MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral

MHRA-100891-PIP01-23

Scope of the Application

Active Substance(s)

MODIFIED MESSENGER RIBONUCLEIC ACID ENCODING HUMAN PROPIONYL-COENZYME A CARBOXYLASE ALPHA AND BETA SUBUNITS ENCAPSULATED INTO LIPID NANOPARTICLES

Condition(s)

Treatment of propionic 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 the Decision

Pursuant to the Human Medicines Regulations 2012, Moderna Biotech Spain, S.L. submitted to the licensing authority on 20/05/2024 14:51 BST an application for a Paediatric Investigation Plan

The procedure started on 05/06/2024 07:53 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to agree a paediatric investigation plan and grant a deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100891-PIP01-23

Of 11/09/2024 07:59 BST

On the adopted decision for MODIFIED MESSENGER RIBONUCLEIC ACID ENCODING HUMAN PROPIONYL-COENZYME A CARBOXYLASE ALPHA AND BETA SUBUNITS ENCAPSULATED INTO LIPID NANOPARTICLES (MHRA-100891-PIP01-23) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for MODIFIED MESSENGER RIBONUCLEIC ACID ENCODING HUMAN PROPIONYL-COENZYME A CARBOXYLASE ALPHA AND BETA SUBUNITS ENCAPSULATED INTO LIPID NANOPARTICLES, Dispersion for injection , INTRAVENOUS USE .

This decision is addressed to Moderna Biotech Spain, S.L., C/ Julián Camarillo nº 31, Madrid, SPAIN, 28037

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of propionic acidaemia

2.2 Indication(s) targeted by the PIP:

Treatment of propionic acidaemia

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Dispersion for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	6	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-3927-P002) Non-interventional, multicentre, retrospective cohort study describing patient characteristics, clinical outcomes, and event rates in participants with PA. Study 3 (mRNA-3927-P101 Part 1) Open-label, dose optimisation study to evaluate the safety and tolerability of mRNA-3927 in participants with PA. Study 4 (mRNA-3927-P101 Part 2) Dose expansion portion to evaluate the efficacy of mRNA-3927 in participants with PA. Study 5 (mRNA-3927-P101 Part 2 : Infant cohort) Open-label trial to assess the safety and clinical activity of mRNA-3927 in participants with early-onset PA aged less than 1 year of age. Study 6 (mRNA-3927-P101-EXT) Open-label extension study to evaluate the long-term safety and clinical activity of mRNA-3927 in participants previously enrolled in

		the mRNA-3927-P101 study (PIP study 5).
Extrapolation, Modeling & Simulation Studies	1	Study 7 (PKPD_mRNA-3927_PA_P101) Population pharmacokinetic and pharmacodynamic analysis using data from paediatric patients from P101 for dose finding in paediatric patients from birth to less than 18 years of age.
Other Studies	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	31/08/2033
Deferral of one or more studies contained in the paediatric investigation plan:	Yes