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 plan (MHRA-100333-PIP01-21-M01) and to the deferral

MHRA-100566-PIP01-22-M01

Scope of the Application

Active Substance(s)

MIRABEGRON

Condition(s)

Treatment of neurogenic detrusor overactivity

Pharmaceutical Form(s)

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

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 29/06/2022 17:17 BST an application for a Modification

The procedure started on 31/08/2022 08:23 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-100566-PIP01-22-M01

Of 20/09/2022 08:49 BST

On the adopted decision for MIRABEGRON (MHRA-100566-PIP01-22-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 (including modification of a waiver or deferral included in that paediatric investigation plan)

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

This decision is addressed to Astellas Pharma Ltd, SPACE, 68 Chertsey road, Woking, GU215BJ, United Kingdom, Woking, UNITED KINGDOM, GU215BJ

ANNEX I

1. Waiver

1.1 Condition:

Treatment of neurogenic detrusor overactivity The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 months of age Pharmaceutical form(s): Prolonged-release tablet; Granules for oral suspension 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.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of neurogenic detrusor overactivity

2.2 Indication(s) targeted by the PIP:

Treatment of detrusor overactivity in children with neurogenic bladder dysfunction

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

The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

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

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	(Studies for mirabegron the same as in EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.) Study 1 Development of an oral age-appropriate prolonged-release microgranule-based suspension with a compatible delivery device. Study 2 Development of a prolonged-release tablet.
Non-Clinical Studies	2	(Studies for mirabegron the same as in EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.) 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	5	(Studies for mirabegron the same as in EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.) Study 7 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 11 Open label, baseline controlled, multicentre, dose titration

		study followed by a fixed dose observation period to evaluate efficacy, safety and pharmacokinetics of mirabegron in children from 3 years to less than 18 years of age with neurogenic detrusor overactivity on clean intermittent catheterisation (CIC). Study 12 Open label, multicentre, baseline-controlled sequential dose titration study followed by a fixed dose observation period to evaluate pharmacokinetics, efficacy and safety of mirabegron prolonged-release microgranule-based suspension in children from 6 months to less than 3 years of age with neurogenic detrusor overactivity. Study 13 Open label, randomised bioavailability and food effect study to evaluate the relative bioavailability of a prototype oral prolonged-release microgranule-based suspensions and the prolonged-release tablet in healthy adults from 18 years to less than 26 years of age. Study 14 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 years to less than 12 years of age and in children with neurogenic detrusor overactivity from 3 years to less than 12 years of age. [Studies 5, 6, 8 9 and 10 were deleted due to splitting of the PIP.]
Extrapolation, Modeling & Simulation Studies	0	Not applicable
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:	31/03/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes