EMA/145474/2022

European Medicines Agency decision

P/0107/2022

of 13 April 2022

on the acceptance of a modification of an agreed paediatric investigation plan for amikacin (sulfate) (Arikayce liposomal), (EMEA-000525-PIP01-08-M08) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/31/2011 issued on 28 January 2011, the decision P/0185/2012 issued on 21 August 2012, the decision P/0248/2014 issued on 30 September 2014, the decision P/0030/2015 issued on 30 January 2015, the decision P/0346/2018 issued on 8 November 2018 and the decision P/0358/2021 issued on 8 September 2021,

Having regard to the application submitted by Insmed Netherlands B.V. on 19 November 2021 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 25 February 2022, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for amikacin (sulfate), (Arikayce liposomal), nebuliser dispersion , inhalation use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

A product-specific waiver for amikacin (sulfate), (Arikayce liposomal), nebuliser dispersion, inhalation 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 Insmed Netherlands B.V., Stadsplateau 7, 3521 AZ – Utrecht, The Netherlands.

EMA/PDCO/709057/2021 Corr
Amsterdam, 25 February 2022

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

EMEA-000525-PIP01-08-M08

Scope of the application

Active substance(s):

Amikacin (sulfate)

Invented name:

Arikayce liposomal

Condition(s):

Treatment of *Pseudomonas aeruginosa* lung infection/colonisation in cystic fibrosis patients

Treatment of nontuberculous mycobacterial lung infection

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Nebuliser dispersion

Route(s) of administration:

Inhalation use

Name/corporate name of the PIP applicant:

Insmed Netherlands B.V.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Insmed Netherlands B.V. submitted to the European Medicines Agency on 19 November 2021 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/31/2011 issued on 28 January 2011, the decision P/0185/2012 issued on 21 August 2012, the decision P/0248/2014 issued on 30 September 2014, the decision P/0030/2015 issued on 30 January 2015, the decision P/0346/2018 issued on 8 November 2018 and the decision P/0358/2021 issued on 8 September 2021.

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

The procedure started on 4 January 2022.

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.
   - to grant a waiver for one or more subsets of the paediatric population of its own motion in accordance with Article 12 of said Regulation and concluded in accordance with Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   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 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

1.1. Condition:

Treatment of *Pseudomonas aeruginosa* lung infection/colonisation in cystic fibrosis patients

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- nebuliser dispersion, inhalation use;
- on the grounds that the specific medicinal product is likely to be ineffective.

1.2. Condition:

Treatment of nontuberculous mycobacterial lung infection

The waiver applies to:

- children from birth to less than 6 years of age;
- nebuliser dispersion, inhalation use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of *Pseudomonas aeruginosa* lung infection/colonisation in cystic fibrosis patients

A waiver was granted for all subsets of the paediatric population from birth to less than 18 years of age for this condition and PIP studies 3, 4, 5, 6, 8, 9 and 10 were deleted during modification EMEA-000525-PIP01-M08.

PIP study 7 was deleted during modification EMEA-000525-PIP01-08-M03.

2.2. Condition:

Treatment of nontuberculous mycobacterial lung infection

2.2.1. Indication(s) targeted by the PIP

Treatment of nontuberculous mycobacterial (NTM) lung infection in cystic fibrosis patients

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

From 6 years to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Nebuliser dispersion

2.2.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	**Study 1** 2-year inhalation carcinogenicity study in rats **Study 2** Juvenile rodent inhalation toxicity and toxicokinetic study
Clinical studies	***Study 11*** *– deleted during modification EMEA-000525-PIP01-08-M07*
Extrapolation, modelling and simulation studies	**Study 12** Extrapolation study of pharmacokinetic (PK) data of liposomal amikacin for inhalation (LAI) from adult and paediatric patients with Pseudomonas infection/colonisation in cystic fibrosis (CF) to paediatric patients with CF and nontuberculous mycobacterial (NTM) lung disease
Other studies	Not applicable
Other measures	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By April 2016
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

Treatment of non-tuberculous mycobacterial lung infections

Authorised indication(s):

Arikayce liposomal is indicated for the treatment of non-tuberculous mycobacterial (NTM) lung infections caused by Mycobacterium avium Complex (MAC) in adults with limited treatment options who do not have cystic fibrosis (see sections 4.2, 4.4 and 5.1). Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Authorised pharmaceutical form(s):

Nebuliser dispersion

Authorised route(s) of administration:

Inhalation use