EMA/463926/2010

European Medicines Agency decision

P/128/2010

of 28 July 2010

on the agreement of a paediatric investigation plan and on the granting of a waiver for bosentan monohydrate (Tracleer) (EMEA-000425-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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8670
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

European Medicines Agency decision

P/128/2010

of 28 July 2010

on the agreement of a paediatric investigation plan and on the granting of a waiver for bosentan monohydrate (Tracleer) (EMEA-000425-PIP02-10) 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 application submitted by Actelion Registration Ltd on 23 March 2010 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 June 2010, in accordance with Article 18 of Regulation (EC) No 1901/2006, 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 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 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 bosentan monohydrate (Tracleer), film-coated tablet, dispersible 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 waiver for bosentan monohydrate (Tracleer), film-coated tablet, dispersible 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

This decision is addressed to Actelion Registration Ltd, 389 Chiswick High Road, W44 4AL London, United Kingdom.

Done at London, 28 July 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/PDCO/299267/2010

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

EMEA-000425-PIP02-10

Scope of the application

Active substance(s):

Bosentan monohydrate

Invented name:

Tracleer

Condition(s):

Pulmonary Arterial Hypertension (PAH)

Systemic sclerosis

Interstitial pulmonary fibrosis

Pharmaceutical form(s):

Film-coated tablet

Dispersible tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Actelion Registration Ltd

Information about the authorised medicinal product: see Annex II

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8670
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Actelion Registration Ltd submitted for agreement to the European Medicines Agency on 23 March 2010 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 15 April 2010.

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 waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Articles 11(1)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population. 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 annexes and appendix.

London, 11 June 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)

Pulmonary Arterial Hypertension (PAH)

Systemic sclerosis

Other interstitial pulmonary diseases with fibrosis

2. Waiver

2.1. Condition

Pulmonary Arterial Hypertension (PAH)

The waiver applies to:

- Infants from 28 days to less than 3 months
- for Film-coated tablet and Dispersible tablet; for oral use
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.
- Adolescents from 12 to less than 18 years
- for Film-coated tablet and Dispersible tablet; for oral use
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

2.2. Condition

Systemic sclerosis

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age.
- for Film-coated tablet and Dispersible tablet; for oral use
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2.3. Condition

Interstitial pulmonary fibrosis

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age.
- for Film-coated tablet and Dispersible tablet; Oral use
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

3. Paediatric Investigation Plan

3.1. Condition to be investigated

Pulmonary Arterial Hypertension (PAH)

3.1.1. Indication targeted by the PIP

Treatment of Pulmonary Arterial Hypertension (PAH)

Treatment of Persistent Pulmonary Hypertension of the Newborn (PPHN)

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

From birth to less than 28 days of age.

From 3 months to less than 12 years of age.

3.1.3. Pharmaceutical form(s)

Film-coated tablet

Dispersible tablet

3.1.4. Studies

Area	**Number of studies**	**Description**
Quality	1	Study 1: *Study on nasogastric tube administration of the bosentan dispersible tablet*
Non-clinical	3	Study 2: *24 days dose-range-finding toxicity study in juvenile rats* Study 3: *94 days toxicity study in juvenile rats* Study 4: *PK/safety and efficacy study in a model of chronic pulmonary hypertension in newborn sheep*
Clinical	2	Study 5: Open-label, randomised multicentre, multiple dose trial to evaluate pharmacokinetics, safety of bosentan in children from 3 months to less than 12 years of age with Pulmonary Arterial Hypertension (PAH) Study 6: Double blind, randomised multicentre, add-on placebo controlled, trial to evaluate pharmacokinetics, safety, efficacy, of bosentan in neonates with persistent pulmonary hypertension of the newborn (PPHN).

4. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	By June 2014
Deferral for one or more studies contained in the paediatric investigation plan:	No

Annex II

Information about the authorised medicinal product

EU Number	Invented name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/02/220/001	Tracleer	62.5 mg	Film-coated tablet	Oral use	blister (PVC/PE/PVDC/alu)	14 tablets
EU/1/02/220/002	Tracleer	62.5 mg	Film-coated tablet	Oral use	blister (PVC/PE/PVDC/alu)	56 tablets
EU/1/02/220/003	Tracleer	62.5 mg	Film-coated tablet	Oral use	blister (PVC/PE/PVDC/alu)	112 tablets
EU/1/02/220/004	Tracleer	125 mg	Film-coated tablet	Oral use	blister (PVC/PE/PVDC/alu)	56 tablets
EU/1/02/220/005	Tracleer	125 mg	Film-coated tablet	Oral use	blister (PVC/PE/PVDC/alu)	112 tablets
EU/1/02/220/006	Tracleer	32 mg	Dispersible tablet	Oral use	blister (alu/alu)	56 tablets