIC POPULATION AND CONDITION(S) COVERED BY THE WAIVER

A. CONDITION(S)

Ewing sarcoma family of tumours (including Ewing sarcoma of bone, peripheral primitive neuroectodermal tumour, extraskeletal Ewing sarcoma, and Askin tumour)

B. WAIVER

- **Condition**

Ewing sarcoma family of tumours (including Ewing sarcoma of bone, peripheral primitive neuroectodermal tumour, extraskeletal Ewing sarcoma, and Askin tumour)

The waiver applies to:

- Preterm newborn infants, term newborn infants (from birth to less than 28 days), infants and toddlers (from 28 days to less than 24 months), for powder for concentrate for solution for infusion for intravenous use,

on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

C. PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

Ewing sarcoma family of tumours (including Ewing sarcoma of bone, peripheral primitive neuroectodermal tumour, extraskeletal Ewing sarcoma, and Askin tumour)

- **Proposed PIP indication**

Treatment of Ewing sarcoma family of tumours (including Ewing sarcoma of bone, peripheral primitive neuroectodermal tumour, extraskeletal Ewing sarcoma, and Askin tumour)

- **Subset(s) of the paediatric population concerned by the paediatric development**

From 2 years to less than 18 years

- **Formulation(s)**

Powder for concentrate for solution for infusion, intravenous use

- **Studies**

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	3	Embryo-foetal development toxicity study In-vivo targeting, scintigraphic and immunoPET imaging study Juvenile toxicity study
Clinical	4	Open-label, multi-centre, single-arm, multiple ascending-dose trial to evaluate the pharmacokinetics, safety and activity of the IGF-1R

		antagonist RO4858696 in children from 2 years to less than 18 years of age with advanced solid tumours Open-label, single-arm, multi-center, multi-cohort trial to evaluate pharmacokinetics, safety and activity of RO4858696 in children from 2 years to less than 18 years (and in adults) with recurrent or refractory Ewing sarcoma family of tumours, osteosarcoma, synovial sarcoma, rhabdomyosarcoma and other sarcomas. Double-blind, randomised, multi-center trial to evaluate safety and efficacy of RO4858696 add-on to cyclophosphamide and topotecan in children from 2 years to less than 18 years (and in adults) with first relapse of an Ewing sarcoma family of tumour Double-blind, placebo-controlled, randomised add-on, multi-centre trial to evaluate safety and efficacy of RO4858696 add-on to multimodal standard therapy in children from 2 years to less than 18 years with newly-diagnosed, metastatic to bone Ewing sarcoma family of tumour

Measures to address long term follow-up of potential safety issues and efficacy in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	**By December 2016**
Deferral for some or all studies contained in the paediatric investigation plan:	**Yes**