

EMA/508733/2014

European Medicines Agency decision

P/0248/2014

of 30 September 2014

on the acceptance of a modification of an agreed paediatric investigation plan for amikacin (sulfate) (EMEA-000525-PIP01-08-M03) 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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/31/2011 issued on 28 January 2011, and decision P/0185/2012 issued on 21 August 2012,

Having regard to the application submitted by Insmmed Incorporated on 27 May 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 15 August 2014, 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 and to the deferral and to the waiver.
- (2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral and the 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 amikacin (sulfate), nebuliser suspension, inhalation use, including changes to the deferral, and the waiver, 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 Insmmed Incorporated, Princeton Corporate Plaza, 9 Deer Park Drive, Suite C, 08852-1919 - Monmouth Junction, New Jersey, United States of America.

Done at London, 30 September 2014

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

EMA/PDCO/335629/2014

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

EMA-000525-PIP01-08-M03

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:

Insméd Incorporated

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Insméd Incorporated submitted to the European Medicines Agency on 27 May 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 and decision P/0185/2012 issued on 21 August 2012.

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

The procedure started on 18 June 2014.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified; a new condition has been included. A waiver for a new paediatric subset has been added.

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 and to the deferral and to the waiver in the scope set out in the Annex I of this opinion.

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.

London, 15 August 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 (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 <i>Pseudomonas aeruginosa</i>-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 <i>Pseudomonas aeruginosa</i>-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 <i>Pseudomonas aeruginosa</i>. (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 <i>Pseudomonas aeruginosa</i>. (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 <i>Pseudomonas aeruginosa</i>. (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 <i>Pseudomonas aeruginosa</i> 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 <i>Pseudomonas aeruginosa</i>. (TR02-115).
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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 simulation	1	Study 12 Extrapolation study of pharmacokinetic (PK) data of liposomal amikacin for inhalation (LAI) from adult and paediatric patients with

studies		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