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

MHRA-100238-PIP01-21-M02

Scope of the Application

Active Substance(s)

AVELUMAB

Condition(s)

Treatment of malignant neoplasms of the central nervous system, Treatment of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms), Treatment of malignant neoplasms of the lymphoid tissue.

Pharmaceutical Form(s)

Concentrate for solution for infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Merck Serono Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Merck Serono Limited submitted to the licensing authority on 12/08/2024 14:33 BST an application for a Modification

The procedure started on 10/09/2024 08:37 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 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-100238-PIP01-21-M02

Of 23/10/2024 08:54 BST

On the adopted decision for AVELUMAB (MHRA-100238-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 AVELUMAB, Concentrate for solution for infusion , INTRAVENOUS .

This decision is addressed to Merck Serono Limited, 5 New Square, Bedfont Lakes Business Park, Feltham, Feltham, UNITED KINGDOM, TW14 8HA

ANNEX I

1. Waiver

1.1 Condition:

Condition: Treatment of malignant neoplasms of the lymphoid tissue. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 18 years of age. Pharmaceutical form(s): Concentrate for solution for infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: On the grounds clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfill a therapeutic need of the specified paediatric subset(s). Condition: Treatment of malignant neoplasms of the central nervous system. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age. Pharmaceutical form(s): Concentrate for solution for infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: On the grounds clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s)

2. Paediatric Investigation Plan:

2.1 Condition(s):

Condition 1: Treatment of all conditions included in the category of malignant neoplasms (except central nervous system tumours, haematopoietic and lymphoid tissue neoplasms). Condition 2: Treatment of malignant neoplasms of the central nervous system.

2.2 Indication(s) targeted by the PIP:

Condition 1: Treatment of paediatric patients from birth to less than 18 years old with a relapsed or refractory solid tumour or with a solid tumour as part of the first line treatment. Condition 2: Treatment of paediatric patients from 2 years to less than 18 years old with a refractory or relapsed tumour of the central nervous system or with a tumour of the central nervous system as part of first line treatment.

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

Condition 1: The paediatric population from birth to less than 18 years of age. Condition 2: The paediatric population from 2 years to less than 18 years

2.4 Pharmaceutical Form(s):

Concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	3	Study 1 Exploratory toxicity/efficacy non-clinical study in a syngeneic mouse model. Study 2 Collection and analysis of data from literature and databases of paediatric tumour samples relative to tumour genetic mutations and tumour gene and neoantigens expression. Study 3 Non-clinical biomarker study in paediatric tumour tissues.
Clinical Studies	2	Study 4 Open-label study to evaluate pharmacokinetics, pharmacodynamics, safety and anti-cancer activity of avelumab in paediatric patients from birth to less than 18 years of age with a refractory or relapsed solid tumour, including lymphomas and tumours of the

		central nervous system, or for which no effective treatment is known. Study 5 This study was deleted during procedure EMEA-001849-PIP02-15-M03. Study 7 (This study was added during procedure EMEA-001849-PIP02-15-M03) Open-label, single-arm study to evaluate pharmacokinetics, safety and tolerability (dose-escalation part) and safety and anti-tumour activity (expansion part) of avelumab used in combination with lenvatinib in paediatric patients from 2 years to less than 18 years of age with a primary central nervous system malignancy that has progressed after at least one prior therapy.
Extrapolation, Modeling & Simulation Studies	1	Study 6 Adult population pharmacokinetic PK (POPPK) model study.
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:	30/09/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes