EMA/716808/2010

European Medicines Agency decision

P/270/2010

of 02 December 2010

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for pralatrexate (EMEA-000619-PIP02-10) 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 application submitted by Allos Therapeutics Limited on 12 April 2010 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 12 November 2010, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a 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

A paediatric investigation plan for pralatrexate, solution for infusion, intravenous use, solution for injection, intrathecal 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, is hereby agreed.

Article 2

A deferral for pralatrexate, solution for infusion, intravenous use, solution for injection, intrathecal 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, is hereby granted.

Article 3

A waiver for pralatrexate, solution for infusion, intravenous use, solution for injection, intrathecal 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, is hereby granted.

Article 4

This decision is addressed to Allos Therapeutics Limited, 71 Knowl Piece, Wilbury Way, Hitchin, Herts, SG4 0TY Hitchin, United Kingdom.

Done at London, 02 December 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/PDCO/612718/2010

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-000619-PIP02-10

Scope of the application

Active substance(s):

Pralatrexate

Condition(s):

Treatment of Hodgkin lymphoma

Treatment of mature B-cell non-Hodgkin lymphoma

Treatment of peripheral T-cell Lymphoma (nodal, other extranodal and leukaemic disseminated)

Treatment of lymphoblastic non-Hodgkin lymphoma

Pharmaceutical form(s):

Solution for infusion

Solution for injection

Route(s) of administration:

Intravenous use

Intrathecal use

Name/corporate name of the PIP applicant:

Allos Therapeutics Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Allos Therapeutics Limited submitted for agreement to the European Medicines Agency on 12 April 2010 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

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The procedure started on 20 May 2010.

Supplementary information was provided by the applicant on 27 August 2010.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

- to agree the paediatric investigation plan in accordance with Article 18 of said Regulation,
- to grant a deferral in accordance with Article 21 of said Regulation,
- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with

Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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 agreed 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 annex(es) and appendix.

London, 12 November 2010

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 Hodgkin lymphoma

The waiver applies to:

- All subsets of the paediatric population,
- For solution for infusion for intravenous use and solution for injection for intrathecal use,
- On the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

1.2. Conditions: Treatment of mature B-cell non-Hodgkin lymphoma, treatment of peripheral T-cell Lymphoma (nodal, other extranodal and leukaemic disseminated) and treatment of lymphoblastic non-Hodgkin lymphoma

The waiver applies to:

- The paediatric population from birth to less than 3 years of age,
- For solution for infusion for intravenous use and solution for injection for intrathecal use,
- On the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified subset.

2. Paediatric Investigation Plan

2.1. Conditions: Treatment of mature B-cell non-Hodgkin lymphoma, treatment of peripheral T-cell Lymphoma (nodal, other extranodal and leukaemic disseminated) and treatment of lymphoblastic non-Hodgkin lymphoma

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with first relapse or primary refractory mature B-cell non-Hodgkin lymphoma, treatment of peripheral T-cell lymphoma (nodal, other extranodal and leukaemic disseminated) and treatment of lymphoblastic non-Hodgkin lymphoma

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

From 3 years to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Solution for infusion for intravenous use and solution for injection for intrathecal use

2.1.4. Studies

Area	Number of studies	Description
Quality	1	Study 1: Development of a formulation for intrathecal use
Non-clinical	4	Study 2: In vitro polyglutamation and retention study Study 3: Development of a pralatrexate polyglutamation assay Study 4: Juvenile toxicity study Study 5: Intrathecal pralatrexate toxicology study
Clinical	3	Study 6: Open-label, multi-centre, single-arm, dose-finding trial to evaluate safety, pharmacokinetics and activity of high-dose pralatrexate with and without leucovorin rescue in paediatric patients from three years of age on with defined first relapsed or primary refractory non-Hodgkin lymphoma, including diffuse large B-cell lymphoma (DLBCL), anaplastic large cell lymphoma (ALCL), T-cell lymphoblastic lymphoma (T-LBL) and precursor B-cell lymphoblastic lymphoma (pB-LBL) Study 7: Active-controlled, randomized, multicentre, open-label, parallel-group trial to evaluate pharmacodynamics, safety and efficacy of high-dose pralatrexate with leucovorin rescue in paediatric patients from three years of age on with untreated first relapsed or with primary refractory non-Hodgkin lymphoma (DLBCL, ALCL, T-LBL or pB-LBL) Study 8: Open-label, multi-centre, single-arm, dose-finding trial to evaluate pharmacokinetics and safety in patients from three years of age on with CNS involvement of previously treated non-Hodgkin lymphoma (DLBCL, ALCL or T-LBL)

3. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 2021
Deferral for one or more studies contained in the paediatric investigation plan:	Yes