EMA/666528/2016

European Medicines Agency decision

P/0288/2016

of 4 November 2016

on the acceptance of a modification of an agreed paediatric investigation plan for mirabegron (Betmiga), (EMEA-000597-PIP03-15-M02) 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/0117/2015 issued on 5 June 2015 and the decision P/0269/2015 issued on 27 November 2015,

Having regard to the application submitted by Astellas Pharma Europe B.V. on 24 June 2016 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 16 September 2016, 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.

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

[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, 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., Sylviusweg 62, 2333 BE – Leiden, The Netherlands.

EMA/PDCO/453754/2016
London, 16 September 2016

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

EMEA-000597-PIP03-15-M02

Scope of the application

Active substance(s):

Mirabegron

Invented name:

Betmiga

Condition(s):

Treatment of neurogenic detrusor overactivity

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

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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 24 June 2016 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 and the decision P/0269/2015 issued on 27 November 2015.

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

The procedure started on 19 July 2016.

Scope of the modification

Some measures 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 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 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;
- for 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;
- for 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	Number of measures	Description
Quality-related studies	2	**Study 1** *(Same as Study 1 of mirabegron EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.)* Development of an oral age-appropriate prolonged-release microgranula-based suspension with a compatible delivery device.

		Study 2 *(Same as Study 2 of mirabegron EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.)* Development of a prolonged-release tablet.
Non-clinical studies	2	**Study 3** *(Same as Study 3 of mirabegron EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.)* 14 day repeated dose feasibility and dose range finding study in juvenile rats. **Study 4** *(Same as Study 4 of mirabegron EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.)* 13 week repeated dose toxicity and toxicokinetics study in juvenile rats.
Clinical studies	5	**Study 7** *(Same as Study 7 of mirabegron EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.)* 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 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 5 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 microgranula-based suspension in children from 6 months to less than 5 years of age with neurogenic detrusor overactivity. **Study 13** *(Same as Study 13 of mirabegron EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.)*

		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** *(Same as Study 14 of mirabegron EMEA-000597-PIP02-10 and subsequent modifications for the condition treatment of idiopathic overactive bladder.)* 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 March 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