EMA/532839/2021

European Medicines Agency decision

P/0405/2021

of 1 October 2021

on the acceptance of a modification of an agreed paediatric investigation plan for brigatinib (Alunbrig), (EMEA-002296-PIP01-17-M03) 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 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/0350/2018 issued on 15 November 2018, the decision P/0430/2019 issued on 5 December 2019 and the decision P/0483/2020 issued on 9 December 2020,

Having regard to the application submitted by Takeda Pharm A/S on 4 June 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with 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 brigatinib (Alunbrig), age-appropriate liquid 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 Takeda Pharm A/S, Delta Park 45, 2665 - Vallensbaek Strand, Denmark.

EMA/PDCO/324479/2021
Amsterdam, 10 September 2021

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

EMEA-002296-PIP01-17-M03

Scope of the application

Active substance(s):

Brigatinib

Invented name:

Alunbrig

Condition(s):

Treatment of anaplastic large cell lymphoma

Treatment of inflammatory myofibroblastic tumours

Treatment of non-small cell lung cancer

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Age-appropriate liquid dosage form

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Takeda Pharm A/S

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Takeda Pharm A/S submitted to the European Medicines Agency on 4 June 2021 an application for modification of the agreed paediatric investigation plan with a waiver as set out in the European Medicines Agency's decision P/0350/2018 issued on 15 November 2018, the decision P/0430/2019 issued on 5 December 2019 and the decision P/0483/2020 issued on 9 December 2020.

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

The procedure started on 12 July 2021.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

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 non-small cell lung cancer

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- age-appropriate liquid 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).

1.2. Condition

Treatment of anaplastic large cell lymphoma

The waiver applies to:

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

1.3. Condition

Treatment of inflammatory myofibroblastic tumours

The waiver applies to:

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

Treatment of anaplastic large cell lymphoma

2.1.1. Indication(s) targeted by the PIP

Treatment in combination with standard chemotherapy in paediatric patients from 1 year of age and older with newly diagnosed ALK+ ALCL at high risk for recurrence

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)

Age-appropriate liquid dosage form

Film-coated tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate liquid dosage form (oral solution) for paediatric patients unable to swallow the film-coated tablets.
Non-clinical studies	0	Not applicable.
Clinical studies	2	**Study 2 (Brigatinib-1002)** Open-label, single arm trial to evaluate i. the pharmacokinetics and safety of brigatinib used in monotherapy in paediatric patients from 1 to less than 18 years of age (and in adults) with relapsed/refractory ALCL or a relapsed/refractory/recurrent solid tumour harbouring an ALK mutation (phase 1-dose escalation, part A) ii. the anti-tumour activity of brigatinib used in monotherapy in an expansion cohort of paediatric patients from 1 to less than 18 years of age (and in adults) with unresectable/recurrent (including patients with metastatic disease) IMT harbouring an ALK mutation and in an expansion cohort of paediatric patients from 1 to less than 18 years of age (and in adults) with relapsed/refractory ALCL harbouring an ALK mutation (phase 2, part B) **Study 3 (Brigatinib-1003)** Open-label, trial including a dose-escalating phase to evaluate the pharmacokinetics and safety of brigatinib used in combination with standard therapy (ALCL99 protocol) (phase 1-dose confirmation of brigatinib used in combination with ALCL99 protocol, phase 1 part) followed by a randomised, controlled phase to evaluate the efficacy and safety of brigatinib used in combination with ALCL99 protocol compared to ALCL99 protocol alone (phase 2 part) in paediatric patients from 1 year to less than 18 years of age (and adults) with newly-diagnosed high risk ALK positive anaplastic large cell lymphoma.
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition

Treatment of inflammatory myofibroblastic tumours

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from 1 year of age and older with ALK+ unresectable or recurrent or metastatic inflammatory myofibroblastic tumours

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

From 1 year to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Age-appropriate liquid dosage form

Film-coated tablet

2.2.4. Measures

Area	**Number of measures**	**Description**
Quality-related studies	1	**Study 1** Same as for condition 'Treatment of anaplastic large cell lymphoma'.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 2** Same as for condition 'Treatment of anaplastic large cell lymphoma'.
Extrapolation, modelling and simulation studies	0	Not applicable.
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 December 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 non-small cell lung cancer

Authorised indication(s):

- Alunbrig is indicated as monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib.
- Alunbrig is indicated as monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with an ALK inhibitor.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use