EMA/654967/2017

European Medicines Agency decision

P/0309/2017

of 30 October 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for acalabrutinib (EMEA-001796-PIP03-16) 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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An agency of the European Union

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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 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 application submitted by ACERTA PHARMA, BV on 13 June 2016 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 September 2017, in accordance with Article 18 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation 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 deferral 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 deferral.

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

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

Has adopted this decision:

Article 1

A paediatric investigation plan for acalabrutinib, capsule, hard, age-appropriate oral liquid dosage form, age-appropriate oral solid 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 deferral for acalabrutinib, capsule, hard, age-appropriate oral liquid dosage form, age-appropriate oral solid 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

A waiver for acalabrutinib, capsule, hard, age-appropriate oral liquid dosage form, age-appropriate oral solid 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 4

This decision is addressed to ACERTA PHARMA, BV. Kloosterstraat 9, 5349 AB – Oss, The Netherlands.

EMA/PDCO/432392/2017
London, 15 September 2017

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

EMEA-001796-PIP03-16

Scope of the application

Active substance(s):

Acalabrutinib

Condition(s):

Treatment of mature B cell neoplasms

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral liquid dosage form

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

ACERTA PHARMA, BV

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, ACERTA PHARMA, BV submitted for agreement to the European Medicines Agency on 13 June 2016 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 19 July 2016.

Supplementary information was provided by the applicant on 26 June 2017. The applicant proposed modifications to the paediatric investigation plan.

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 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 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)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population.

   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(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 annex 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, 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.

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 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes