EMA/644037/2011

European Medicines Agency decision

P/213/2011

of 2 September 2011

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for eslicarbazepine (acetate) (Zebinix, Exalief) (EMEA-000696-PIP02-10) 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 application submitted by BIAL - Portela & Ca, SA on 15 November 2010 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 15 July 2011, in accordance with Article 18 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 eslicarbazepine (acetate) (Zebinix, Exalief), oral suspension, tablet, oral 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 eslicarbazepine (acetate) (Zebinix, Exalief), oral suspension, tablet, oral 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 eslicarbazepine (acetate) (Zebinix, Exalief), oral suspension, tablet, oral 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 BIAL - Portela & Ca, SA, À Av. da Siderurgia Nacional, 4745-457 - S. Mamede do Coronado, Portugal.

Done at London, 2 September 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)

EMA/644037/2011

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

EMEA-000696-PIP02-10

Scope of the application

Active substance(s):

Eslicarbazepine (acetate)

Invented name:

Zebinix, Exalief

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

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Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, BIAL - Portela & Ca, SA submitted for agreement to the European Medicines Agency on 15 November 2010 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 22 December 2010.

Supplementary information was provided by the applicant on 29 April 2011. The applicant proposed modifications to the paediatric investigation plan.

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 18 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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   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 annex(es) and appendix.

London, 15 July 2011

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman
(Signature on file)

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

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 ineffective.
- 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	Number of studies	Description
Quality	1	**Study 1** Provision of the final qualitative and quantitative contents of the oral suspension of eslicarbazepine acetate (ESL).
Non-clinical	2	**Study 2** Toxicity and toxicokinetic study of 28 days repeat doses of eslicarbazepine acetate (ESL) in juvenile dogs. **Study 3** 12 months repeat oral dose toxicity and toxicokinetic study of eslicarbazepine acetate (ESL) in juvenile Beagle dogs.
Clinical	7	**Study 4** 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** 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).

Area	Number of studies	Description
		Study 6 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** 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** Double-blind, randomised, placebo-controlled, parallel-group, multicentre clinical trial to evaluate efficacy and safety of eslicarbazepine acetate (ESL) as adjunctive therapy for refractory partial seizures in children aged from 7 months to less than 24 months with a one year open-label extension phase. **Study 9** Double-blind, randomised, placebo-controlled, parallel-group, multicentre clinical trial to evaluate safety and tolerability of eslicarbazepine acetate (ESL) as adjunctive therapy for refractory partial seizures in children aged from 1 month to less than 7 months with a one year open-label extension phase. **Study 10** 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** Open-label, multicentre study to evaluate tolerability and safety of eslicarbazepine acetate (ESL) as monotherapy for young children 1 month to 4 years with newly diagnosed partial-onset seizures. **Study 12** Double blind study in paediatric epileptic subjects aged from 5 years to less than 8 years to compare the subject preference for eslicarbazepine acetate (ESL) oral suspension formulation with alternative flavours.

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 December 2018
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 indications:

Exalief is indicated as adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation.

Zebinix is indicated as adjunctive therapy in adults with partial-onset seizures with or without secondary generalisations.

EU Number	(Invented) name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Package size
EU/1/09/520/001	Exalief	400 mg	Tablet	Oral use	blister (alu/alu)	7 tablets
EU/1/09/520/002	Exalief	400 mg	Tablet	Oral use	blister (alu/alu)	14 tablets
EU/1/09/520/003	Exalief	400 mg	Tablet	Oral use	blister (alu/alu)	28 tablets
EU/1/09/520/004	Exalief	400 mg	Tablet	Oral use	blister (PVC/alu)	7 tablets
EU/1/09/520/005	Exalief	400 mg	Tablet	Oral use	blister (PVC/alu)	14 tablets
EU/1/09/520/006	Exalief	400 mg	Tablet	Oral use	blister (PVC/alu)	28 tablets
EU/1/09/520/007	Exalief	600 mg	Tablet	Oral use	blister (alu/alu)	30 tablets
EU/1/09/520/008	Exalief	600 mg	Tablet	Oral use	blister (alu/alu)	60 tablets
EU/1/09/520/009	Exalief	600 mg	Tablet	Oral use	blister (PVC/alu)	30 tablets
EU/1/09/520/010	Exalief	600 mg	Tablet	Oral use	blister (PVC/alu)	60 tablets
EU/1/09/520/011	Exalief	600 mg	Tablet	Oral use	bottle (HDPE)	90 tablets
EU/1/09/520/012	Exalief	800 mg	Tablet	Oral use	blister (alu/alu)	20 tablets
EU/1/09/520/013	Exalief	800 mg	Tablet	Oral use	blister (alu/alu)	30 tablets
EU/1/09/520/014	Exalief	800 mg	Tablet	Oral use	blister (alu/alu)	60 tablets
EU/1/09/520/015	Exalief	800 mg	Tablet	Oral use	blister (alu/alu)	90 tablets
EU/1/09/520/016	Exalief	800 mg	Tablet	Oral use	blister (PVC/alu)	20 tablets
EU/1/09/520/017	Exalief	800 mg	Tablet	Oral use	blister (PVC/alu)	30 tablets
EU/1/09/520/018	Exalief	800 mg	Tablet	Oral use	blister (PVC/alu)	60 tablets
EU/1/09/520/019	Exalief	800 mg	Tablet	Oral use	blister (PVC/alu)	90 tablets
EU/1/09/520/020	Exalief	800 mg	Tablet	Oral use	bottle (HDPE)	90 tablets

EU Number	(Invented) name	Strength	Pharma-Ceutical Form	Route of Administration	Packaging	Package size
EU/1/09/514/001	Zebinix	400 mg	Tablet	Oral use	blister (alu/alu)	7 tablets
EU/1/09/514/002	Zebinix	400 mg	Tablet	Oral use	blister (alu/alu)	14 tablets
EU/1/09/514/003	Zebinix	400 mg	Tablet	Oral use	blister (alu/alu)	28 tablets
EU/1/09/514/004	Zebinix	400 mg	Tablet	Oral use	blister (PVC/alu)	7 tablets
EU/1/09/514/005	Zebinix	400 mg	Tablet	Oral use	blister (PVC/alu)	14 tablets
EU/1/09/514/006	Zebinix	400 mg	Tablet	Oral use	blister (PVC/alu)	28 tablets
EU/1/09/514/007	Zebinix	600 mg	Tablet	Oral use	blister (alu/alu)	30 tablets
EU/1/09/514/008	Zebinix	600 mg	Tablet	Oral use	blister (alu/alu)	60 tablets

EU/1/09/514/009	Zebinix	600 mg	Tablet	Oral use	blister (PVC/alu)	30 tablets
EU/1/09/514/010	Zebinix	600 mg	Tablet	Oral use	blister (PVC/alu)	60 tablets
EU/1/09/514/011	Zebinix	600 mg	Tablet	Oral use	bottle (HDPE)	90 tablets
EU/1/09/514/012	Zebinix	800 mg	Tablet	Oral use	blister (alu/alu)	20 tablets
EU/1/09/514/013	Zebinix	800 mg	Tablet	Oral use	blister (alu/alu)	30 tablets
EU/1/09/514/014	Zebinix	800 mg	Tablet	Oral use	blister (alu/alu)	60 tablets
EU/1/09/514/015	Zebinix	800 mg	Tablet	Oral use	blister (alu/alu)	90 tablets
EU/1/09/514/016	Zebinix	800 mg	Tablet	Oral use	blister (PVC/alu)	20 tablets
EU/1/09/514/017	Zebinix	800 mg	Tablet	Oral use	blister (PVC/alu)	30 tablets
EU/1/09/514/018	Zebinix	800 mg	Tablet	Oral use	blister (PVC/alu)	60 tablets
EU/1/09/514/019	Zebinix	800 mg	Tablet	Oral use	blister (PVC/alu)	90 tablets
EU/1/09/514/020	Zebinix	800 mg	Tablet	Oral use	bottle (HDPE)	90 tablets