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-101073-PIP01-23-M01

Scope of the Application

Active Substance(s)

MIRABEGRON

Condition(s)

Treatment of idiopathic overactive bladder

Pharmaceutical Form(s)

Prolonged-release granules for oral suspension, Prolonged-release tablet

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Astellas Pharma Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Astellas Pharma Ltd submitted to the licensing authority on 06/07/2023 09:24 BST an application for a Modification

The procedure started on 07/11/2023 10:47 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-101073-PIP01-23-M01

Of 20/11/2023 11:05 GMT

On the adopted decision for MIRABEGRON (MHRA-101073-PIP01-23-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.

This decision applies to a Modification for MIRABEGRON, Prolonged-release granules for oral suspension, Prolonged-release tablet , ORAL USE .

This decision is addressed to Astellas Pharma Ltd, 300 Dashwood Lang Road, Bourne Business Park, Addlestone, UNITED KINGDOM, KT15 2NX

ANNEX I

1. Waiver

1.1 Condition:

Treatment of idiopathic overactive bladder. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 5 years of age. Pharmaceutical form(s): Prolonged-release granules for oral suspension Route(s) of administration: ORAL USE Reason for granting waiver: On the grounds the specific medicinal product does not represent a significant therapeutic benefit over existing treatments Paediatric Subset(s): The paediatric population from birth to less than 6 years of age. Pharmaceutical form(s): Prolonged-release tablet Route(s) of administration: ORAL USE Reason for granting waiver: On the grounds the specific medicinal product does not represent a significant therapeutic benefit over existing treatments

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of idiopathic overactive bladder

2.2 Indication(s) targeted by the PIP:

Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in patients with overactive bladder syndrome.

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

The paediatric population from 5 years to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Prolonged-release granules for oral suspension Prolonged-release tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	(The following quality studies are the same as the quality studies in procedure MHRA-100566-PIP01-22-M01.) Study 1 Development of an oral age-appropriate prolonged-release microgranular-based suspension with a compatible delivery device. Study 2 Development of a prolonged-release tablet.
Non-Clinical Studies	2	(The following non-clinical studies are the same as the non-clinical studies in procedure MHRA-100566-PIP01-22-M01.) Study 3 14 day repeated dose feasibility and dose range finding study in juvenile rats. Study 4 13 week repeated dose toxicity and toxicokinetics study in juvenile rats.
Clinical Studies	4	Study 5 This study was deleted during procedure EMEA-000597-PIP02-10-M02. Study 6 This study was deleted during procedure EMEA-000597-PIP02-10-M02. Study 7 (This study is the same as Study 7 in procedure MHRA-100566-PIP01-22-M01.) Open label, multicentre single

		ascending dose study to evaluate pharmacokinetics, safety and tolerability of mirabegron prolonged-release tablets in children from 5 years to less than 18 years of age with overactive bladder or neurogenic detrusor overactivity. Study 8 This study was deleted during procedure EMEA-000597-PIP02-10-M03. Study 9 Double blind, randomised, multicentre, parallel group, placebo controlled sequential dose titration study to evaluate pharmacokinetics, safety and efficacy of mirabegron in children from 5 years to less than 18 years of age with overactive bladder. Study 10 This study was deleted during procedure EMEA-000597-PIP02-10-M07. Study 11 This study was deleted during procedure EMEA-000597-PIP02-10-M04. Study 12 This study was deleted during procedure EMEA-000597-PIP02-10-M04 Study 13 (This study is the same as Study 13 in procedure MHRA-100566-PIP01-22-M01.) Open label, randomised bioavailability and food effect study to evaluate the relative bioavailability of a prototype oral prolonged-release micro granular-based suspensions and the prolonged-release tablet in healthy adults from 18 years to less than 26 years of age. Study 14 (This study is the same as Study 14 in procedure MHRA-100566-PIP01-22-M01.) Open label, single dose study to evaluate pharmacokinetics, safety and tolerability of mirabegron prolonged-release granules for oral suspension in children with overactive bladder from 5 to less than 12 years of age and in children with neurogenic detrusor overactivity from 3 years to less than 12 years of age.
Extrapolation, Modeling & Simulation Studies	1	Study 15 Extrapolation study to evaluate the use of mirabegron in adolescents from 12 years to less than 18 years of age with overactive bladder.
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:	30/06/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes