EMA/554972/2021

European Medicines Agency decision

P/0408/2021

of 8 October 2021

on the acceptance of a modification of an agreed paediatric investigation plan for acalabrutinib (Calquence), (EMEA-001796-PIP03-16-M02) 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.

European Medicines Agency decision

P/0408/2021

of 8 October 2021

on the acceptance of a modification of an agreed paediatric investigation plan for acalabrutinib (Calquence), (EMEA-001796-PIP03-16-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0309/2017 issued on 30 October 2017 and the decision P/0062/2019 issued on 15 March 2019,

Having regard to the application submitted by Acerta Pharma, BV on 12 July 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 10 September 2021, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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 acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for acalabrutinib (Calquence), capsule, hard, age-appropriate oral liquid dosage form, age-appropriate oral solid dosage form, film-coated tablet, oral use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Acerta Pharma, BV, Pivot Park, Kloosterstraat 9, 5349 AB- OSS, Netherlands.

EMA/PDCO/415096/2021
Amsterdam, 10 September 2021

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-001796-PIP03-16-M02

Scope of the application

Active substance(s):

Acalabrutinib

Invented name:

Calquence

Condition(s):

Treatment of mature B cell neoplasms

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral liquid dosage form

Age-appropriate oral solid dosage form

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Acerta Pharma, BV

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Acerta Pharma, BV submitted to the European Medicines Agency on 12 July 2021 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0309/2017 issued on 30 October 2017 and the decision P/0062/2019 issued on 15 March 2019.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 17 August 2021.

Scope of the modification

Pharmaceutical form was amended; new pharmaceutical form was added.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

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

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) 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 mature B cell neoplasms

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- capsule, hard, age-appropriate oral liquid dosage form, age-appropriate oral solid dosage form, film-coated tablet, oral use;
- 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

Treatment of mature B cell neoplasms

2.1.1. 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 lymphoma or primary mediastinal lymphoma

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

From 1 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard, age-appropriate oral liquid dosage form, age-appropriate oral solid dosage form, film-coated tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an age-appropriate oral liquid formulation to be used in children from 1 to less than 18 years of age. **Study 2** Development of an age-appropriate oral solid dosage form (mini-tablets or dispersible tablets or granules) to be used in children from 1 to less than 18 years of age.

Non-clinical studies	2	**Study 3** Efficacy study in mouse xenograft models of paediatric (and adult) B cell malignancies. **Study 4** Efficacy study in mouse models of CNS lymphoma.
Clinical studies	2	**Study 5** Open-label, single arm dose-escalation (phase 1) trial to evaluate the pharmacokinetics, pharmacodynamics, safety and anti-tumour activity of acalabrutinib as add-on to rituximab, ifosfamide, carboplatin and etoposide (R-ICE) or rituximab, vincristine, ifosfamide, carboplatin, idarubicin and dexamethasone (R-VICI) regimens in paediatric patients from 1 to less than 18 years of age (and young adults) with a relapsed or refractory mature B-cell neoplasm and an expansion cohort (phase 2). **Study 6** Open-label, single arm trial to evaluate the pharmacokinetics, pharmacodynamics, safety and anti-tumour activity of acalabrutinib as add-on to multi-agent Lymphoma-Malins-B (LMB) chemotherapy + rituximab in paediatric patients from 1 to less than 18 years of age (and young adults) with a newly-diagnosed mature B-cell neoplasm.
Extrapolation, modelling and simulation studies	2	**Study 7** Modelling and simulation study to better define the dose of acalabrutinib to be used in children from 1 to less than 18 years of age with a refractory or relapsed mature B-cell neoplasm. **Study 8** Extrapolation study to support and evaluate the use of acalabrutinib in children from 1 to less than 18 years of age with a newly-diagnosed mature B-cell neoplasm.
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:	Yes
Date of completion of the paediatric investigation plan:	By September 2028
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of mature B cell neoplasms

Authorised indication(s):

- Calquence as monotherapy or in combination with obinutuzumab is indicated for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL).
- Calquence as monotherapy is indicated for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy.

Authorised pharmaceutical form(s):

Capsule, hard

Authorised route(s) of administration:

Oral use