EMA/203739/2013

# European Medicines Agency decision

P/0102/2013

of 30 April 2013

on the acceptance of a modification of an agreed paediatric investigation plan for ivabradine (hydrochloride) (Procoralan) (EMEA-000628-PIP01-09-M04) 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.**

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
**Telephone** +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
**E-mail** info@ema.europa.eu **Website** www.ema.europa.eu

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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/157/2010 issued on 27 August 2010, the decision P/81/2011 issued on 6 April 2011, the decision P/0032/2012 issued on 2 February 2012 and the decision P/0099/2012 issued on 30 May 2012,

Having regard to the application submitted by Les Laboratoires Servier on 17 December 2012 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 15 March 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 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

***Article 2***

This decision is addressed to Les Laboratoires Servier, 50 rue Carnot, 92284 Suresnes Cedex, France.

Done at London, 30 April 2013

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

EMA/PDCO/169043/2013

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

EMEA-000628-PIP01-09-M04

## Scope of the application

**Active substance(s):**

Ivabradine (hydrochloride)

**Invented name:**

Procoralan

**Condition(s):**

Treatment of coronary artery disease

Treatment of angina pectoris

Treatment of chronic heart failure

**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

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
**Telephone** +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
**E-mail** info@ema.europa.eu **Website** www.ema.europa.eu

**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 17 December 2012 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, the decision P/81/2011 issued on 6 April 2011, the decision P/0032/2012 issued on 2 February 2012 and the decision P/0099/2012 issued on 30 May 2012.

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

The procedure started on 16 January 2013.

## Scope of the modification

Some measures and 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 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.

London, 15 March 2013

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

# 1. Waiver

## *1.1. Condition: Treatment of 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: Treatment of 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: Treatment of 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.

# 2. Paediatric Investigation Plan

## *2.1. Condition to be investigated: Treatment of 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:**<br>A monocentre, open-label, randomised, two-period, cross-over bioavailability study in healthy male volunteers to support the paediatric formulation development (PKH-16257-086).<br>**Study 2:**<br>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). |

## 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 March 2014 |
| 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 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.

2. Treatment of coronary artery disease

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.

3. Treatment of chronic heart failure

Authorised indications:

Ivabradine is indicated in chronic heart failure NYHA II to IV class with systolic dysfunction, in patients in sinus rhythm and whose heart rate is ≥ 75 bpm, in combination with standard therapy including beta-blocker therapy or when beta-blocker therapy is contraindicated or not tolerated.

## Authorised pharmaceutical form(s):

Film-coated tablet

## Authorised route(s) of administration:

Oral use