EMADOC-1700519818-1911730

European Medicines Agency decision

EMA/PE/0000232896

of 21 February 2025

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for antisense oligonucleotide against patatin like phospholipase domain containing protein 3 gene (PNPLA3), conjugated to N-acetylgalactosamine (AZD2693), sodium salt 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.

European Medicines Agency decision

EMA/PE/0000232896

of 21 February 2025

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for antisense oligonucleotide against patatin like phospholipase domain containing protein 3 gene (PNPLA3), conjugated to N-acetylgalactosamine (AZD2693), sodium salt 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the application submitted by AstraZeneca AB on 31 May 2024 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 31 January 2025, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 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 on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(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.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[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

A paediatric investigation for antisense oligonucleotide against patatin like phospholipase domain containing protein 3 gene (PNPLA3), conjugated to N-acetylgalactosamine (AZD2693), sodium salt, 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 antisense oligonucleotide against patatin like phospholipase domain containing protein 3 gene (PNPLA3), conjugated to N-acetylgalactosamine (AZD2693), sodium salt, 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

A waiver for antisense oligonucleotide against patatin like phospholipase domain containing protein 3 gene (PNPLA3), conjugated to N-acetylgalactosamine (AZD2693), sodium salt, 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 4

This decision is addressed to AstraZeneca AB, 151 85 – Sodertalje, Sweden.

EMADOC-1700519818-1728315 [1]Corr
Amsterdam, 31 January 2025

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

EMA/PE/0000232896

Scope of the application

Active substance(s):

Antisense oligonucleotide against patatin like phospholipase domain containing protein 3 gene (PNPLA3), conjugated to N-acetylgalactosamine (AZD2693), sodium salt

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of metabolic dysfunction-associated steatohepatitis

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

AstraZeneca AB

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, AstraZeneca AB submitted for agreement to the European Medicines Agency on 31 May 2024 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 8 July 2024.

[1] 17 February 2025

Supplementary information was provided by the applicant on 17 October 2024. The applicant proposed modifications to the paediatric investigation plan

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;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not present a significant therapeutic benefit over exiting treatments for paediatric patients.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 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

1.1. Condition:

Treatment of metabolic dysfunction-associated steatohepatitis (MASH)

The waiver applies to:

- the paediatric population from birth to less than 8 years of age;
- solution of injection, subcutaneous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition:

Treatment of metabolic dysfunction-associated steatohepatitis (MASH)

2.1.1. Indication(s) targeted by the PIP

Treatment of non-cirrhotic MASH with fibrosis, for homozygous carriers of the PNPLA3 rs738409 148M risk allele

Treatment of cirrhotic MASH for homozygous carriers of the PNPLA3 rs738409 148M risk allele

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

From 8 years to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	**Description**
Quality-related studies	**Study 1** Development of an age-appropriate formulation for paediatric patients from 8 years to less than 18 years of age
Non-clinical studies	Not applicable
Clinical studies	**Study 2** Open-label, non-randomised, single-dose trial to evaluate pharmacokinetics and safety of antisense oligonucleotide against patatin like phospholipase domain containing protein 3 gene (PNPLA3), conjugated to N-acetylgalactosamine (AZD2693) in

	children from 8 years to less than 18 years of age who have presumed metabolic dysfunction-associated steatohepatitis (MASH). **Study 3** Double-blind, randomised, multiple dose, placebo-controlled trial to evaluate safety and efficacy of AZD2693 as add-on to best standard of care compared to placebo in children from 8 years to less than 18 years of age with a diagnosis of non-cirrhotic MASH, and who are homozygous carriers of the PNPLA3 rs738409 148M risk allele.
Modelling and simulation analyses	**Study 4** Modelling and simulation analysis to be conducted in support of the development of AZD2693 for treatment of children from 8 years to less than 18 years of age with MASH.
Other studies	Not applicable
Extrapolation plan	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2039
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.