EMA/559076/2010

European Medicines Agency decision

P/172/2010

of 10 September 2010

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for mirabegron, EMEA-000597-PIP02-10 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 application submitted by Astellas Pharma Europe B.V. on 30 April 2010 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 6 August 2010, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for mirabegron, oral liquid, tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for mirabegron, oral liquid, tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for mirabegron, oral liquid, tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Astellas Pharma Europe B.V., Elisabethhof 19, Leiderdorp - 2353 EW, The Netherlands.

Done at London, 10 September 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/559076/2010

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-000597-PIP02-10

Scope of the application

Active substance(s):

Mirabegron

Condition(s):

Treatment of idiopathic overactive bladder

Treatment of neurogenic detrusor overactivity

Pharmaceutical form(s):

Oral liquid

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 16(1) of Regulation (EC) No 1901/2006 as amended, Astellas Pharma Europe B.V. submitted for agreement to the European Medicines Agency on 30 April 2010 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 10 June 2010.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation,
   - to grant a deferral in accordance with Article 21 of said Regulation,
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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 annex(es) and appendix.

London, 6 August 2010

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

Annex I

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

1. Condition(s)

Treatment of idiopathic overactive bladder

Treatment of neurogenic detrusor overactivity

2. Waiver

2.1. Condition(s)

Treatment of idiopathic overactive bladder

The waiver applies to:

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

2.2. Condition(s)

Treatment of neurogenic detrusor overactivity

The waiver applies to:

- The paediatric population from birth to less than 6 months of age,
- for oral liquid, 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 tablet, oral use,
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

3. Paediatric Investigation Plan

3.1. Condition to be investigated

Treatment of Idiopathic overactive bladder

3.1.1. 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

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

From 5 years to less than 18 years of age.

3.1.3. Pharmaceutical form(s)

Oral liquid

Tablet

3.1.4. Studies

Area	Number of studies	Description
Quality	2	*Study 1* Development of an oral age-appropriate modified release microgranula-based suspension with a compatible delivery device. *Study 2* Development of a modified release tablet.
Non-clinical	2	*Study 3* 14 day repeated dose feasibility and dose range finding study in juvenile rats. *Study 4* 13 week repeated dose toxicity and toxicokinetics study in juvenile rats.
Clinical	6	*Study 5* Open label, randomised, formulation taste and pharmacokinetics study to evaluate the taste and pharmacokinetics of different mirabegron modified release microgranula-based suspensions in healthy young adults from 18 to less than 26 years of age combined with open label, single dose study to evaluate the taste of prototype oral modified release liquid placebo formulation(s) in children from 6 months to less than 18 years of age.

		Study 6 Open label, randomised bioavailability and food effect study to compare relative bioavailability of the liquid formulation and tablet in healthy young adults from 18 to less than 26 years of age. *Study 7* Open label, multicentre single ascending dose study to evaluate pharmacokinetics, safety and tolerability of mirabegron modified release microgranula-based suspension in children from 5 to less than 18 years of age with overactive bladder. *Study 8 (Extension of Study 7)* Open label extension of multicentre single ascending dose study with mirabegron modified release microgranula-based suspension in children from 5 to less than 18 years of age with overactive bladder. *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 modified 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 modified release microgranula-based suspension in children from 5 to less than 18 years of age with overactive bladder.

3.2. Condition to be investigated

Treatment of neurogenic detrusor overactivity

3.2.1. Indication(s) targeted by the PIP

Treatment of detrusor overactivity in children with neurogenic bladder dysfunction

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

From 6 months to less than 18 years of age.

3.2.3. Pharmaceutical form(s)

Oral liquid

Tablet

3.2.4. Studies

Area	Number of studies	Description
Quality	2	*Study 1 (Same study as for condition idiopathic overactive bladder)* Development of an oral age-appropriate modified release microgranula-based suspension with a compatible delivery device. *Study 2 (Same study as for condition idiopathic overactive bladder)* Development of a modified release tablet.
Non-clinical	2	*Study 3 (Same study as for condition idiopathic overactive bladder)* 14 day repeated dose feasibility and dose range finding study in juvenile rats. *Study 4 (Same study as for condition idiopathic overactive bladder)* 13 week repeated dose toxicity and toxicokinetics study in juvenile rats.
Clinical	4	*Study 5 (Same study as for condition idiopathic overactive bladder)* Open label, randomised, formulation taste and pharmacokinetics study to evaluate the taste and pharmacokinetics of different mirabegron oral modified release microgranula-based suspensions in healthy young adults from 18 to less than 26 years of age combined with open label, single dose study to evaluate the taste of prototype oral modified release liquid placebo formulation(s) in children from 6 months to less than 18 years of age. *Study 6 (Same study as for condition idiopathic overactive bladder)* Open label, randomised bioavailability and food effect study to compare relative bioavailability of the liquid formulation and tablet in healthy young adults from 18 to less than 26 years of age. *Study 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 modified release microgranula-based suspension in children from 5 to less than 18 years of age with neurogenic detrusor overactivity. *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 modified release microgranula-based suspension in children from 6 months to less than 5 years of age with neurogenic detrusor overactivity.

4. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues and of efficacy in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By March 2024
Deferral for one or more studies contained in the paediatric investigation plan:	Yes