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

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral

MHRA-100270-PIP01-21

Scope of the Application

Active Substance(s)

crinecerfont

Condition(s)

Treatment of congenital adrenal hyperplasia

Pharmaceutical Form(s)

Capsule, hard, Oral solution

Route(s) of Administration

Oral use; Gastric use

Name / Corporate name of the PIP applicant

Neurocrine Biosciences, Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Neurocrine Biosciences, Inc. submitted to the licensing authority on 18/10/2021 18:00 BST an application for a

The procedure started on 07/03/2022 12:18 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 agree a paediatric investigation plan and grant a 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-100270-PIP01-21

Of 04/04/2022 08:40 BST

On the adopted decision for crinecerfont (MHRA-100270-PIP01-21) 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 a paediatric investigation plan

This decision applies to a for crinecerfont, Capsule, hard, Oral solution , Oral use .

This decision is addressed to Neurocrine Biosciences, Inc., 12780 El Camino Real, San Diego, United States, CA 92130

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of congenital adrenal hyperplasia

2.2 Indication(s) targeted by the PIP:

Treatment of congenital adrenal hyperplasia

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

The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard, Oral solution

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Assess feasibility of administration of crinecerfont oral solution using a feeding tube.
Non-Clinical Studies	2	Study 2 (20259410) Determination of exposure levels and tolerability in rats after single and 4-day repeat dosing of crinecerfont. Study 3 (2020-TX-284) Evaluation of the effects in rats on reproductive and neurobehavioural development and function.
Clinical Studies	3	Study 4 (CAH2006) Randomised trial to evaluate the PK, efficacy and safety of crinecerfont with an initial 28 week placebo-controlled period followed by 24 week open label treatment. Study 5 (CAH2011) Open label study to assess the safety, tolerability, sparse PK, and PD of crinecerfont in children from birth to less than 2 years of age. Study 6 (CAH3008) Open label study to collect long-term safety data for up to 3 years in subjects with 21 -hydroxylase deficiency (21-OHD) causing congenital adrenal hyperplasia (CAH) who have completed treatment in Study CAH2006 or Study CAH2011.
Extrapolation, Modeling & Simulation Studies	4	Study 7 Population PK analysis update with paediatric data in children from 2 years to less than 18 years Study 8 Population PK analysis update with paediatric data in children less than 2 years Study 9 Paediatric Exposure- Response analysis update with data from adult and paediatric study in ages 2 years to less than 18 years. Study 10 Paediatric Exposure- Response analysis update with data from paediatric study in ages less than 2

		years combined with data from adults and older paediatric ages.
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:	No
Date of completion of the paediatric investigation plan:	31/08/2029
Deferral of one or more studies contained in the paediatric investigation plan:	Yes