EMA/472143/2016

European Medicines Agency decision

P/0215/2016

of 12 August 2016

on the acceptance of a modification of an agreed paediatric investigation plan for dinutuximab (Unituxin) (EMEA-001285-PIP01-12-M02) 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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on the acceptance of a modification of an agreed paediatric investigation plan for dinutuximab (Unituxin) (EMEA-001285-PIP01-12-M02) 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/0295/2012 issued on 18 December 2012 and the decision P/0208/2013 issued on 3 September 2013,

Having regard to the application submitted by United Therapeutics Europe Limited on 1 April 2016 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 24 June 2016, 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 dinutuximab (Unituxin), solution for infusion, 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 United Therapeutics Europe Limited, Unither House, Curfew Bell Road, Chertsey, KT16 9FG – Surrey, United Kingdom.

EMA/PDCO/244049/2016 Corr
London, 24 June 2016

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

EMEA-001285-PIP01-12-M02

Scope of the application

Active substance(s):

Dinutuximab

Invented name:

Unituxin

Condition(s):

Treatment of neuroblastoma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

United Therapeutics Europe Limited

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, United Therapeutics Europe Limited submitted to the European Medicines Agency on 1 April 2016 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/0295/2012 issued on 18 December 2012, and the decision P/0208/2013 issued on 3 September 2013.

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

The procedure started on 26 April 2016.

Scope of the modification

Some 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;

   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 annex 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 neuroblastoma

The waiver applies to:

- the paediatric population from birth to less than 28 days;
- 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 population.

2. Paediatric Investigation Plan

2.1. Condition

Treatment of neuroblastoma

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with high-risk neuroblastoma as part of a consolidation therapy in combination with GM-CSF, interleukin-2 and retinoic acid after achieving at least a partial response and after high-dose chemotherapy with autologous haematopoietic stem cell transplantation

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

From 28 days to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for infusion

2.1.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	7	**Study 1:** Open-label, single-arm study to evaluate toxicity and activity of chimeric anti-disialoganglioside (GD2) monoclonal antibody NSC623408 in combination with GM-CSF in patients from 2 years to less than 18 years of age (and adults) with recurrent neuroblastoma

		Study 2: Open-label, dose-escalating study to evaluate tolerability of NSC623408 in combination with GM-CSF in patients from 28 days to less than 18 years of age with neuroblastoma **Study 3:** Open-label, dose escalating study to evaluate tolerability of NSC623408 in combination with GM-CSF and interleukin-2 in patients from 28 days to less than 18 years of age with neuroblastoma **Study 4:** Open-label, randomized, active-controlled study to evaluate efficacy and toxicity of NSC623408 in combination with GM-CSF, interleukin-2 and isotretinoin versus isotretinoin alone in patients from 28 days to less than 18 years of age with high-risk neuroblastoma. **Study 5:** Open-label, single-arm study to evaluate safety and activity of NSC623408 in combination with GM-CSF, interleukin-2 and isotretinoin in patients from 28 days to less than 18 years of age with high-risk neuroblastoma. **Study 6:** Open-label, single-arm study to evaluate safety of NSC623408 in combination with GM-CSF, interleukin-2 and isotretinoin in patients from 28 days to less than 18 years of age with high-risk neuroblastoma. **Study 7:** Open-label, randomized cross-over study to evaluate pharmacokinetics, tolerability and safety of NSC764038 compared to NSC623408 in patients from 28 days to less than 10 years of age with high-risk neuroblastoma.

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 February 2014.
Deferral for one or more studies contained in the paediatric investigation plan:	Yes.

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of neuroblastoma

Authorised indication(s):

- The product is indicated for the treatment of high-risk neuroblastoma in patients aged 12 months to 17 years, who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and autologous stem cell transplantation (ASCT). It is administered in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and isotretinoin.

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous infusion