EMA/598732/2020

European Medicines Agency decision

P/0492/2020

of 22 December 2020

on the refusal of a modification of an agreed paediatric investigation plan for fluciclovine (18F) (Axumin), (EMEA-001644-PIP02-14-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 European Medicines Agency's decision P/0256/2015 issued on 30 October 2015 and the decision P/0285/2019 issued on 16 August 2019,

Having regard to the application submitted by Blue Earth Diagnostics Ireland Ltd on 30 July 2020 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and proposing a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 November 2020, 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 refusal of changes to the agreed paediatric investigation plan and to the deferral and on the refusal of a waiver.

(2) It is therefore appropriate to adopt a decision on the refusal of changes to the agreed paediatric investigation plan, including changes to the deferral.

(3) It is therefore appropriate to adopt a decision refusing 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

Changes to the agreed paediatric investigation plan for fluciclovine (18F) (Axumin), solution for injection, intravenous use, including changes to the deferral, 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, are hereby refused.

Article 2

A waiver for fluciclovine (18F) (Axumin), solution for injection, intravenous use, the details of which are set out in the opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby refused.

Article 3

This decision is addressed to Blue Earth Diagnostics Ireland Ltd, 6th Floor, 2 Grand Canal Square, 2 – Dublin, Ireland.

EMA/PDCO/486818/2020
Amsterdam, 13 November 2020

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

EMEA-001644-PIP02-14-M02

Scope of the application

Active substance(s):

Fluciclovine (18F)

Invented name:

Axumin

Condition(s):

Diagnosis of amino acid metabolism in solid malignant tumours

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Blue Earth Diagnostics Ireland Ltd

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Blue Earth Diagnostics Ireland Ltd submitted to the European Medicines Agency on 30 July 2020 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0256/2015 issued on 30 October 2015 and the decision P/0285/2019 issued on 16 August 2019.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral and proposed a waiver for all subsets of the paediatric population.

The procedure started on 15 September 2020.

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 refuse the changes proposed by the applicant regarding the paediatric investigation plan and the deferral;
   - to refuse the granting of a waiver for all subsets of the paediatric population and the above mentioned condition as it does not meet the grounds detailed in Article 11(1) of Regulation (EC) No 1901/2006 as amended.

   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 remain unchanged and are set out in the Annex I.

3. The scientific conclusions and the grounds for refusal are set out in the Annex I and the summary report appended to this opinion.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes 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

The request for the waiver applied to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- solution for injection, intravenous use;

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- (a) the specific medicinal product is likely to be ineffective or unsafe in the paediatric population;
- (b) the disease or condition for which the specific medicinal product is intended occurs only in adult populations;
- (c) the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

Because:

- the specific medicinal product is not likely to be ineffective or unsafe;
- the disease or condition for which the specific medicinal product is intended, does occur in the paediatric population(s);
- measures would be justified by the expected therapeutic benefit and clinical trials may be feasible;
- the specific medicinal product may represent a significant therapeutic benefit as the needs are not met;
- clinical studies may fulfil a therapeutic need of the paediatric population.

The waiver request is therefore refused by the PDCO.

2. Paediatric investigation plan

2.1. Condition:

Diagnosis of amino acid metabolism in solid malignant tumours

2.1.1. Indication(s) targeted by the PIP

Diagnosis of primary and recurrent brain tumours

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)

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Quality study to evaluate dilution of solution for injection, to introduce a dilution procedure for accurate dosing in younger children and to evaluate the effect of dilution on osmolality and pH
Non-clinical studies	0	Not applicable
Clinical studies	1	**Study 2** Open-label two cohort trial to evaluate pharmacokinetics, safety and diagnostic performance of fluciclovine (18F) as add-on to MRI compared to MRI alone in children from birth to less than 18 years of age with suspected primary or recurrent malignant brain tumours
Extrapolation, modelling and simulation studies	1	**Study 3** Analysis of existing in house and literature data on diagnostic performance of fluciclovine (18F) in children from birth to less than 18 years of age with malignant brain tumours
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 June 2022
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. Diagnosis of prostate cancer

Authorised indication(s):

- Axumin is indicated for Positron Emission Tomography (PET) imaging to detect recurrence of prostate cancer in adult men with a suspected recurrence based on elevated blood prostate specific antigen (PSA) levels after primary curative treatment.

Authorised pharmaceutical form(s):

Solution for injection

Authorised route(s) of administration:

Intravenous use