

EMA/62972/2012

European Medicines Agency decision

P/0032/2012

of 2 February 2012

on the acceptance of a modification of an agreed paediatric investigation plan for ivabradine (hydrochloride) (Procoralan), (EMA-000628-PIP01-09-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.

European Medicines Agency decision

P/0032/2012

of 2 February 2012

on the acceptance of a modification of an agreed paediatric investigation plan for ivabradine (hydrochloride) (Procoralan), (EMA-000628-PIP01-09-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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/157/2010 issued on 27 August 2010, and the decision P/81/2011 issued on 6 April 2011,

Having regard to the application submitted by Les Laboratoires Servier on 24 October 2011 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 13 January 2012, 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 ivabradine (hydrochloride) (Procoralan), film-coated tablet, solution for injection, oral solution, intravenous use, 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 Les Laboratoires Servier, 50, rue Carnot, 92284 - Suresnes Cedex, France.

Done at London, 2 February 2012

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

EMA/PDCO/37372/2012

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

EMA-000628-PIP01-09-M02

Scope of the application

Active substance(s):

Ivabradine (hydrochloride)

Invented name:

Procoralan

Condition(s):

Coronary artery disease

Angina pectoris

Chronic heart failure

Reduction of heart rate during Multislice Computed Tomography Coronary Angiography (MSCT CA)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Solution for injection

Oral solution

Route(s) of administration:

Intravenous use

Oral use

Name/corporate name of the PIP applicant:

Les Laboratoires Servier

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Les Laboratoires Servier submitted to the European Medicines Agency on 24 October 2011 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/157/2010 issued on 27 August 2010, and the decision P/81/2011 issued on 6 April 2011.

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

The procedure started on 16 November 2011.

Scope of the modification

Some measures 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 annex(es) and appendix.

London, 13 January 2012

On behalf of the Paediatric Committee
Dr Daniel Brasseur, 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: Coronary artery disease

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age;
- for film-coated tablet for oral use, for solution for injection for intravenous use and for oral solution for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

1.2. Condition: Angina pectoris

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age;
- for film-coated tablet for oral use, for solution for injection for intravenous use and for oral solution for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

1.3. Condition: Chronic heart failure

The waiver applies to:

- Neonates and infants from birth to less than 6 months of age;
- for film-coated tablet for oral use, for solution for injection for intravenous use and for oral solution for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

1.4. Condition: Reduction of heart rate during Multislice Computed Tomography Coronary Angiography (MSCT CA)

The waiver applies to:

- Neonates and infants from birth to less than 2 years of age;
- for film-coated tablet for oral use, for solution for injection for intravenous use and for oral solution for 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 to be investigated: Chronic heart failure

2.1.1. Indication targeted by the PIP

Treatment of chronic heart failure

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)

Oral solution for oral use

2.1.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable
Non-clinical	0	Not applicable
Clinical	2	Study 1: A monocentre, open-label, randomised, two-period, cross-over bioavailability study in healthy male volunteers to support the paediatric formulation development (PKH-16257-086) Study 2: A randomised, double-blind, placebo controlled, multicentre PK/PD and dose-finding study in children from 6 months to less than 18 years of age with chronic heart failure (CL2-16257-090)

2.2. Condition to be investigated: Reduction of heart rate during Multislice Computed Tomography Coronary Angiography (MSCT CA)

2.2.1. Indication targeted by the PIP

Reduction of heart rate during Multislice Computed Tomography Coronary Angiography (MSCT CA)

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

From 2 to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Solution for injection for intravenous use

2.2.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	3	Study 3: A preliminary 4-week toxicity study by oral route (gavage) in juvenile Wistar rats (35438 RSR – TOX-16257-040-FRA) Study 4: A preliminary 2 or 4-week toxicity study by oral route (gavage) in juvenile Wistar rats (35658 EPR – PF-09-16257-168-RRTK) Study 5: A 10-week toxicity study by oral route (gavage) in juvenile Wistar rats followed by a 3-week recovery period (35439 RSR – TOX-16257-042-FRA)
Clinical	1	Study 6: A double blind, non-randomised multicentre, non-controlled PK/PD and dose-finding study in children from 2 to less than 18 years of age undergoing MSCT-CA examination (CL2-16257-085)

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By September 2013
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Angina pectoris.

Authorised indications:

Symptomatic treatment of chronic stable angina pectoris in coronary artery disease adults with normal sinus rhythm:

- In adults unable to tolerate or with a contra-indication to the use of beta-blockers.
- Or in combination with beta-blockers in patients inadequately controlled with an optimal beta-blocker dose and whose heart rate is >60 bpm.

EU Number	Invented name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/05/316/001	Procoralan	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	14 tablets
EU/1/05/316/002	Procoralan	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	28 tablets
EU/1/05/316/003	Procoralan	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	56 tablets
EU/1/05/316/004	Procoralan	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	84 tablets
EU/1/05/316/005	Procoralan	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	98 tablets
EU/1/05/316/006	Procoralan	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	100 tablets
EU/1/05/316/007	Procoralan	5 mg	Film-coated tablet	Oral use	blister (alu/PVC)	112 tablets