EMA/466413/2019

European Medicines Agency decision

P/0320/2019

of 11 September 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for pegvorhyaluronidase alfa (EMEA-001883-PIP03-17) 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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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 Halozyme Inc on 23 March 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 July 2019, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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.

(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.

[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 pegvorhyaluronidase alfa, concentrate for solution for infusion, intravenous 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 pegvorhyaluronidase alfa, concentrate for solution for infusion, intravenous 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 Halozyme Inc, 11388 Sorrento Valley Road, CA 92121 - San Diego, United States.

EMA/PDCO/288332/2019 Corr
Amsterdam, 26 July 2019

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

EMEA-001883-PIP03-17

Scope of the application

Active substance(s):

Pegvorhyaluronidase alfa

Condition(s):

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms).

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Halozyme Inc

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Halozyme Inc submitted for agreement to the European Medicines Agency on 23 March 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 2 May 2018.

Supplementary information was provided by the applicant on 23 April 2019. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

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 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

   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 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.

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

Not applicable.

2. Paediatric investigation plan

2.1. Condition

Treatment of all conditions included in the category of malignant neoplasms (except central nervous system, haematopoietic and lymphoid tissue neoplasms)

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from birth to less than 18 years of age with a relapsed/refractory or newly-diagnosed non-CNS solid tumour containing hyaluronan, in combination with cytotoxic anticancer therapies

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate strength
Non-clinical studies	3	**Study 2** In *vitro* study to evaluate the presence of hyaluronan in clinical tissue samples of paediatric tumours (rhabdomyosarcoma, Wilms tumour, Ewing sarcoma, neuroblastoma and medulloblastoma). **Study 3** In *vivo* study to determine the presence of hyaluronan using histochemical staining in tumour tissues from established animal models of paediatric solid tumours found to contain hyaluronan in clinical samples from Study 2. **Study 4** In *vivo* study to evaluate the efficacy of pegvorhyaluronidase alfa (PEGPH20) in combination with vincristine, irinotecan, and temozolomide in selected hyaluronan-containing mouse models of paediatric solid tumours identified in Studies 2 and 3.

Clinical studies	3	**Study 5** Open label, single arm trial to evaluate the safety, pharmacokinetics and anti-tumour activity of pegvorhyaluronidase alfa (PEGPH20) used in combination with a vincristine, irinotecan, temozolomide regimen with a dose-escalation phase and expansion phase in paediatric patients from birth to less than 18 years of age with a relapsed or refractory non-CNS solid tumour. **Study 6** Open label, randomised controlled trial to evaluate the efficacy, safety and pharmacokinetics of pegvorhyaluronidase alfa (PEGPH20) used in combination with a vincristine, irinotecan, temozolomide regimen compared to a vincristine, irinotecan, temozolomide regimen alone in paediatric patients from 6 months to less than 18 years of age with relapsed or refractory rhabdomyosarcoma. **Study 7** Open label, randomised controlled trial to evaluate the efficacy, safety and pharmacokinetics of pegvorhyaluronidase alfa (PEGPH20) used in combination with an ifosfamide, vincristine, actinomycin-d, and doxorubicin regimen compared to an ifosfamide, vincristine, actinomycin-d, and doxorubicin regimen alone in paediatric patients from birth to less than 18 years of age with newly-diagnosed rhabdomyosarcoma.
Extrapolation, modelling and simulation studies	1	**Study 8** Modelling and simulation study to evaluate the use and support dosing regimen of pegvorhyaluronidase alfa (PEGPH20) in the paediatric population from birth to less than 18 years of age with a relapsed/refractory or newly-diagnosed non-CNS solid tumour.
Other studies	0	Not applicable.
Other measures	0	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 November 2031
Deferral for one or more measures contained in the paediatric investigation plan:	Yes