EMA/34215/2021

European Medicines Agency decision

P/0036/2021

of 27 January 2021

on the acceptance of a modification of an agreed paediatric investigation plan for crizotinib (Xalkori) (EMEA-001493-PIP03-18-M01) 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 P/0399/2019 issued on 4 December 2019,

Having regard to the application submitted by Pfizer Europe MA EEIG on 11 September 2020 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 11 December 2020, 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 crizotinib (Xalkori), capsule, hard, age-appropriate oral dosage form, 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 Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 – Bruxelles, Belgium.

EMA/PDCO/515845/2020
Amsterdam, 11 December 2020

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

EMEA-001493-PIP03-18-M01

Scope of the application

Active substance(s):

Crizotinib

Invented name:

Xalkori

Condition(s):

Treatment of anaplastic large cell lymphoma

Treatment of inflammatory myofibroblastic tumour

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Pfizer Europe MA EEIG

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Pfizer Europe MA EEIG submitted to the European Medicines Agency on 11 September 2020 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/0399/2019 issued on 4 December 2019.

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

The procedure started on 13 October 2020.

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 anaplastic large cell lymphoma (ALCL)

The waiver applies to:

- the paediatric population from birth to less than 12 months of age;
- capsule, hard, age-appropriate oral 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).

1.2. Condition:

Treatment of inflammatory myofibroblastic tumour (IMT)

The waiver applies to:

- the paediatric population from birth to less than 12 months of age;
- capsule, hard, age-appropriate oral 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 anaplastic large cell lymphoma

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with relapsed/refractory systemic ALK-positive ALCL

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

From 12 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard

Age-appropriate oral dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an oral age appropriate paediatric formulation
Non-clinical studies	0	Not applicable
Clinical studies	4	**Study 2 (Study ADVL0912)** Single arm, multiple dose, two-phase trial to evaluate the recommended Phase 2 dose (RP2D), pharmacokinetics, safety and activity of crizotinib in children from 12 months to less than 18 years of age (and adults) with relapsed/refractory solid tumours (including IMT) and relapsed/refractory ALCL **Study 3 (Study A8081013)** Single arm trial to evaluate safety and activity of crizotinib in children from age 15 years to less than 18 years of age (and adults) with relapsed/ refractory ALK-positive ALCL or other advanced malignancies known to have an ALK-genetic event (including IMT) **Study 4 (Bioavailability/taste Study – A8081069)** Open label, crossover study to evaluate palatability and relative bioavailability of two paediatric microsphere formulations of crizotinib in healthy participants **Study 5 (Bioequivalence Study)** Bioequivalence single dose cross-over study with crizotinib in adults comparing the selected age-appropriate formulation with the formulated capsule
Extrapolation, modelling and simulation studies	0	Not applicable
Other studies	2	**Study 6** A literature review summarising all available published paediatric safety and efficacy results from crizotinib in the intended indication of relapsed/refractory ALK-positive ALCL and relapsed/refractory or inoperable ALK-positive IMT **Study 7 (modified during EMEA-001493-PIP03-18-M01)** A literature review in paediatric patients with relapsed or refractory ALK-positive ALCL or with unresectable, recurrent, or refractory ALK-positive IMT, treated with other standard of care, other regimens and treatment options
Other measures	0	Not applicable

2.2. Condition:

Treatment of inflammatory myofibroblastic tumour

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with unresectable or relapsed/refractory ALK-positive IMT

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

From 12 months to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Capsule, hard

Age-appropriate oral dosage form

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	4	**Study 2 (Study ADVL0912)** Same as for condition "treatment of anaplastic large cell lymphoma" **Study 3 (Study A8081013)** Same as for condition "treatment of anaplastic large cell lymphoma" **Study 4 (Bioavailability/taste Study – A8081069)** Same as for condition "treatment of anaplastic large cell lymphoma" **Study 5 (Bioequivalence Study)** Same as for condition "treatment of anaplastic large cell lymphoma"
Extrapolation, modelling and simulation studies	0	Not applicable
Other studies	1	**Study 6** Same as for condition "treatment of anaplastic large cell lymphoma"
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 June 2022
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 lung cancer

Authorised indication(s):

As monotherapy is indicated for:

- The first-line treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC)
- The treatment of adults with previously treated ALK-positive advanced NSCLC
- The treatment of adults with ROS1-positive advanced NSCLC

Authorised pharmaceutical form(s):

Hard capsule

Authorised route(s) of administration:

Oral use