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 and to the deferral.

MHRA-100343-PIP01-21-M02

Scope of the Application

Active Substance(s)

MACITENTAN

Condition(s)

Treatment of pulmonary arterial hypertension, Treatment of systemic sclerosis, Treatment of idiopathic pulmonary fibrosis

Pharmaceutical Form(s)

Film-coated tablet, Dispersible tablet

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Janssen-Cilag Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Janssen-Cilag Limited submitted to the licensing authority on 02/02/2023 13:04 GMT an application for a Modification

The procedure started on 12/06/2023 14:16 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-100343-PIP01-21-M02

Of 05/07/2023 13:14 BST

On the adopted decision for MACITENTAN (MHRA-100343-PIP01-21-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 MACITENTAN, Film-coated tablet, Dispersible tablet , ORAL USE .

This decision is addressed to Janssen-Cilag Limited, 50-100 Holmers Farm Way, High Wycombe, UNITED KINGDOM, HP12 4EG

ANNEX I

1. Waiver

1.1 Condition:

1.1 Condition: Treatment of pulmonary arterial hypertension The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 month of age. Pharmaceutical form(s): Film-coated tablet Dispersible tablet Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments; 1.2 Condition: Treatment of systemic sclerosis. The waiver applies / applied to: Paediatric Subset(s): All subsets of the paediatric population from birth to less than 18 years of age. Pharmaceutical form(s): Film-coated tablet Dispersible tablet Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s). 1.3 Condition: Treatment of idiopathic pulmonary fibrosis The waiver applies / applied to: Paediatric Subset(s): All subsets of the paediatric population from birth to less than 18 years of age. Pharmaceutical form(s): Film-coated tablet Dispersible tablet Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of pulmonary arterial hypertension

2.2 Indication(s) targeted by the PIP:

Treatment of pulmonary arterial hypertension

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):

Film-coated tablet Dispersible tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of a dispersible tablet formulation. Study 2 This study was deleted during procedure EMEA-001032-PIP01-10-M02.
Non-Clinical Studies	2	Study 3 25-day dose range finding toxicity study in juvenile rats. Study 4 Toxicity study in juvenile rats.
Clinical Studies	2	Study 5 This study was deleted during procedure EMEA-001032-PIP01-10-M02. Study 6 This study was deleted during procedure EMEA-001032-PIP01-10-M02. Study 7 This study was deleted during procedure EMEA-001032-PIP01-10-M02. Study 8 Open-label, randomised, multicentre, active-controlled, parallel-group study to evaluate pharmacokinetics, safety and efficacy of macitentan in children from 1 month to less than 18 years of age with pulmonary arterial hypertension. Study 11: (This

		study was added during procedure MHRA-100343-PIP01-21-M02.) Open-label, multicentre, single-arm, uncontrolled study to evaluate pharmacokinetics, and safety of macitentan in children from 1 month to less than 2 years of age with PAH.
Extrapolation, Modeling & Simulation Studies	2	Study 9 (This study was added during procedure MHRA-100343-PIP01-21-M01) Population pharmacokinetic modelling and simulation study to support extrapolation and the use of macitentan in children from 1 month to less than 18 years of age with pulmonary arterial hypertension. Study 10 (This study was added during procedure MHRA-100343-PIP01-21-M01) Pharmacodynamic similarity/ comparison study.
Other Studies	1	Study 12: (This study was added during procedure MHRA-100343-PIP01-21-M02) Combined descriptive analysis of pharmacokinetics, safety, and efficacy of macitentan in children from 1 month to less than 2 years of age with PAH treated with macitentan.
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:	30/04/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes