MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100567-PIP01-22-M01

Scope of the Application

Active Substance(s)

Dinutuximab beta

Condition(s)

Treatment of neuroblastoma

Pharmaceutical Form(s)

Solution for infusion for intravenous use Concentrate for solution for infusion Powder and solvent for solution for injection for intravenous use Powder for solution for infusion for intravenous use

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

EUSA Pharma (UK) Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, EUSA Pharma (UK) Ltd submitted to the licensing authority on 08/06/2022 14:41 BST an application for a Modification

The procedure started on 02/02/2023 08:11 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100567-PIP01-22-M01

Of 17/03/2023 12:01 GMT

On the adopted decision for Dinutuximab beta (MHRA-100567-PIP01-22-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for Dinutuximab beta , Solution for infusion Concentrate for solution for infusion Powder and solvent for solution for injection Powder for solution for infusion , INTRAVENOUS USE .

This decision is addressed to EUSA Pharma (UK) Ltd, Breakspear Park, Breakspear Way, Hemel, UNITED KINGDOM, HP2 4TZ

ANNEX I

1. Waiver

1.1 Condition:

Treatment of neuroblastoma The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 28 days Pharmaceutical form(s): Solution for infusion Concentrate for solution for infusion Powder and solvent for solution for injection Powder for solution for infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: 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). Reason for Refusing Waiver: Not Applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of neuroblastoma

2.2 Indication(s) targeted by the PIP:

Treatment of neuroblastoma in minimal residual disease in patients from 1 month of age onwards in combination with aldesleukin and isotretinoin by means of a pain-minimising ch14.18/CHO (APN311) administration schedule.

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 1 month to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Solution for infusion Concentrate for solution for infusion Powder and solvent for solution for injection Powder for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	1	Study 1 (23939) Repeat-dose juvenile toxicity study
Clinical Studies	3	Study 2 (2009-015936-14 / APN311-201) Open-label, multi-centre, multiple-dose, single-arm trial to evaluate safety, toxicity and activity of APN311 in combination with aldesleukin in children from 1 month to less than 18 years of age (and young adults) with a neuroblastoma that is refractory to standard treatment or that has relapsed after high-dose therapy with allogeneic haploidentical stem cell transplantation. Study 3 (2009-018077-31 / APN311-202) Open-label, multi-centre, dose-escalating/dose schedule-varying trial to evaluate pharmacokinetics, pharmacodynamics, safety, toxicity and activity of APN311 in combination with aldesleukin and isotretinoin in children from 1 year to less than 18 years of age (and young adults) with a

		neuroblastoma after at least one high-dose therapy with stem cell rescue. Study 4 (APN311-304) Open-label, multi-centre trial to evaluate pharmacokinetics, pharmacodynamics, safety, toxicity and activity of APN311 in children from 12 months to less than 18 years of age (and young adults) with a neuroblastoma that is refractory to standard therapy or that has relapsed or with a neuroblastoma that is refractory to or that has relapsed after at least one high-dose therapy with stem cell rescue.
Extrapolation, Modeling & Simulation Studies	0	Not applicable.
Other Studies	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	30/04/2019
Deferral of one or more studies contained in the paediatric investigation plan:	Yes