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 of change(s) to the agreed paediatric investigation plan (MHRA-100482-PIP01-22-M01) and to the deferral

MHRA-100482-PIP01-22-M02

Scope of the Application

Active Substance(s)

acetyl-L-leucine ((s)-(acetylamino)-4-methylpentanoic acid)

Condition(s)

Treatment of Niemann-Pick Disease Type C (NPC)

Pharmaceutical Form(s)

Age-appropriate oral liquid dosage form

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

IntraBio Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, IntraBio Ltd submitted to the licensing authority on 04/06/2024 15:46 BST an application for a Modification

The procedure started on 05/08/2024 10:31 BST

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-100482-PIP01-22-M02

Of 23/09/2024 16:17 BST

On the adopted decision for acetyl-L-leucine ((s)-(acetylamino)-4-methylpentanoic acid) (MHRA-100482-PIP01-22-M02) 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 acetyl-L-leucine ((s)-(acetylamino)-4-methylpentanoic acid) , Age-appropriate oral liquid dosage form , ORAL USE .

This decision is addressed to IntraBio Ltd, 10 Earlsfort Terrace, Dublin 2, IRELAND, D02 T380

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of Niemann-Pick Disease type C (NPC)

2.2 Indication(s) targeted by the PIP:

Treatment of Niemann-Pick Disease type C (NPC)

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):

Age-appropriate oral liquid dosage form.

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 A study to assess compatibility of the formulation with the feeding tube. Study 2 Development of a lower strength and volume formulation appropriate for dosing children weighing under 5 kg.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	Study 3 (IB1001-201) Observer-blind, non-comparative trial to evaluate pharmacokinetics (PK), safety and activity of the active substance in children from 6 years to less than 18 years of age (and adults) with Niemann-Pick Disease Type C (NPC). Study 4 (IB1001-301) Double-blind, randomised, placebo-controlled, cross-over trial to evaluate pharmacokinetics, safety and efficacy of the active substance in children from 4 years to less than 18 years of age with Niemann-Pick Disease Type C (NPC), followed by an open-label extension study including children from birth to less than 18 years of age. Study 5 (IB1001-401) Deleted during procedure MHRA-100482-PIP01-22-M02
Extrapolation, Modeling & Simulation Studies	1	Study 6 (TW-2020-IntraB-001) Modelling and Simulation study of population pharmacokinetics (PK) to support dose selection in children under 5 kg body weight and to evaluate the use of the product in children from birth to less than

		4 years of age with Niemann-Pick Disease Type C.
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:	31/03/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes