EMA/44366/2015

European Medicines Agency decision

P/0030/2015

of 30 January 2015

on the acceptance of a modification of an agreed paediatric investigation plan for amikacin (sulfate) (EMEA-000525-PIP01-08-M04) 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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on the acceptance of a modification of an agreed paediatric investigation plan for amikacin (sulfate) (EMEA-000525-PIP01-08-M04) 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 European Medicines Agency's decision P/31/2011 issued on 28 January 2011, decision P/0185/2012 issued on 21 August 2012 and decision P/0248/2014 issued on 30 September 2014,

Having regard to the application submitted by Insmed Incorporated on 19 December 2014 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 16 January 2015, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for amikacin (sulfate), nebuliser suspension, 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

This decision is addressed to Insmed Limited, Overseas House, 66-68 High Road, WD23 1GG - Bushey Heath,United Kingdom.

Done at London, 30 January 2015

For the European Medicines Agency
Zaide Frias
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/801541/2014

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

EMEA-000525-PIP01-08-M04

Scope of the application

Active substance(s):

Amikacin (sulfate)

Condition(s):

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

Treatment of nontuberculous mycobacterial lung infection

Pharmaceutical form(s):

Nebuliser suspension

Route(s) of administration:

Inhalation use

Name/corporate name of the PIP applicant:

Insmed Incorporated

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Insmed Incorporated submitted to the European Medicines Agency on 19 December 2014 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, decision P/0185/2012 issued on 21 August 2012 and decision P/0248/2014 issued on 30 September 2014,

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

The procedure started on 6 January 2015.

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Scope of the modification

Some measures 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.

   The Icelandic and the Norwegian Paediatric Committee members agree 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.

London, 16 January 2015

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 (PIP)

1. Waiver

1.1. Condition:

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

The waiver applies to:

- Children from birth to less than 3 months of age;
- for nebuliser suspension for inhalation use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

1.2. Condition:

Treatment of nontuberculous mycobacterial (NTM) lung infection

The waiver applies to:

- Children from birth to less than 6 years of age;
- for nebuliser suspension for 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

2.1.1. Indication(s) targeted by the PIP

Treatment of initial (early) *Pseudomonas aeruginosa* lung infection/colonisation in cystic fibrosis patients

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

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

From 3 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Nebuliser suspension

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	2	**Study 1** 2-year inhalation carcinogenicity study in rats. **Study 2** Juvenile rodent inhalation toxicity and toxicokinetic study.
Clinical studies	7	**Study 3** Multidose safety and tolerability study of dose escalation of liposomal amikacin for inhalation in cystic fibrosis patients (children from 6 years to less than 18 years and adults) with chronic lung infections due to *Pseudomonas aeruginosa*-double blind portion. (TR02-105). **Study 4** Multidose safety and tolerability study of dose escalation of liposomal amikacin for inhalation in cystic fibrosis patients (children from 6 years to less than 18 years and adults) with chronic lung infections due to *Pseudomonas aeruginosa*-open label portion. (TR02-105). **Study 5** Multidose safety and tolerability study of dose escalation of liposomal amikacin for inhalation in cystic fibrosis patients (children from 6 years to less than 18 years and adults)with chronic lung infections due to *Pseudomonas aeruginosa*. (TR02-106). **Study 6** Randomised, active controlled, multicentre study to assess the efficacy, safety and tolerability of liposomal amikacin for inhalation in cystic fibrosis patients (children from 6 years to less than 18 years and adults) with chronic lung infection due to *Pseudomonas aeruginosa*. (TR02-108). **Study 8** Long term safety and tolerability study of open label liposomal amikacin for inhalation in cystic fibrosis patients (children from 6 years to less than 18 years and adults) with chronic lung infection due to *Pseudomonas aeruginosa*. (TR02-110). **Study 9** Randomised, active controlled, multi-centre study to assess the efficacy

		and safety of liposomal amikacin for inhalation for the treatment of first or early infections of *Pseudomonas aeruginosa* in children aged from 3 months to less than 18 years with cystic fibrosis. (TR02-114). **Study 10** Open label, multi-cycle study of safety, tolerability and efficacy of liposomal amikacin for inhalation in cystic fibrosis children aged from 3 years to less than 6 years old, with chronic infection due to *Pseudomonas aeruginosa*. (TR02-115).

2.2. Condition:

Treatment of nontuberculous mycobacterial (NTM) 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 suspension

2.2.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	2	**Study 1** 2-year inhalation carcinogenicity study in rats. • as described for condition 2.1. **Study 2** Juvenile rodent inhalation toxicity and toxicokinetic study. • as described for condition 2.1.
Clinical studies	1	**Study 11** Randomized, double blind, placebo-controlled, multicentre study to evaluate efficacy and safety and pharmacokinetics of liposomal amikacin for inhalation in children from 6 to less than 18 years with CF and NTM lung infection and adults with NTM lung infections with a 6 months safety follow-up phase. (INS-216).
Extrapolation, modelling and	1	**Study 12** Extrapolation study of pharmacokinetic (PK) data of liposomal amikacin

simulation studies		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	0	Not applicable.
Other measures	0	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 January 2019
Deferral for one or more studies contained in the paediatric investigation plan:	Yes