EMA/784278/2013

European Medicines Agency decision

P/0011/2014

of 22 January 2014

on the acceptance of a modification of an agreed paediatric investigation plan for mirabegron (Betmiga) (EMEA-000597-PIP02-10-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/172/2010 issued on 10 September 2010, and the decision P/0191/2013 issued on 9 August 2013,

Having regard to the application submitted by Astellas Pharma Europe B.V. on 13 September 2013 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 6 December 2013, 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), polonged-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 is addressed to Astellas Pharma Europe B.V., Sylviusweg 62, 2333 BE – Leiden, The Netherlands.

Done at London, 22 January 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/577181/2013 Corr

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

EMEA-000597-PIP02-10-M02

Scope of the application

Active substance(s):

Mirabegron

Invented name:

Betmiga

Condition(s):

Treatment of idiopathic overactive bladder

Treatment of neurogenic detrusor overactivity

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Polonged-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 13 September 2013 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 and the decision P/0191/2013 issued on 9 August 2013.

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

The procedure started on 10 October 2013.

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 Icelandic and the Norwegian Paediatric Committee members agree 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.

London, 6 December 2013

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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

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;
- 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.

1.2. 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 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	2	**Measure 1** Development of an oral age-appropriate prolonged-release microgranula-based suspension with a compatible delivery device. **Measure 2** Development of a prolonged-release tablet.
Non-clinical	2	**Measure 3** 14 day repeated dose feasibility and dose range finding study in juvenile rats. **Measure 4** 13 week repeated dose toxicity and toxicokinetics study in juvenile rats.
Clinical	5	*[Measure 5 deleted in procedure EMEA-000597-PIP02-10-M02]* *[Measure 6 deleted in procedure EMEA-000597-PIP02-10-M02]* **Measure 7** Open label, multicentre single ascending dose study to evaluate pharmacokinetics, safety and tolerability of mirabegron prolonged-release microgranula-based suspension in children from 5 to less than 18 years of age with overactive bladder. **Measure 8** (Extension of Measure 7) Open label extension of multicentre single ascending dose study with mirabegron prolonged-release microgranula-based suspension in children from 5 to less than 18 years of age with overactive bladder. **Measure 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.

		Measure 10 (Extension of Measure 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. **Measure 13** Open label, randomised bioavailability and food effect study to evaluate the relative bioavailability of 1 or 2 prototype oral prolonged-release microgranula-based suspensions and the prolonged-release tablet in healthy adults from 18 to less than 26 years of age.

2.2. Condition: treatment of neurogenic detrusor overactivity

2.2.1. Indication(s) targeted by the PIP

Treatment of detrusor overactivity in children with neurogenic bladder dysfunction.

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

From 6 months to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

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

2.2.4. Measures

Area	Number of measures	Description
Quality	2	**Measure 1** (Same measure as for treatment of idiopathic overactive bladder) Development of an oral age-appropriate prolonged-release microgranula-based suspension with a compatible delivery device. **Measure 2** (Same measure as for treatment of idiopathic overactive bladder) Development of a prolonged-release tablet.
Non-clinical	2	**Measure 3** (Same measure as for treatment of idiopathic overactive bladder) 14 day repeated dose feasibility and dose range finding study in juvenile rats. **Measure 4** (Same measure as for treatment of idiopathic overactive bladder) 13 week repeated dose toxicity and toxicokinetics study in juvenile rats.

Clinical	3	*[Measure 5 deleted in procedure EMEA-000597-PIP02-10-M02]* *[Measure 6 deleted in procedure EMEA-000597-PIP02-10-M02]* **Measure 11** Double blind, randomised, multicentre, active controlled (oxybutynin) 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 5 to less than 18 years of age with neurogenic detrusor overactivity. **Measure 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. **Measure 13** (same measure as for treatment of idiopathic overactive bladder) Open label, randomised bioavailability and food effect study to evaluate the relative bioavailability of 1 or 2 prototype oral prolonged-release microgranula-based suspensions and the prolonged-release tablet in healthy adults from 18 to less than 26 years of age.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety 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):

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