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-100494-PIP01-22-M01) and to the deferral

MHRA-100494-PIP01-22-M02

Scope of the Application

Active Substance(s)

NIVOLUMAB

Condition(s)

Treatment of malignant neoplasms of lymphoid tissue , Treatment of malignant neoplasms of the central nervous system

Pharmaceutical Form(s)

Concentrate for solution for infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Bristol-Myers Squibb Pharma EEIG

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Bristol-Myers Squibb Pharma EEIG submitted to the licensing authority on 29/04/2024 11:51 BST an application for a Modification

The procedure started on 04/06/2024 15:07 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-100494-PIP01-22-M02

Of 31/07/2024 08:30 BST

On the adopted decision for NIVOLUMAB (MHRA-100494-PIP01-22-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 NIVOLUMAB, Concentrate for solution for infusion , INTRAVENOUS USE .

This decision is addressed to Bristol-Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, IRELAND, D15 T867

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of malignant neoplasms of lymphoid tissue The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 months of age Pharmaceutical form(s): Concentrate for solution for infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: on the grounds that 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). Condition 2: 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 6 months of age Pharmaceutical form(s): Concentrate for solution for infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: on the grounds that 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 malignant neoplasms of lymphoid tissue 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 with a relapsed or refractory Hodgkin lymphoma in the age group from 5 years to less than 18 years Treatment of paediatric patients with a relapsed or refractory non-Hodgkin lymphoma in the age group from 6 months to less than 18 years old Condition 2: Treatment of paediatric patients from 6 months to less than 18 years of age with a recurrent or progressive high-grade glioma

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

For both Conditions: The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

For both Conditions: Concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	3	Same study for both conditions Study 1 (CA209070) (Same as study 2 in EMEA-001407-PIP01-12) Open-label, multi-centre trial to evaluate pharmacokinetics, pharmacodynamics, toxicity, safety and anti-cancer activity of nivolumab and of nivolumab in combination with ipilimumab in paediatric patients from 1 year to less than 18 years of age with a refractory or relapsed malignant solid tumour, with an expansion phase evaluating nivolumab in paediatric patients from 1 year to less than 18 years of age (and adults) with refractory or relapsed Ewing sarcoma, osteosarcoma, rhabdomyosarcoma or neuroblastoma, for which no

		effective treatment is known. Study for Condition 2 Study 2 (CA209908) Multi-centre, open-label, single-arm trial of nivolumab to evaluate safety, pharmacodynamics and anti-tumour activity in patients from 6 months to less than 18 years of age (and adults) with a recurrent or refractory central nervous system tumour. Studies for Condition 1 Study 3 Deleted during procedure EMEA-001407-PIP02-15-M04. Study 4 (CA209744) Open label, single arm trial to assess the safety and activity of nivolumab combined with brentuximab vedotin in paediatric patients from 5 years to less than 18 years (and adults) with a relapsed or refractory Hodgkin lymphoma followed by brentuximab vedotin in combination with bendamustine in case of suboptimal response.
Extrapolation, Modeling & Simulation Studies	0	Not applicable.
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:	31/12/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes