MHRA
10 South Colonnade
Canary Wharf
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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-100031-PIP01-21-M02

Scope of the Application

Active Substance(s)

PALBOCICLIB

Condition(s)

Treatment of Ewing sarcoma (EWS)

Pharmaceutical Form(s)

Capsule, hard; Film-coated tablet; Age-appropriate oral dosage form

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Pfizer Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Pfizer Limited submitted to the licensing authority on 18/03/2022 17:01 GMT an application for a Modification

The procedure started on 14/11/2022 07:44 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

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-100031-PIP01-21-M02

Of 17/11/2022 15:23 GMT

On the adopted decision for PALBOCICLIB (MHRA-100031-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 PALBOCICLIB, Capsule, hard; Film-coated tablet; Age-appropriate oral dosage form , ORAL USE .

This decision is addressed to Pfizer Limited, Ramsgate Road, Sandwich, UNITED KINGDOM, CT13 9NJ

ANNEX I

1. Waiver

1.1 Condition:

Treatment of Ewing sarcoma The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Capsule, hard; Film-coated tablet; Age-appropriate oral dosage form 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):

Treatment of Ewing sarcoma

2.2 Indication(s) targeted by the PIP:

Treatment of refractory or recurrent Ewing sarcoma

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

The paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard; Film-coated tablet; Age-appropriate oral dosage form

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an oral solution formulation for paediatric patients unable to swallow the capsules.
Non-Clinical Studies	2	Study 2 In vivo study to assess the anti-tumour activity of palbociclib used in combination with irinotecan and temozolomide compared irinotecan and temozolomide alone in Ewing sarcoma xenografts. Study 3 In vitro study to evaluate the anti-tumour activity of palbociclib used in with irinotecan in Ewing sarcoma (EWS) cell lines.
Clinical Studies	1	Study 4 (A5481092) Open-label, single-arm, dose-escalation trial to evaluate the safety, pharmacokinetics and anti-tumour activity of palbociclib used in combination with temozolomide and irinotecan in children from 2 years to less than 18 years of age (and young adults) with a recurrent or refractory solid tumour, with a dose-finding phase (dose-escalation and dose determination parts) and expansion cohorts (dose expansion parts) (phase 1 portion) and open-label, randomised trial to evaluate the efficacy, safety, and pharmacokinetics of palbociclib

		in combination with irinotecan and temozolomide compared to irinotecan and temozolomide alone in children from 2 years to less than 18 years of age (and young adults) with recurrent/refractory Ewing sarcoma, for whom no standard therapy is available (randomised phase 2 portion) Study 5 Deleted in procedure MHRA-100030-PIP01-21-M02.
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:	30/04/2025
Deferral of one or more studies contained in the paediatric investigation plan:	No