EMA/268706/2014

European Medicines Agency decision

P/0164/2014

of 25 June 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for expanded autologous bone marrow-derived osteoblastic cells (EMEA-001329-PIP02-13) 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
An agency of the European Union

European Medicines Agency decision

P/0164/2014

of 25 June 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for expanded autologous bone marrow-derived osteoblastic cells (EMEA-001329-PIP02-13) 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 Bone Therapeutics S.A. on 15 April 2013 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 25 April 2014, 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 expanded autologous bone marrow-derived osteoblastic cells, suspension for injection, intraosseous 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 expanded autologous bone marrow-derived osteoblastic cells, suspension for injection, intraosseous 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 3

A waiver for expanded autologous bone marrow-derived osteoblastic cells, suspension for injection, intraosseous 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 4

This decision is addressed to Bone Therapeutics S.A., Rue Adrienne Bollland, 8, B-6041 - Gosselies, Belgium.

Done at London, 25 June 2014

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

EMA/PDCO/75737/2014 corr

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

EMEA-001329-PIP02-13

Scope of the application

Active substance(s):

Expanded autologous bone marrow-derived osteoblastic cells

Condition(s):

Treatment of non-traumatic osteonecrosis

Pharmaceutical form(s):

Suspension for injection

Route(s) of administration:

Intraosseous use

Name/corporate name of the PIP applicant:

Bone Therapeutics S.A.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Bone Therapeutics S.A. submitted for agreement to the European Medicines Agency on 15 April 2013 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 12 September 2013.

Supplementary information was provided by the applicant on 3 February 2014. The applicant proposed modifications to the paediatric investigation plan and requested a waiver.

A meeting with the Paediatric Committee took place on 23 April 2014.

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
An agency of the European Union

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 and appendix.

London, 25 April 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

1. Waiver

1.1. Condition: treatment of non-traumatic osteonecrosis

The waiver applies to:

- the paediatric population from birth to less than 10 years;
- for suspension for injection, intraosseous 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 non-traumatic osteonecrosis

2.1.1. Indication(s) targeted by the PIP

Treatment of non-traumatic osteonecrosis.

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

From 10 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Suspension for injection.

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	0	
Non-clinical studies	8	**Study 1: PAED-PREOB-VT-007** In vitro proliferation assay to test for the presence of immortalised cells in paediatric expanded autologous bone marrow-derived osteoblastic cells. **Study 2: PAED-PREOB-VT-008** In vitro soft-agar assay to test whether the manufacturing process of paediatric expanded autologous bone marrow-derived osteoblastic cells generates immortalised cells. **Study 3: PAED-PREOB-VV-001** Injection of paediatric expanded autologous bone marrow-derived osteoblastic cells in juvenile nude rats to test whether they are tumorigenic.

		Study 4: PAED-PREOB-VT-009 In vitro proliferation assay to test whether the manufacturing process of expanded autologous bone marrow-derived osteoblastic cells selects for and/or amplifies residual tumour cells. **Study 5: PAED-PREOB-VT-010** In vitro soft-agar assay to test whether the manufacturing process of expanded autologous bone marrow-derived osteoblastic cells allows retention and/or causes proliferation of residual tumour cells. **Study 6: PAED-PREOB-VV-002** In vivo tumourigenicity study in juvenile nude rats. **Study 7: PAED-PREOB-VV-003** Study with juvenile nude rats with closed femoral shaft fracture to test whether paediatric expanded autologous bone marrow-derived osteoblastic cells engraft at bone fracture site and whether they invade vital organs or growth plates. **Study 8: PAED-PREOB-VV-004** Study with juvenile nude rats to test whether paediatric expanded autologous bone marrow-derived osteoblastic cells interfere with the growth plate when administered close to it.
Clinical studies	1	**Study 9: PAED-PREOB-ON3** Multi-centre, randomised, controlled trial to evaluate efficacy and safety of expanded autologous bone marrow-derived osteoblastic cells in children from 10 to less than 18 years of age with acute lymphocytic leukaemia and non-traumatic osteonecrosis.
Extrapolation, modelling & simulation studies		Not applicable.
Other studies	2	**Study 10: PAED-PREOB-VT-004** Assessment of the impact of corticosteroids on the quality of adult expanded autologous bone marrow-derived osteoblastic cells. **Study 11: PAED-PREOB-VT-005** Identification of remnant tumour cells in the bone marrow of paediatric patients with cancer history and assessment of chromosomal abnormalities in bone marrow samples derived from children with acute lymphocytic leukaemia and osteonecrosis. **Study 12** Detection of tumour cells in paediatric human bone marrow-derived osteoblastic cells.
Other measures		Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes