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

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan (MHRA-100258-PIP01-21-M01) and to the deferral

MHRA-100258-PIP01-21-M02

Scope of the Application

Active Substance(s)

Fully human IgG1 RB-1 YTE anti-RSV F monoclonal antibody (MK-1654)

Condition(s)

Prevention of lower respiratory tract infection caused by respiratory syncytial virus

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

INTRAMUSCULAR USE

Name / Corporate name of the PIP applicant

Merck Sharp & Dohme (UK) Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Merck Sharp & Dohme (UK) Limited submitted to the licensing authority on 18/12/2023 14:07 GMT an application for a Modification

The procedure started on 16/02/2024 16:02 GMT

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 accept change(s) to the agreed paediatric investigation plan and to the 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-100258-PIP01-21-M02

Of 01/03/2024 15:14 GMT

On the adopted decision for Fully human IgG1 RB-1 YTE anti-RSV F monoclonal antibody (MK-1654) (MHRA-100258-PIP01-21-M02) 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 modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for Fully human IgG1 RB-1 YTE anti-RSV F monoclonal antibody (MK-1654), Solution for injection , INTRAMUSCULAR USE .

This decision is addressed to Merck Sharp & Dohme (UK) Limited, 120 Moorgate, London, UNITED KINGDOM, EC2M 6UR

ANNEX I

1. Waiver

1.1 Condition:

Prevention of lower respiratory tract infection caused by respiratory syncytial virus (RSV). The waiver applies / applied to: Paediatric Subset(s): The paediatric population from 2 years to less than 18 years of age. Pharmaceutical form(s): Solution for injection. Route(s) of administration: INTRAMUSCULAR USE. Reason for granting waiver: 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(s):

Prevention of lower respiratory tract infection caused by respiratory syncytial virus (RSV).

2.2 Indication(s) targeted by the PIP:

Prevention of medically attending lower respiratory tract infecting (MALRI) caused by respiratory syncytial virus (RSV).

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

The paediatric population from birth to less than 2 years of age.

2.4 Pharmaceutical Form(s):

Solution 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	3	Study 1 (PN002) Safety, tolerability, and pharmacokinetic study of MK-1654 in pre-term (born from 29 to less than 37 weeks gestational age) and full-term infants (born from 37 weeks gestational age onwards) for prevention of lower respiratory tract infection caused by respiratory syncytial virus (RSV). Study 2 (PN004) Double-blind, randomised, placebo-controlled study to evaluate the efficacy and safety of MK-1654 in healthy pre-term (born at 29 to 35 weeks gestational age) and late pre-term and full-term infants (born from 35 weeks gestational age onwards) for prevention of lower respiratory tract infection caused by RSV. Study 3 (PN007) Multicentre, randomised, partially blinded, palivizumab-controlled study to evaluate the safety, efficacy, and pharmacokinetics of MK-1654 in infants and children at increased risk for severe RSV disease for prevention of lower respiratory tract infection caused by RSV.

Extrapolation, Modeling & Simulation Studies	4	Study 4 Paediatric population PK Model of MK-1654 serum concentrations. Study 5 Paediatric population PK/PD Model relating the MK-1654 serum concentrations with Serum Neutralizing (SN) Antibody titer. Study 6 A model-based meta-analysis (MBMA) for RSV and clinical trial simulations (CTS) to inform dose selection of the palivizumab-controlled study. Study 7 Partial extrapolation of efficacy based on evaluating similarity of MK-1654 PK.
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:	30/06/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes