EMA/562327/2023

European Medicines Agency decision

P/0540/2023

of 29 December 2023

on the agreement of a paediatric investigation plan and on the granting of a deferral for modified mRNA encoding human methylmalonyl-coenzyme A mutase containing a polymorphism at position 671 (mRNA-3705), (EMEA-003437-PIP01-23) 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 application submitted by Moderna Biotech Spain, S.L. on 24 April 2023 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 10 November 2023, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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 agreement of a paediatric investigation plan and on the granting of a deferral.

(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.

[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 plan for modified mRNA encoding human methylmalonyl-coenzyme A mutase containing a polymorphism at position 671 (mRNA-3705), dispersion for injection, intravenous 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 agreed.

Article 2

A deferral for modified mRNA encoding human methylmalonyl-coenzyme A mutase containing a polymorphism at position 671 (mRNA-3705), dispersion for injection, intravenous 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 Moderna Biotech Spain, S.L., Calle del Principe De Vergara 132 Plt 12, 28002 – Madrid, Spain.

EMA/PDCO/389491/2023 Corr[1]
Amsterdam, 10 November 2023

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

EMEA-003437-PIP01-23

Scope of the application

Active substance(s):

Modified mRNA encoding human methylmalonyl-coenzyme A mutase containing a polymorphism at position 671 (mRNA-3705)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of methylmalonic acidaemia

Pharmaceutical form(s):

Dispersion for injection

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Moderna Biotech Spain, S.L.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Moderna Biotech Spain, S.L. submitted for agreement to the European Medicines Agency on 24 April 2023 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 22 May 2023.

Supplementary information was provided by the applicant on 7 August 2023. The applicant proposed modifications to the paediatric investigation plan.

[1] 14 December 2023

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.

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 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

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of methylmalonic acidaemia

2.1.1. Indication(s) targeted by the PIP

Treatment of isolated methylmalonic acidaemia due to methylmalonyl-coenzyme A mutase deficiency

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)

Dispersion for injection

2.1.4. Measures.

Area	Description
Quality-related studies	Not applicable.
Non-clinical studies	Not applicable.
Clinical studies	**Study 1:** mRNA-3704-P001 Ambispective, longitudinal, natural history study of patients with methylmalonic acidaemia (MMA) and propionic acidaemia (PA) in North America and Europe. **Study 2:** mRNA-3705-P002 Non-interventional, multicentre, retrospective cohort study describing patient characteristics, clinical outcomes, and event rates in participants with MMA from birth to less than 18 years of age (and in adults). **Study 3:** mRNA-3705-P101 Part 1 Open-label, dose optimization study to evaluate the safety and tolerability of mRNA-3705 in participants with MMA from 1 year to less than 18 years of age (and in adults). **Study 4:** mRNA-3705-P101 Part 2 Dose expansion portion to evaluate the clinical activity of mRNA-3705 in participants with MMA from 1 year to less than 18 years of age (and in adults).

	Study 5: mRNA-3705-P101 Infant cohort Open-label trial to assess the safety and clinical activity of mRNA-3705 in participants with early-onset MMA from birth from birth to less than 1 year of age. **Study 6:** mRNA-3705-P101-EXT Open-label extension study to evaluate the long-term safety and clinical activity of mRNA-3705 in participants previously enrolled in the mRNA-3705-P101 study (PIP study 5).
Modelling and simulation studies	**Study 7:** PKPD_mRNA-3705_MMA_P101 Population pharmacokinetic and pharmacodynamic analysis using data from paediatric patients from studies 3, 4 and 5 for dose finding in paediatric patients from birth to less than 18 years of age.
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 August 2034
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.