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-100164-PIP01-21-M02)

MHRA-100164-PIP01-21-M03

Scope of the Application

Active Substance(s)

NIRMATRELVIR; RITONAVIR

Condition(s)

Treatment of coronavirus disease 2019 (COVID-19), Prevention of coronavirus disease 2019 (COVID-19)

Pharmaceutical Form(s)

Film-coated tablet Age-appropriate oral formulation

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Pfizer Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Pfizer Limited submitted to the licensing authority on 04/08/2023 09:08 BST an application for a Modification

The procedure started on 09/11/2023 15:53 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

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-100164-PIP01-21-M03

Of 13/02/2024 10:08 GMT

On the adopted decision for NIRMATRELVIR; RITONAVIR (MHRA-100164-PIP01-21-M03) 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 NIRMATRELVIR; RITONAVIR, Film-coated tablet Age-appropriate oral formulation , ORAL USE .

This decision is addressed to Pfizer Limited, Ramsgate Road, Sandwich, Kent, UNITED KINGDOM, CT139NJ

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Condition 1: Treatment of coronavirus disease 2019 (COVID-19) Condition 2: Prevention of coronavirus disease 2019 (COVID-19)

2.2 Indication(s) targeted by the PIP:

Condition 1: Treatment of coronavirus disease 2019 (COVID-19) Condition 2: Prevention of coronavirus disease 2019 (COVID-19)

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

For both conditions: All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

For both conditions: Film-coated tablet Age-appropriate oral formulation

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	(Same study for both conditions) Study 1 Development of an age-appropriate pharmaceutical form for nirmatrelvir in combination with ritonavir for the paediatric population from birth to less than 6 years of age.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	1	(Same study for both conditions) Study 2 (C4671026) Open label study to evaluate the pharmacokinetics (PK), safety and efficacy of nirmatrelvir (with ritonavir) for the treatment of children from birth to less than 18 years of age with coronavirus disease 2019 and at risk for progression to severe COVID-19.
Extrapolation, Modeling & Simulation Studies	4	(Same studies for both conditions) Study 3 Population PK modelling and simulation study to simulate multidose administration of nirmatrelvir with ritonavir across in children from birth to less than 18 years of age with COVID-19 to inform dose for paediatric clinical study 2. Study 4 Population PK modelling to simulate multiple-dose administration of nirmatrelvir with ritonavir in children from birth to less than 18 years of age with COVID-19 for the treatment of COVID-19 and in healthy children for the prevention of COVID-19 to select final

		paediatric dose recommendations by matching exposures in adults. (Study for Condition 1 only)Study 5 Extrapolation study of efficacy and safety of nirmatrelvir with ritonavir from adults to children from birth to less than 18 years of age with COVID-19 who are at risk for progression to severe COVID-19. (Study for Condition 2 only) Study 6 Extrapolation study of efficacy and safety of nirmatrelvir with ritonavir from healthy adults to healthy children from birth to less than 18 years of age for the prevention of COVID-19.
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:	31/12/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes