EMA/104845/2024

European Medicines Agency decision

P/0085/2024

of 15 March 2024

on the acceptance of a modification of an agreed paediatric investigation plan for mirabegron (Betmiga), (EMEA-000597-PIP03-15-M06) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0117/2015 issued on 5 June 2015, the decision P/0269/2015 issued on 27 November 2015, the decision P/0288/2016 issued on 4 November 2016, the decision P/0056/2017 issued on 17 March 2017, the decision P/0402/2021 issued on 1 October 2021 and the decision P/0187/2022 issued on 25 May 2022,

Having regard to the application submitted by Astellas Pharma Europe B.V. on 10 November 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 23 February 2024, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for mirabegron (Betmiga), prolonged-release granules for oral suspension, prolonged-release tablet, oral use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/172/2010 issued on 10 September 2010, including subsequent modifications thereof.

Article 3

This decision is addressed to Astellas Pharma Europe B.V., 62 Sylviusweg, 2333 BE – Leiden, The Netherlands.

EMA/PDCO/540735/2023
Amsterdam, 23 February 2024

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-000597-PIP03-15-M06

Scope of the application

Active substance(s):

Mirabegron

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of neurogenic detrusor overactivity

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 Europe B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Astellas Pharma Europe B.V. submitted to the European Medicines Agency on 10 November 2023 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0117/2015 issued on 5 June 2015, the decision P/0269/2015 issued on 27 November 2015, the decision P/0288/2016 issued on 4 November 2016, the decision P/0056/2017 issued on 17 March 2017, the decision P/0402/2021 issued on 1 October 2021 and the decision P/0187/2022 issued on 25 May 2022.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 3 January 2024.

Scope of the modification

Some timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of neurogenic detrusor overactivity

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- prolonged-release granules for oral suspension, prolonged-release tablet, oral use;
- 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:

Treatment of neurogenic detrusor overactivity

2.1.1. Indication(s) targeted by the PIP

Treatment of detrusor overactivity in children with neurogenic bladder dysfunction

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Prolonged-release granules for oral suspension

Prolonged-release tablet

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an oral age-appropriate prolonged-release microgranula-based suspension with a compatible delivery device. **Study 2** Development of a prolonged-release tablet.
Non-clinical studies	**Study 3 (178-TX-054)** 14-day repeated dose feasibility and dose range finding study in juvenile rats. **Study 4 (178-TX-055)** 13 week repeated dose toxicity and toxicokinetics study in juvenile rats.

Clinical studies	*[**Study 5** was deleted due to splitting of the PIP.]* *[**Study 6** was deleted due to splitting of the PIP.]* **Study 7 (178-CL-202)** Open label, multicentre single ascending dose study to evaluate pharmacokinetics, safety and tolerability of mirabegron prolonged-release tablets in children from 5 to less than 18 years of age with overactive bladder or neurogenic detrusor overactivity. *[**Study 8** was deleted due to splitting of the PIP.]* *[**Study 9** was deleted due to splitting of the PIP.]* *[**Study 10** was deleted due to splitting of the PIP.]* **Study 11 (178-CL-206)** 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 to less than 18 years of age with neurogenic detrusor overactivity on clean intermittent catheterisation (CIC). **Study 12 (178-CL-207)** 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 microgranula-based suspension in children from 6 months to less than 3 years of age with neurogenic detrusor overactivity. **Study 13 (178-CL-201)** Open label, randomised bioavailability and food effect study to evaluate the relative bioavailability of a prototype oral prolonged-release microgranula-based suspensions and the prolonged-release tablet in healthy adults from 18 to less than 26 years of age. **Study 14 (178-CL-203)** 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 to less than 12 years of age.
Extrapolation, modelling and simulation studies	Not applicable
Other studies	Not applicable
Other measures	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of idiopathic overactive bladder

Authorised indication(s):

- Betmiga is indicated in symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome.

Authorised pharmaceutical form(s):

Prolonged-release tablets

Authorised route(s) of administration:

Oral use