



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/724286/2017

European Medicines Agency decision

P/0350/2017

of 1 December 2017

on the refusal of a modification of an agreed paediatric investigation plan for mirabegron (Betmiga), (EMA-000597-PIP02-10-M06) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 726/2004¹,

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency²,

Having regard to the European Medicines Agency's decision P/172/2010 issued on 10 September 2010, the decision P/0191/2013 issued on 9 August 2013, the decision P/0011/2014 issued on 22 January 2014, the decision P/0014/2015 issued on 30 January 2015, the decision P/0116/2015 issued on 5 June 2015 and the decision P/0287/2016 issued on 4 November 2016,

Having regard to the application submitted by Astellas Pharma Europe B.V. on 20 July 2017 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 13 October 2017, 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 refusal of changes to the agreed paediatric investigation plan and to the deferral.
- (2) It is therefore appropriate to adopt a decision on the refusal of changes to the agreed paediatric investigation plan, including changes to the deferral.

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 the details of which are set out in the opinion of the Paediatric Committee of the European Medicines

¹ OJ L 378, 27.12.2006, p.1.

² OJ L 136, 30.4.2004, p. 1.

Agency annexed hereto, together with its appendices, are hereby refused.

Article 2

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



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/466325/2017

London, 13 October 2017

Opinion of the Paediatric Committee on the refusal of a modification of an agreed Paediatric Investigation Plan EMA-000597-PIP02-10-M06

Scope of the application

Active substance(s):

Mirabegron

Invented name:

Betmiga

Condition(s):

Treatment of idiopathic overactive bladder

Authorised indication(s):

See Annex II

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.

Information about the authorised medicinal product:

See Annex II



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 20 July 2017 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/172/2010 issued on 10 September 2010, the decision P/0191/2013 issued on 9 August 2013, the decision P/0011/2014 issued on 22 January 2014, the decision P/0014/2015 issued on 30 January 2015, the decision P/0116/2015 issued on 5 June 2015 and the decision P/0287/2016 issued on 4 November 2016.

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

The procedure started on 15 August 2017.

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 refuse the changes proposed by the applicant regarding the paediatric investigation plan and the deferral.

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

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver remain unchanged and are set out in the Annex I.
3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

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 idiopathic overactive bladder

The waiver applies to:

- the paediatric population from birth to less than 5 years of age;
- prolonged-release granules for oral suspension, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

The waiver applies to:

- the paediatric population from birth to less than 6 years of age;
- 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 idiopathic overactive bladder

2.1.1. 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

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

From 5 years 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	Number of measures	Description
Quality-related studies	2	Study 1 <i>(Same as Study 1 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity)</i>

		Development of an oral age-appropriate prolonged-release microgranula-based suspension with a compatible delivery device Study 2 <i>Same as Study 2 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity</i> Development of a prolonged-release tablet
Non-clinical studies	2	Study 3 <i>(Same as Study 3 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity)</i> 14 day repeated dose feasibility and dose range finding study in juvenile rats Study 4 <i>(Same as Study 4 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity)</i> 13 week repeated dose toxicity and toxicokinetics study in juvenile rats
Clinical studies	5	<i>[Study 5 deleted in procedure EMEA-000597-PIP02-10-M02]</i> <i>[Study 6 deleted in procedure EMEA-000597-PIP02-10-M02]</i> Study 7 <i>(Same as Study 7 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity)</i> 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 <i>[Study 8 deleted in procedure EMEA-000597-PIP02-10-M03]</i> Study 9 Double blind, randomised, multicentre, parallel group, placebo and active controlled (oxybutynin) sequential dose titration study to evaluate pharmacokinetics, safety and efficacy of mirabegron prolonged-release microgranula-based suspension in children from 5 to less than 18 years of age with overactive bladder

		Study 10 (Extension of Study 9) Open label long-term safety study to evaluate safety and efficacy of mirabegron prolonged-release microgranula-based suspension in children from 5 to less than 18 years of age with overactive bladder <i>[Study 11 deleted in procedure EMEA-000597-PIP02-10-M04]</i> <i>[Study 12 deleted in procedure EMEA-000597-PIP02-10-M04]</i> Study 13 <i>(Same as Study 13 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity)</i> 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 <i>(Same as Study 14 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity)</i> 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	0	Not applicable
Other studies	0	Not applicable
Other measures	0	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 September 2021
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):

- 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