MHRA
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Canary Wharf
London
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United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100203-PIP01-21-M01

Scope of the Application

Active Substance(s)

Avacopan

Condition(s)

Treatment of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis

Pharmaceutical Form(s)

Age appropriate oral solid dosage form; Age appropriate oral liquid dosage form; Capsule; hard

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Vifor Fresenius Medical Care Renal Pharma France

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Vifor Fresenius Medical Care Renal Pharma France submitted to the licensing authority on 29/07/2021 11:58 BST an application for a Modification

The procedure started on 01/11/2021 11:34 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-100203-PIP01-21-M01

Of 10/11/2021 12:09 GMT

On the adopted decision for Avacopan (MHRA-100203-PIP01-21-M01) 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 Avacopan, Age appropriate oral solid dosage form; Age appropriate oral liquid dosage form; Capsule; hard , Oral use .

This decision is addressed to Vifor Fresenius Medical Care Renal Pharma France, 100–101 Terrasse Boieldieu Tour Franklin La Défense 8, Paris la Défense Cedex, France, 92042

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis

2.2 Indication(s) targeted by the PIP:

Treatment of adult and paediatric patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA)

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

All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Age appropriate oral solid dosage form; Age appropriate oral liquid dosage form; Capsule, hard

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Development of age-appropriate oral solid dosage form for use in the paediatric population from 2 years to less than 12 years of age and of an appropriate dispensing device for granules. Study 2 Development of age-appropriate oral liquid dosage form for use in the paediatric population from birth to less than 12 years of age and of an administration device with suitable graduation for the liquid formulation.
Non-Clinical Studies	3	Study 3 44-week nasogastric / oral toxicity study in cyno monkeys with 6-week recovery Study 4 Determination of PK parameters of the age-appropriate oral solid dosage form and the age-appropriate oral liquid dosage form in dogs. Study 5 13-week oral toxicity study in juvenile hamsters with 4-week recovery phase
Clinical Studies	4	Study 6 Double-blind, double dummy, randomised, placebo controlled trial to evaluate safety and efficacy of avacopan as add-on to standard of care compared to prednisone as add-on to standard of care in children from 12 years to less than 18 years of age (and adults) with active ANCA-associated vasculitis. Study 7 Open-label, 3-period, 3-way, crossover, single-dose bioavailability study in adult healthy

		volunteers to evaluate the PK profile of paediatric formulations. Study 8 Open label, uncontrolled trial to evaluate pharmacokinetics, safety and activity of a single dose of avacopan, followed by multiple doses in children from 6 to less than 18 years of age with active ANCA-associated vasculitis. Study 9 Open label, uncontrolled trial to evaluate pharmacokinetics, safety and activity of a single dose of avacopan, followed by multiple doses in children from birth to less than 6 years of age with active ANCA-associated vasculitis.
Extrapolation, Modeling & Simulation Studies	4	Study 10 Population PK modelling to support dosing in adolescents from 12 years to less than 18 years of age Study 11 Population PK modelling to support dosing in children from 6 years to less than 12 years of age Study 12 Population PK modelling to support dosing in children from birth to less than 6 years of age Study 13 Extrapolation study to provide efficacy assumptions in the paediatric population from birth to less than 12 years of age with active ANCA-associated vasculitis based on extrapolation from adults and adolescent patients.
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:	Yes
Date of completion of the paediatric investigation plan:	31/12/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes