EMA/8294/2022

European Medicines Agency decision

P/0020/2022

of 31 January 2022

on the agreement of a paediatric investigation plan and on the granting of a waiver for ribociclib (Kisqali), (EMEA-002765-PIP02-21) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Novartis Europharm Limited on 11 February 2021 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 17 December 2021, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for ribociclib (Kisqali), film coated tablet, age-appropriate oral liquid dosage form, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A waiver plan for ribociclib (Kisqali), film coated tablet, age-appropriate oral liquid dosage form, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, D04A9N6 – Dublin, Ireland.

EMA/PDCO/526697/2021
Amsterdam, 17 December 2021

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a waiver

EMEA-002765-PIP02-21

Scope of the application

Active substance(s):

Ribociclib

Invented name:

Kisqali

Condition(s):

Treatment of neuroblastoma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film coated tablet

Age-appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm Limited

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted for agreement to the European Medicines Agency on 11 February 2021 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 23 March 2021.

Supplementary information was provided by the applicant on 13 September 2021. The applicant proposed modifications to the paediatric investigation plan and waiver.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of neuroblastoma

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- film coated tablet, age-appropriate oral liquid dosage form, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered.

2. Paediatric investigation plan

2.1. Condition:

Treatment of neuroblastoma

2.1.1. Indication(s) targeted by the PIP

Treatment of relapsed or refractory neuroblastoma (NB) in patients aged 12 months and above in combination with temozolomide and topotecan (TOTEM).

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 1 year to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film coated tablet, age-appropriate oral liquid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age appropriate oral liquid dosage form
Non-clinical studies	1	**Study 2** Definitive juvenile toxicity study
Clinical studies	3	**Study 3** Open-label, single arm trial (Part A) to determine the recommended Phase 2 dose (RP2D) and evaluate pharmacokinetics, safety and activity of ribociclib as add-on to topotecan and temozolomide (TOTEM) in children from 1 year to less than 18 years of age (and

		adults) with relapsed or refractory neuroblastoma (and other solid tumours). **Study 4** Open-label, single arm trial (Part B) to evaluate activity, safety and pharmacokinetics of ribociclib in combination with topotecan and temozolomide (TOTEM) at the RP2D in children from 1 year to less than 18 years of age (and adults) with relapsed or refractory neuroblastoma (and other solid tumours). **Study 5** Double-blind, randomised, placebo controlled trial to evaluate pharmacokinetics, safety and efficacy of ribociclib in combination with topotecan and temozolomide (TOTEM) compared to placebo plus TOTEM in children from 1 year to less than 18 years of age (and adults) with relapsed or refractory neuroblastoma.
Extrapolation, modelling and simulation studies	1	**Study 6** Modelling and simulation study to evaluate the use of ribociclib in combination with TOTEM in children from 1 year to less than 18 years of age (and adults) with relapsed or refractory neuroblastoma.
Other studies	0	Not applicable
Other measures	0	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By January 2028
Deferral for one or more measures contained in the paediatric investigation plan:	No

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of breast cancer

Authorised indication(s):

- Treatment of women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy.

  In pre or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone releasing hormone (LHRH) agonist

Authorised pharmaceutical form(s):

Film coated tablet

Authorised route(s) of administration:

Oral use