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-100049-PIP01-21-M02

Scope of the Application

Active Substance(s)

IBRUTINIB

Condition(s)

Treatment of mature B-cell neoplasm

Pharmaceutical Form(s)

Film-coated tablet; Capsule, hard

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Janssen-Cilag Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Janssen-Cilag Limited submitted to the licensing authority on 08/10/2021 14:40 BST an application for a Modification

The procedure started on 07/03/2022 13:30 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-100049-PIP01-21-M02

Of 17/03/2022 16:58 GMT

On the adopted decision for IBRUTINIB (MHRA-100049-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 IBRUTINIB, Film-coated tablet; Capsule, hard , Oral use .

This decision is addressed to Janssen-Cilag Limited, 50-100 Holmers Farm Way, High Wycombe, United Kingdom, HP12 4EG

ANNEX I

1. Waiver

1.1 Condition:

Treatment of mature B-cell neoplasm The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Capsule, hard; Film-coated tablet Route(s) of administration: Oral 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 mature B-cell neoplasm

2.2 Indication(s) targeted by the PIP:

Treatment of children from 1 year to less than 18 years of age with newly-diagnosed and relapsed/ refractory mature B-cell lymphoma, that is, diffuse large B-cell lymphoma or Burkitt and Burkitt-like lymphoma

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

The paediatric population from 1 year to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard; Film-coated tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Study 1 (CMCPED01) Removed in procedure MHRA-100049-PIP01-21-M01
Non-Clinical Studies	1	Study 2 In vitro and in vivo non-clinical efficacy studies of ibrutinib, including in combination, in models of paediatric malignant diseases
Clinical Studies	1	Study 3 Multi-centre, randomised add-on study with run-in phase to evaluate pharmacokinetics, pharmacodynamics, toxicity, safety and anti-tumour activity of ibrutinib as add-on to RICE or RVICI regimens in paediatric patients from 1 year to less than 18 years (and young adults) with a relapsed or refractory mature B cell lymphoma Study 4 (PCI-32765PEDXXXX) Removed in procedure MHRA-100049-PIP01-21-M01
Extrapolation, Modeling & Simulation Studies	1	Study 5 Physiologically-based pharmacokinetic (PBPK) model
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:	31/12/2021
Deferral of one or more studies contained in the paediatric investigation plan:	Yes