MHRA
10 South Colonnade
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 (MHRA-100203-PIP01-21-M01) and to the deferral and grant a waiver

MHRA-100203-PIP01-21-M02

Scope of the Application

Active Substance(s)

AVACOPAN

Condition(s)

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis

Pharmaceutical Form(s)

Capsule, hard; Age-appropriate oral liquid dosage form

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 17/11/2023 21:32 GMT an application for a Modification

The procedure started on 11/01/2024 15:40 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 and grant a waiver.

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-M02

Of 22/01/2024 14:25 GMT

On the adopted decision for AVACOPAN (MHRA-100203-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 AVACOPAN, Capsule, hard; Age-appropriate oral liquid dosage form , ORAL USE .

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

ANNEX I

1. Waiver

1.1 Condition:

Treatment of anti-neutrophil cytoplasmic auto-antibody (ANCA)-associated vasculitis. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 years of age. Pharmaceutical form(s): Capsule, hard Age-appropriate oral liquid dosage form Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of anti-neutrophil cytoplasmic auto-antibody (ANCA)-associated vasculitis.

2.2 Indication(s) targeted by the PIP:

Treatment of patients with active microscopic polyangiitis (MPA). Treatment of patients with active granulomatosis with polyangiitis (GPA) where treatment with rituximab or cyclophosphamide containing regimen is indicated.

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

The paediatric population from 6 years to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Capsule, hard Age-appropriate oral liquid dosage form

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Deleted during procedure MHRA-100203-PIP01-21-M02. Study 2 Development of age-appropriate oral liquid dosage form for use in the paediatric population from 6 years to less than 18 years of age.
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	3	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 in children from 12 to less than 18 years of age (and adults) with active anti-neutrophil cytoplasmic antibody (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 liquid paediatric formulation. Study 8 Deleted during procedure MHRA-100203-PIP01-21-M02. Study 9 Deleted during procedure MHRA-100203-PIP01-21-M02. Study 14 Added during procedure MHRA-100203-PIP01-21-M02. Open label, uncontrolled single-arm study to evaluate pharmacokinetics, safety and activity of avacopan as add-on to standard of care in children from 6 years to less than 18 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 to less than 18 years of age. Study 11 Population PK modelling to support dosing in children from 6 to less than 12 years of age. Study 12 Deleted during procedure MHRA-100203-PIP01-21-M02. Study 13 Extrapolation study to provide efficacy assumptions in the paediatric population from 6 years to less than 18 years of age with active ANCA-associated vasculitis based on extrapolation from adult population.
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:	31/07/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes