MHRA
10 South Colonnade
Canary Wharf
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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-101785-PIP01-25

Scope of the Application

Active Substance(s)

(R)-3-(1-cyclopropyl-3-(2-fluoro-4-(trifluoromethoxy)benzyl)ureido)piperidine-1-carboxamide (JNT-517)

Condition(s)

Treatment of hyperphenylalaninemia

Pharmaceutical Form(s)

Oral powder, Tablet, Granules for oral suspension

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Otsuka Pharmaceutical Netherlands B.V.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Otsuka Pharmaceutical Netherlands B.V. submitted to the licensing authority on 17/01/2025 20:30 GMT an application for a

The procedure started on 17/02/2025 17:48 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-101785-PIP01-25

Of 03/06/2025 09:51 BST

On the adopted decision for (R)-3-(1-cyclopropyl-3-(2-fluoro-4-(trifluoromethoxy)benzyl)ureido)piperidine-1-carboxamide (JNT- 517) (MHRA-101785-PIP01-25) 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 (R)-3-(1-cyclopropyl-3-(2-fluoro-4-(trifluoromethoxy)benzyl)ureido)piperidine-1-carboxamide (JNT- 517), Oral powder, Tablet, Granules for oral suspension , ORAL USE .

This decision is addressed to Otsuka Pharmaceutical Netherlands B.V., Herikerbergweg 292, Amsterdam, NETHERLANDS, 1101 CT

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of hyperphenylalaninemia

2.2 Indication(s) targeted by the PIP:

Reduction of plasma phenylalanine concentrations in patients with phenylketonuria who have uncontrolled plasma phenylalanine concentrations.

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

All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Oral powder Tablet Granules for oral suspension

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of age-appropriate formulation (granules for oral suspension) for use in children below 12 years of age or adolescents unable to swallow tablets.
Non-Clinical Studies	1	Study 2 Definitive juvenile animal study
Clinical Studies	3	Study 3 (JNT517-201) Randomised, double-blind, placebo-controlled study to evaluate efficacy and safety of JNT-517 in adolescents from 12 to less than 18 years of age with phenylketonuria (PKU). Study 4 (JNT517-301) Randomised, double-blind, placebo-controlled, two-part study to evaluate efficacy and safety of JNT-517 in children from 4 years to less than 18 years of age (and adults) with PKU. Study 5 (JNT517-302) Open-label, single-arm study to evaluate safety and efficacy of JNT-517 in paediatric participants from birth to less than 4 years of age with PKU.
Extrapolation, Modeling & Simulation Studies	3	Study 6 (JNT517-M&S-1) Modelling and simulation analyses to support dosing of JNT517 in children from 4 years to less than 18 years of age with PKU. Study 7 (JNT517-M&S-2) Modelling and simulation analyses to support dosing of JNT517 in children from birth to less than 4 years of age with

		PKU. Extrapolation Plan Studies 3, 4, 5, 6 and 7 are part of an extrapolation plan covering the paediatric population from birth to less than 18 years of age.
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:	31/01/2032
Deferral of one or more studies contained in the paediatric investigation plan:	Yes