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-100200-PIP01-21-M01

Scope of the Application

Active Substance(s)

REGORAFENIB

Condition(s)

Treatment of all malignant neoplasms (except haematopoietic and lymphoid tissue)

Pharmaceutical Form(s)

Film-coated tablet, Granules

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Bayer Plc

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Bayer Plc submitted to the licensing authority on 27/09/2021 23:09 BST an application for a

The procedure started on 29/07/2022 14:40 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-100200-PIP01-21-M01

Of 19/09/2022 09:19 BST

On the adopted decision for REGORAFENIB (MHRA-100200-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 for REGORAFENIB, Film-coated tablet, Granules , Oral use .

This decision is addressed to Bayer Plc, 400 South Oak Way, Reading, United Kingdom, RG2 6AD

ANNEX I

1. Waiver

1.1 Condition:

Treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and 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): Granules; Film-coated tablet Route(s) of administration: Oral use Reason for granting waiver: on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of all conditions contained in the category of malignant neoplasms (except haematopoietic and lymphoid tissue)

2.2 Indication(s) targeted by the PIP:

Treatment of paediatric patients with a solid malignant tumour(s) integrated with anti-cancer therapy

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

The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Granules; Film-coated tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of granules for oral use as age-appropriate formulation.
Non-Clinical Studies	2	Study 2 Juvenile toxicity study. Study 3 Pharmacology testing of regorafenib in paediatric tumour models including biomarker exploration and combination testing.
Clinical Studies	2	Study 5 Multi-centre, open-label, dose-escalating, cohort-expanding trial to evaluate pharmacokinetics, pharmacodynamics, tolerability, safety and tumour activity of regorafenib in the paediatric population with a solid malignant tumour refractory to standard therapy Study 6 Deleted in procedure EMEA-001178-PIP01-11-M03. Study 7 Multi-centre, randomised, controlled, open label trial to evaluate the activity, safety and efficacy of regorafenib in combination with vincristine and irinotecan (VI) compared to VI alone in the paediatric population from 6 months to less than 18 years with a first and subsequent relapses of rhabdomyosarcoma.
Extrapolation, Modeling & Simulation Studies	1	Study 4 Physiologically-based pharmacokinetic model to predict pharmacokinetics in the paediatric population from 6 months to less than 18 years of age.
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