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 and to the deferral

MHRA-100455-PIP01-22-M01

Scope of the Application

Active Substance(s)

IXAZOMIB

Condition(s)

Treatment of multiple myeloma, Treatment of lymphoid malignancies (excluding multiple myeloma)

Pharmaceutical Form(s)

Capsule, hard, Powder for solution for injection

Route(s) of Administration

Oral use; Gastric use; Intravenous sue

Name / Corporate name of the PIP applicant

Takeda UK Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Takeda UK Limited submitted to the licensing authority on 02/03/2022 12:30 GMT an application for a Modification

The procedure started on 10/10/2022 15:54 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-100455-PIP01-22-M01

Of 20/10/2022 11:30 BST

On the adopted decision for IXAZOMIB (MHRA-100455-PIP01-22-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 IXAZOMIB, Capsule, hard, Powder for solution for injection , Gastric use, Oral use .

This decision is addressed to Takeda UK Limited, 1 Kingdom Street, London, United Kingdom, W2 6BD

ANNEX I

1. Waiver

1.1 Condition:

Treatment of multiple myeloma The waiver applies / applied to: Paediatric Subset(s): All subsets of the paediatric population from birth to less than 18 years of age Pharmaceutical form(s): Capsule, hard; Powder for solution for injection Route(s) of administration: Oral use; Gastric use; Intravenous use Reason for granting waiver: on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of lymphoid malignancies (excluding multiple myeloma)

2.2 Indication(s) targeted by the PIP:

Treatment of paediatric patients from birth to less than 18 years of age with a lymphoid malignancy

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

The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard; Powder for solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Compatibility of ixazomib powder for solution for injection, oral use, gastric use, with flavouring agents or food and with naso-gastric feeding tubes. Generation of data on acceptability and palatability.
Non-Clinical Studies	0	Not applicable
Clinical Studies	4	Study 2 (T2017-002) Uncontrolled, open label study to assess pharmacokinetics and safety of ixazomib capsules for oral use, and of powder for solution for injection, oral use and gastric use, in paediatric patients from birth to less than 18 years of age (and adults if diagnosed at less than 18 years of age) with relapsed/refractory acute lymphoblastic leukaemia or lymphoblastic lymphoma with or without extramedullary disease. Study 3 Deleted during procedure EMEA-001410-PIP02-17-M03 Study 4 (T2017-002) Open-label, single arm study to assess the efficacy of the addition of ixazomib, capsules for oral use, and powder for solution for injection, oral use and gastric use, to reinduction chemotherapy in paediatric patients from birth to less than 18 years of age (and adults if diagnosed at less than 18 years of age) with relapsed/ refractory (RR) acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LLy) with or without extramedullary disease. Study 5

		Randomised, controlled, open-label study to assess event free survival (EFS) of patients from birth to less than 18 years of age (and adults if diagnosed at less than 18 years of age) with relapsed or refractory (RR) acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LLy) with or without extramedullary disease treated with ixazomib in combination with vincristine, dexamethasone, L-asparaginase, and doxorubicin (VXLD) chemotherapy versus VXLD chemotherapy alone. Study 6 Randomised, controlled study of modified augmented Berlin-Frankfurt-Münster (ABFM) regimen with bortezomib during induction/ consolidation and intensification followed by maintenance therapy with/without ixazomib in patients from birth to less than 18 years of age (and adults if diagnosed at less than 18 years of age) with newly diagnosed ALL or LLy with or without extramedullary disease.
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:	No
Date of completion of the paediatric investigation plan:	31/12/2031
Deferral of one or more studies contained in the paediatric investigation plan:	Yes