EMA/191160/2018

European Medicines Agency decision

P/0125/2018

of 11 April 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for ixazomib (Ninlaro), (EMEA-001410-PIP02-17) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

European Medicines Agency decision

P/0125/2018

of 11 April 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for ixazomib (Ninlaro), (EMEA-001410-PIP02-17) 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 application submitted by Takeda Pharm A/S on 15 May 2017 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 23 February 2018, in accordance with Article 17 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 ixazomib (Ninlaro), powder for solution for injection, capsule, hard, intravenous use, oral use, gastric 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 ixazomib (Ninlaro), powder for solution for injection, capsule, hard, intravenous use, oral use, gastric 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 ixazomib (Ninlaro), powder for solution for injection, capsule, hard, intravenous use, oral use, gastric 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 Takeda Pharm A/S, Dybendal Alle 10, 2630 – Taastrup, Denmark.

EMA/PDCO/832068/2017
London, 23 February 2018

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

EMEA-001410-PIP02-17

Scope of the application

Active substance(s):

Ixazomib

Invented name:

Ninlaro

Condition(s):

Treatment of multiple myeloma

Treatment of lymphoid malignancies (excluding multiple myeloma)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder for solution for injection

Capsule, hard

Route(s) of administration:

Intravenous use

Oral use

Gastric 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 16(1) of Regulation (EC) No 1901/2006 as amended, Takeda Pharm A/S submitted for agreement to the European Medicines Agency on 15 May 2017 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 20 June 2017.

Supplementary information was provided by the applicant on 11 December 2017. The applicant proposed modifications to the paediatric investigation plan and to the waiver.

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 17(1) 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 occurs only in adult populations.

   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 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 multiple myeloma

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- powder for solution for injection, capsule, hard, intravenous use, oral use, gastric use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subsets.

2. Paediatric investigation plan

2.1. Condition:

Treatment of lymphoid malignancies (excluding multiple myeloma)

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from birth to less than 18 years of age with a lymphoid malignancy

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder for solution for injection

Capsule, hard

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1:** Compatibility of ixazomib powder for solution for injection, oral use, gastric use, with flavouring agents or food and with naso-gastric feeding tubes. Generation of data on acceptability and palatability.
Non-clinical studies	0	Not applicable.

Area	Number of measures	Description
Clinical studies	5	**Study 2:** Uncontrolled, open label study to assess pharmacokinetics and safety of ixazomib capsules for oral use, and of powder for solution for injection, oral use and gastric use, in paediatric patients from birth to less than 18 years of age (and adults if diagnosed at less than 18 years of age) with relapsed/refractory acute lymphoblastic leukaemia or lymphoblastic lymphoma without extramedullary disease. **Study 3:** Uncontrolled, open label study to assess pharmacokinetics and safety of ixazomib powder for solution for injection, intravenous use, in paediatric patients from birth to less than 18 years of age (and adults if diagnosed at less than 18 years of age) with relapsed/refractory acute lymphoblastic leukaemia or lymphoblastic lymphoma without extramedullary disease. **Study 4:** Open-label, single arm study to assess the efficacy of the addition of ixazomib, capsules for oral use, and powder for solution for injection, oral use and gastric use, to reinduction chemotherapy in paediatric patients from birth to less than 18 years of age (and adults if diagnosed at less than 18 years of age) with relapsed/refractory (RR) acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LLy). **Study 5:** Randomised, controlled, open-label study to assess event free survival (EFS) of patients from birth to less than 18 years of age (and adults if diagnosed at less than 18 years of age) with relapsed or refractory (RR) acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LLy) treated with ixazomib in combination with vincristine, dexamethasone, L-asparaginase, and doxorubicin (VXLD) chemotherapy versus VXLD chemotherapy alone. **Study 6:** Randomized, controlled study of modified augmented Berlin-Frankfurt-Münster (ABFM) regimen with bortezomib during induction/consolidation and intensification followed by maintenance therapy with/without ixazomib in patients from birth to less than 18 years of age (and adults if diagnosed at less than 18 years of age) with newly diagnosed ALL or LLy without extramedullary disease
Extrapolation, modelling and simulation studies	0	Not applicable.

Area	Number of measures	Description
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:	No
Date of completion of the paediatric investigation plan:	By December 2031
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):

Treatment of multiple myeloma

Authorised indication:

- Ninlaro in combination with lenalidomide and dexamethasone is indicated for the treatment of adult patients with multiple myeloma who have received at least one prior therapy

Authorised pharmaceutical form(s):

Hard capsule

Authorised route(s) of administration:

Oral use