EMA/793410/2014

European Medicines Agency decision

P/0005/2015

of 30 January 2015

on the acceptance of a modification of an agreed paediatric investigation plan for tiotropium bromide (monohydrate) (Spiriva Respimat, Spiriva), (EMEA-000035-PIP02-09-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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on the acceptance of a modification of an agreed paediatric investigation plan for tiotropium bromide (monohydrate) (Spiriva Respimat, Spiriva), (EMEA-000035-PIP02-09-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0020/2013 issued on 15 February 2013, and the decision P/0101/2014 issued on 11 April 2014,

Having regard to the application submitted by Boehringer Ingelheim International GmbH on 22 September 2014 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 12 December 2014, 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 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 tiotropium bromide (monohydrate) (Spiriva Respimat, Spiriva), inhalation solution, inhalation powder, hard capsule, inhalation 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, 3

This decision is addressed to Boehringer Ingelheim International GmBH, Binger Straße 173, D-55216 - Ingelheim am Rhein, Germany.

Done at London, 30 January 2015

For the European Medicines Agency
Zaide Frias
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/581458/2014

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

EMEA-000035-PIP02-09-M02

Scope of the application

Active substance(s):

Tiotropium bromide (monohydrate)

Invented name:

Spiriva Respimat

Spiriva

Condition(s):

Treatment of asthma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Inhalation solution

Inhalation powder, hard capsule

Route(s) of administration:

Inhalation use

Name/corporate name of the PIP applicant:

Boehringer Ingelheim International GmbH

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, Boehringer Ingelheim International GmbH submitted to the European Medicines Agency on 22 September 2014 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/0020/2013 issued on 15 February 2013, and the decision P/0101/2014 issued on 11 April 2014.

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

The procedure started on 14 October 2014.

Scope of the modification

Some timelines 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 and to the deferral 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, 12 December 2014

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 (PIP)

1. Waiver

1.1. Condition

Treatment of asthma

The waiver applies to:

- the paediatric population from birth to less than one year;
- for inhalation solution, inhalation use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- for inhalation powder, hard capsules, inhalation 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 asthma

2.1.1. Indication(s) targeted by the PIP

Add-on maintenance bronchodilator treatment in patients with asthma, who are not adequately controlled on inhaled corticosteroids

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

From 1 year to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Inhalation solution

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies		Not applicable.
Non-clinical studies		Not applicable.

Clinical studies	7	**Study 1** Randomised, double-blind, placebo-controlled, incomplete-crossover, multiple dose trial to evaluate safety and efficacy in adolescents 12 to less than 18 years with moderate persistent asthma. (205.424) **Study 2** Randomised, double-blind, placebo-controlled, incomplete-crossover, multiple dose trial to evaluate safety and efficacy in children 6 to less than 12 years with moderate persistent asthma. (205.425) **Study 3** Randomised, double-blind, placebo-controlled, parallel-group, multiple dose trial to evaluate safety and efficacy in children 1 to less than 6 years with persistent asthma. (205.443) **Study 4** Randomised, double-blind, placebo-controlled, parallel-group, multiple dose trial to evaluate safety and efficacy in adolescents 12 to less than 18 years with moderate persistent asthma. (205.444) **Study 5** Randomised, double-blind, placebo-controlled, parallel-group, multiple dose trial to evaluate safety and efficacy in children 6 to less than 12 years with moderate persistent asthma. (205.445) **Study 6** Randomised, double-blind, placebo-controlled, parallel-group, multiple dose trial to evaluate safety and efficacy in children 6 to less than 12 years with severe persistent asthma. (205.446) **Study 7** Randomised, double-blind, placebo-controlled, parallel-group, multiple dose trial to evaluate safety and efficacy in adolescents 12 to less than 18 years with severe persistent asthma. (205.456)
Extrapolation, modelling and simulation studies	1	**Study 8** Extrapolation study justifying why the efficacy and safety data with regard to the comparison of tiotropium and LABA as add-on treatment to inhaled corticosteroid can be extrapolated from adult data to the different age subsets of paediatric patients with persistent asthma
Other studies		Not applicable.
Other measures		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 January 2016
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 chronic obstructive pulmonary disease (COPD)

Authorised indications:

- Tiotropium is indicated as a maintenance bronchodilator treatment to relieve symptoms of patients with chronic obstructive pulmonary disease (COPD).

2. Treatment of asthma

Authorised indications:

- Spiriva Respimat is indicated as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 µg budesonide/day or equivalent) and long-acting ß2 agonists and who experienced one or more severe exacerbations in the previous year.

Authorised pharmaceutical formulation(s)

Spiriva Respimat, solution for inhalation

Spiriva Inhalation powder, hard capsule

Authorised route(s) of administration

Inhalation use