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-100145-PIP01-21-M01

Scope of the Application

Active Substance(s)

BRIGATINIB

Condition(s)

Non small cell lung cancer, Anaplastic large cell lymphoma, Inflammatory myofibroblastic tumours

Pharmaceutical Form(s)

Oral solution, Film-coated tablet

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Takeda UK Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Takeda UK Ltd submitted to the licensing authority on 07/06/2021 16:42 BST an application for a Modification

The procedure started on 22/04/2022 07:54 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

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-100145-PIP01-21-M01

Of 20/05/2022 17:05 BST

On the adopted decision for BRIGATINIB (MHRA-100145-PIP01-21-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 BRIGATINIB, Oral solution, Film-coated tablet , Oral use .

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

ANNEX I

1. Waiver

1.1 Condition:

1.1 Condition: Treatment of non-small cell lung cancer (NSCLC) 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): Film-coated tablet; Oral solution 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). 1.2 Condition: Treatment of anaplastic large cell lymphoma (ALCL) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Film-coated tablet; Oral solution Route(s) of administration: Oral 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). 1.3 Condition: Treatment of inflammatory myofibroblastic tumours The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Film-coated tablet; Oral solution Route(s) of administration: Oral 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 2:Treatment of anaplastic large cell lymphoma (ALCL); Condition 3: Treatment of inflammatory myofibroblastic tumours;

2.2 Indication(s) targeted by the PIP:

Condition 2: Treatment in combination with standard chemotherapy in paediatric patients from 1 year of age and older with newly diagnosed ALK+ ALCL at high risk for recurrence; Condition 3: Treatment of paediatric patients from 1 year of age and older with ALK+ unresectable or recurrent inflammatory myofibroblastic tumours

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

For Conditions 2 and 3: The paediatric population from 1 year to less than 18 years of age

2.4 Pharmaceutical Form(s):

For Conditions 2 and 3: Film-coated tablet; Oral solution

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	(Same study for Conditions 2 and 3) Study 1 Development of an age appropriate liquid dosage form (oral solution) for paediatric patients unable to swallow the film-coated tablets.
Non-Clinical Studies	0	Not applicable
Clinical Studies	2	(Same study for Conditions 2 and 3) Study 2 (Brigatinib-1002) Open-label, single arm trial to evaluate: i. the pharmacokinetics and safety of brigatinib used in monotherapy in paediatric patients from 1 to less than 18 years of age (and in adults) with relapsed/refractory ALCL or a relapsed/refractory/recurrent solid tumour harbouring an ALK mutation (phase 1-dose escalation, part A) ii. the anti-tumour activity of brigatinib used in monotherapy in an expansion cohort of paediatric patients from 1 to less than 18 years of age (and in adults) with unresectable/recurrent IMT harbouring an ALK mutation

		and in an expansion cohort of paediatric patients from 1 to less than 18 years of age (and in adults) with relapsed/refractory ALCL harbouring an ALK mutation (phase 2, part B); (For Condition 2 only) Study 3 (Brigatinib-1003) Open-label, trial including a dose-escalating phase to evaluate the pharmacokinetics and safety of brigatinib used in combination with standard therapy (ALCL99 protocol) (phase 1-dose confirmation of brigatinib used in combination with ALCL99 protocol, phase 1 part) followed by a randomised, controlled phase to evaluate the efficacy and safety of brigatinib used in combination with ALCL99 protocol compared to ALCL99 protocol alone (phase 2 part) in paediatric patients from 1 year to less than 18 years of age (and adults) with newly-diagnosed high risk ALK positive anaplastic large cell lymphoma.
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:	31/12/2028
Deferral of one or more studies contained in the paediatric investigation plan:	No