EMADOC-1700519818-2039290

European Medicines Agency decision

EMA/PE/0000236723

of 15 April 2025

on the acceptance of a modification of an agreed paediatric investigation plan for brigatinib (Alunbrig) 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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on the acceptance of a modification of an agreed paediatric investigation plan for brigatinib (Alunbrig) 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 Union procedures for the authorisation and supervision of medicinal products for human 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, the decision P/0483/2020 issued on 9 December 2020 and the decision P/0405/2021 issued on 1 October 2021,

Having regard to the application submitted by Takeda Pharma A/S on 25 Navember 2024 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 28 February 2025, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for brigatinib (Alunbrig), 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 Pharma A/S, Delta Park 45, 2665 - Vallensbaek Strand, Hovedstaden, Denmark.

EMADOC-1700519818-1802004 Corr[1]
Amsterdam, 28 February 2025

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

EMA/PE/0000236723

Scope of the application

Active substance(s):

Brigatinib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of anaplastic large cell lymphoma

Treatment of inflammatory myofibroblastic tumours

Treatment of non-small cell lung cancer

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

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 25 November 2024 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, the

[1] 13 March 2025

decision P/0483/2020 issued on 9 December 2020 and the decision P/0405/2021 issued on 1 October 2021.

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

The procedure started on 2 January 2025.

Scope of the modification

Some measures and timelines 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 Paediatric Committee member of Norway 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 paediatric patients from 1 year of age and older with relapsed/refractory ALK+ ALCL.

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	Description
Quality-related studies	**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	Not applicable.
Clinical studies	**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)*** deleted in modification EMA/PE/0000236723 (corresponding to the 4th PIP modification) of 28 February 2025
Extrapolation, modelling and simulation studies	Not applicable.
Other studies	Not applicable.
Other measures	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	Description
Quality-related studies	**Study 1** Same as for condition 'Treatment of anaplastic large cell lymphoma'.
Non-clinical studies	Not applicable.
Clinical studies	**Study 2** Same as for condition 'Treatment of anaplastic large cell lymphoma'.
Extrapolation, modelling and simulation studies	Not applicable.
Other studies	Not applicable.
Other measures	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 2027
Deferral for one or more measures contained in the paediatric investigation plan:	No

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

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 not treated with an ALK inhibitor.
- Alunbrig is indicated as monotherapy for the treatment of adult patients with ALK-positive advanced NSCLC previously treated with crizotinib.
  - Invented name(s): Alunbrig
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure.