EMA/169198/2022

European Medicines Agency decision

P/0160/2022

of 13 May 2022

on the acceptance of a modification of an agreed paediatric investigation plan for eslicarbazepine acetate (Zebinix), (EMEA-000696-PIP02-10-M08) 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 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/213/2011 issued on 2 September 2011, the decision P/0058/2012 issued on 26 March 2012, the decision P/0284/2012 issued on 23 November 2012, the decision P/0197/2013 issued on 2 September 2013, the decision P/0015/2015 issued on 30 January 2015 and the decision P/0272/2019 issued on 14 August 2019,

Having regard to the application submitted by BIAL - Portela & Ca, SA on 17 December 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 25 March 2022, 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 and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[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 eslicarbazepine acetate (Zebinix), oral suspension, tablet, oral use, including changes to the deferral, 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 BIAL - Portela & Ca, SA, À Av. da Siderurgia Nacional, 4745-457 - S. Mamede do Coronado, Portugal.

EMA/PDCO/6722/2022
Amsterdam, 25 March 2022

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

EMEA-000696-PIP02-10-M08

Scope of the application

Active substance(s):

Eslicarbazepine acetate

Invented name:

Zebinix

Condition(s):

Treatment of epilepsy with partial onset seizures

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Oral suspension

Tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

BIAL - Portela & Ca, SA

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, BIAL - Portela & Ca, SA submitted to the European Medicines Agency on 17 December 2021 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's

decision P/213/2011 issued on 2 September 2011, the decision P/0058/2012 issued on 26 March 2012, the decision P/0284/2012 issued on 23 November 2012, the decision P/0197/2013 issued on 2 September 2013, the decision P/0015/2015 issued on 30 January 2015 and the decision P/0272/2019 issued on 14 August 2019.

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

The procedure started on 31 January 2022.

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 and to the deferral 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 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 epilepsy with partial onset seizures

The waiver applies to:

- all subsets of the paediatric population from birth to less than 1 month years of age;
- for oral suspension, tablet; oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition: treatment of epilepsy with partial onset seizures

2.1.1. Indication(s) targeted by the PIP

Treatment of epilepsy with partial onset seizures with eslicarbazepine acetate (ESL) as adjunctive therapy

Treatment of epilepsy with partial onset seizures with eslicarbazepine acetate (ESL) as monotherapy

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

From 1 month to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Oral suspension

Tablet

2.1.4. Studies

Area	Description
Quality	**Study 1** Development of standardised dosing device(s) for the age-appropriate oral suspension
Non-clinical	**Study 2 (WIL-682001)** Toxicity and toxicokinetic study of 28 days repeat doses of eslicarbazepine acetate (ESL) in juvenile dogs **Study 3 (WIL-682002)** 10-month oral (gavage) toxicity study of ESL in juvenile dogs with a 2-month recovery period

Clinical	**Study 4 (BIA-2093-202)** Open-label, multiple-dose study to evaluate pharmacokinetics, safety and tolerability of eslicarbazepine acetate (ESL) for partial-onset epilepsy in paediatric patients from 2 years to less than 18 years **Study 5 (BIA-2093-208)** Double blind parallel-group, randomised placebo-controlled, multicentre, 2 part study in paediatric patients with partial-onset seizures aged from 6 years to less than 16 years to evaluate efficacy and safety, including effect on cognitive function of eslicarbazepine acetate (ESL) as adjunctive therapy with an open-label extension (48 weeks) **Study 6 (BIA-2093-305)** Double-blind, randomised, placebo-controlled, parallel-group, multi-centre trial to evaluate efficacy and safety of eslicarbazepine acetate (ESL) as adjunctive therapy for refractory partial seizures in children aged 2 years to less than 18 years with a one year open-label extension phase **Study 7 (BIA-2093-211)** Open-label, 2 dose level trial to evaluate pharmacokinetics, safety and tolerability of eslicarbazepine acetate (ESL) as adjunctive therapy in infants with refractory epilepsy with partial-onset seizures aged from 1 month to less than 2 years **Study 8 - Study deleted in procedure EMEA-000696-PIP02-10-M08** **Study 9 - Study deleted in procedure EMEA-000696-PIP02-10-M08** **Study 10 (BIA-2093-313)** Double-blind, randomised, parallel-group, multicenter study to evaluate efficacy and safety of eslicarbazepine acetate (ESL) as monotherapy for children aged from 4 years to less than 18 years with newly diagnosed partial-onset seizures **Study 11 (BIA-2093-314)** Open-label, multicentre study to evaluate tolerability and safety of eslicarbazepine acetate (ESL) as monotherapy for young children aged from 1 month to 4 years with newly diagnosed partial-onset seizures **Study 12 (BIA-2093-212)** Double blind study in children with epilepsy aged from 5 years to less than 8 years to compare the subject preference for eslicarbazepine acetate (ESL) oral suspension formulation with alternative flavours

	Study 13 (BIA-2093-211/EXT) - added in procedure EMEA-000696-PIP02-10-M08 Open-label, uncontrolled study to evaluate safety and tolerability of eslicarbazepine acetate (ESL) as adjunctive therapy in infants with refractory epilepsy with partial-onset seizures aged from 1 month to less than 2 years (extension of Study 7, BIA-2093-211).
Modelling and Simulation	**Study 14 - added in procedure EMEA-000696-PIP02-10-M08 (018041)** A physiologically based pharmacokinetic study to support dose selection of eslicarbazepine acetate (ESL) for children with partial-onset seizures aged 1 month to less than 24 months
Extrapolation	**Study 15 - added in procedure EMEA-000696-PIP02-10-M08 (PH20057)** Predictive population pharmacokinetic (PK) study of eslicarbazepine acetate (ESL) in monotherapy treatment in children with newly diagnosed partial-onset epilepsy from 4 years to less than 18 years of age.
Other Studies	Not applicable
Other Measures	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2026
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

Treatment of epilepsy with partial onset seizures

Authorised indication(s):

- monotherapy in the treatment of partial-onset seizures, with or without secondary generalisation, in adults with newly diagnosed epilepsy;
- adjunctive therapy in adults, adolescents and children aged above 6 years, with partial-onset seizures with or without secondary generalisation.

Authorised pharmaceutical form(s):

Oral suspension

Tablet

Authorised route(s) of administration:

Oral use