EMA/520052/2019

# European Medicines Agency decision

P/0350/2019

of 30 September 2019

on the acceptance of a modification of an agreed paediatric investigation plan for mirabegron (Betmiga), (EMEA-000597-PIP02-10-M07) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

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, the decision P/0287/2016 issued on 4 November 2016 and the decision P/0350/2017 issued on 1 December 2017,

Having regard to the application submitted by Astellas Pharma Europe B.V. on 25 March 2019 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 20 September 2019, 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) of Regulation (EC) No 1901/2006, 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.
[2] OJ L 136, 30.4.2004, p. 1.

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

EMA/PDCO/450007/2019
Amsterdam, 20 September 2019

# Final opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-000597-PIP02-10-M07

## 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 25 March 2019 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, the decision P/0287/2016 issued on 4 November 2016 and the decision P/0350/2017 issued on 1 December 2017.

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

An Opinion was adopted by the Paediatric Committee on 28 June 2019 with 11 votes in favour and 16 votes against, not reaching an absolute majority of committee members in favour or against the proposed modification. Astellas Pharma Europe B.V. received the Paediatric Committee Opinion on 8 July 2019.

On 6 August 2019 Astellas Pharma Europe B.V. submitted to the European Medicines Agency a written request including detailed grounds for a re-examination of the Opinion.

The re-examination procedure started on 22 August 2019.

A meeting with the Paediatric Committee took place on 18 September 2019.

## Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

## Final Opinion

1. The Paediatric Committee, having assessed the detailed grounds for re-examination, in accordance with Article 25(3) of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

1.1. to revise its opinion and

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

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 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 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**<br><br>*(Same as Study 1 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity)* |

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

| | | |
|---|---|---|
| | | *000597-PIP02-10-M07]*<br><br>*[Study 11 was deleted as a result of procedure EMEA-000597-PIP02-10-M04]*<br><br>*[Study 12 was deleted as a result of procedure EMEA-000597-PIP02-10-M04]*<br><br>**Study 13**<br><br>*(Same as Study 13 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity)*<br><br>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<br><br>**Study 14**<br><br>*(Same as Study 14 of mirabegron EMEA-000597-PIP03-15 and subsequent modifications for the condition treatment of neurogenic detrusor overactivity)*<br><br>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 | 1 | **Study 15**<br><br>*(This study was added as a result of procedure EMEA-000597-PIP02-10-M07)*<br><br>Extrapolation study to evaluate the use of mirabegron in adolescents from 12 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 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 2024 |
| 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