EMA/646932/2012

European Medicines Agency decision

P/0256/2012

of 26 October 2012

on the acceptance of a modification of an agreed paediatric investigation plan for aripiprazole (Abilify), (EMEA-000235-PIP02-10-M02) 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 aripiprazole (Abilify), (EMEA-000235-PIP02-10-M02) 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 European Medicines Agency's decision P/99/2011 issued on 14 April 2011, and the decision P/0136/2012 issued on 20 July 2012,

Having regard to the application submitted by Otsuka Pharmaceutical Europe Ltd. on 13 July 2012 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 5 October 2012, 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 aripiprazole (Abilify), tablets, orodispersible tablets, oral solution, solution for injection, powder for suspension for injection, oral use, intramuscular 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 Otsuka Pharmaceutical Europe Ltd., Hunton House Highbridge Business Park, Oxford Road, UB8 1HU – Uxbridge, United Kingdom.

Done at London, 26 October 2012

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/486091/2012

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

EMEA-000235-PIP02-10-M02

Scope of the application

Active substance(s):

Aripiprazole

Invented name:

Abilify

Condition(s):

Treatment of bipolar affective disorder

Treatment of schizophrenia

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablets

Orodispersible tablets

Oral solution

Solution for injection

Powder for suspension for injection

Route(s) of administration:

Oral use

Intramuscular use

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Name/corporate name of the PIP applicant:

Otsuka Pharmaceutical Europe Ltd.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Otsuka Pharmaceutical Europe Ltd. submitted to the European Medicines Agency on 13 July 2012 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/99/2011 issued on 14 April 2011, and the decision P/0136/2012 issued on 20 July 2012.

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

The procedure started on 9 August 2012.

Scope of the modification

Some measures and timelines of one study 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 annex(es) and appendix.

London, 5 October 2012

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 bipolar affective disorder

The waiver applies to:

- Subsets of the paediatric population from birth to less than 10 years of age;
- for tablets, orodispersible tablets and oral solution for oral use;
- for solution for injection and powder for suspension for injection for intramuscular 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).

The waiver applies to:

- Subsets of the paediatric population from 10 to less than 18 years of age;
- for solution for injection and powder for suspension for injection for intramuscular use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

1.2. Condition: Treatment of schizophrenia

The waiver applies to:

- Subsets of the paediatric population from birth to less than 13 years of age;
- for tablets, orodispersible tablets and oral solution for oral use;
- for solution for injection and powder for suspension for injection for intramuscular 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).

The waiver applies to:

- Subsets of the paediatric population from 13 to less than 18 years of age;
- for solution for injection and powder for suspension for injection for intramuscular use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of bipolar affective disorder

2.1.1. Indication(s) targeted by the PIP

Treatment of moderate to severe manic episodes in bipolar I disorder.

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

From 10 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Tablets, orodispersible tablets and oral solution for oral use.

2.1.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	1	**Study 1:** An open-label, multicentre trial to evaluate the safety and tolerability of flexible-dose oral aripiprazole as maintenance treatment in paediatric patients from 10 to less than 18 years of age with bipolar I disorder or with schizophrenia (31-09-267).

2.2. Condition: Treatment of schizophrenia

2.2.1. Indication(s) targeted by the PIP

Treatment of schizophrenia.

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

From 13 to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Tablets, orodispersible tablets and oral solution for oral use.

2.2.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.

Area	Number of studies	Description
Clinical	2	**Study 2:** A double-blind, randomised, multicentre placebo-controlled study to evaluate the long-term efficacy, safety and tolerability of aripiprazole as maintenance treatment in adolescents from 13 to less than 18 years of age with schizophrenia (31-09-266). **Study 3:** An open-label, multicentre trial to evaluate the safety and tolerability of flexible-dose oral aripiprazole as maintenance treatment in paediatric patients from 10 to less than 18 years of age with bipolar I disorder or with schizophrenia (31-09-267) (same as Study 1 specified for the treatment of bipolar I disorder).

3. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By April 2016
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):

1. Treatment of bipolar I disorder

Authorised indications:

- Abilify is indicated for the treatment of moderate to severe manic episodes in Bipolar I Disorder and for the prevention of a new manic episode in patients who experienced predominantly manic episodes and whose manic episodes responded to aripiprazole treatment.
- Abilify solution for injection is indicated for the rapid control of agitation and disturbed behaviours in patients with schizophrenia or in patients with manic episodes in Bipolar I Disorder, when oral therapy is not appropriate. Treatment with aripiprazole solution for injection should be discontinued as soon as clinically appropriate and the use of oral aripiprazole should be initiated.

2. Treatment of schizophrenia

Authorised indications:

- Abilify is indicated for the treatment of schizophrenia in adults and in adolescents 15 years and older.

EU Number	Invented name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/04/276/001	Abilify	5 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	14 x 1
EU/1/04/276/002	Abilify	5 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	28 x 1
EU/1/04/276/003	Abilify	5 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	49 x 1
EU/1/04/276/004	Abilify	5 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	56 x 1
EU/1/04/276/005	Abilify	5 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	98 x 1
EU/1/04/276/006	Abilify	10 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	14 x 1
EU/1/04/276/007	Abilify	10 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	28 x 1

EU Number	Invented name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/04/276/008	Abilify	10 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	49 x 1
EU/1/04/276/009	Abilify	10 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	56 x 1
EU/1/04/276/010	Abilify	10 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	98 x 1
EU/1/04/276/011	Abilify	15 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	14 x 1
EU/1/04/276/012	Abilify	15 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	28 x 1
EU/1/04/276/013	Abilify	15 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	49 x 1
EU/1/04/276/014	Abilify	15 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	56 x 1
EU/1/04/276/015	Abilify	15 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	98 x 1
EU/1/04/276/016	Abilify	30 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	14 x 1
EU/1/04/276/017	Abilify	30 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	28 x 1
EU/1/04/276/018	Abilify	30 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	49 x 1

EU Number	Invented name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/04/276/019	Abilify	30 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	56 x 1
EU/1/04/276/020	Abilify	30 mg	Tablet	Oral use	unit dose perforated blister (alu/alu)	98 x 1
EU/1/04/276/024	Abilify	10 mg	Orodispersible tablet	Oral use	unit dose perforated blister (alu/alu)	14 x 1
EU/1/04/276/025	Abilify	10 mg	Orodispersible tablet	Oral use	unit dose perforated blister (alu/alu)	28 x 1
EU/1/04/276/026	Abilify	10 mg	Orodispersible tablet	Oral use	unit dose perforated blister (alu/alu)	49 x 1
EU/1/04/276/027	Abilify	15 mg	Orodispersible tablet	Oral use	unit dose perforated blister (alu/alu)	14 x 1
EU/1/04/276/028	Abilify	15 mg	Orodispersible tablet	Oral use	unit dose perforated blister (alu/alu)	28 x 1
EU/1/04/276/029	Abilify	15 mg	Orodispersible tablet	Oral use	unit dose perforated blister (alu/alu)	49 x 1
EU/1/04/276/030	Abilify	30 mg	Orodispersible tablet	Oral use	unit dose perforated blister (alu/alu)	14 x 1
EU/1/04/276/031	Abilify	30 mg	Orodispersible tablet	Oral use	unit dose perforated blister (alu/alu)	28 x 1
EU/1/04/276/032	Abilify	30 mg	Orodispersible tablet	Oral use	unit dose perforated blister (alu/alu)	49 x 1

EU Number	Invented name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/04/276/033	Abilify	1 mg/ml	Oral solution	Oral use	bottle (PET)	1 bottle + 1 cup + 1 calibrated dropper
EU/1/04/276/034	Abilify	1 mg/ml	Oral solution	Oral use	bottle (PET)	1 bottle + 1 cup + 1 calibrated dropper
EU/1/04/276/035	Abilify	1 mg/ml	Oral solution	Oral use	bottle (PET)	1 bottle + 1 cup + 1 calibrated dropper
EU/1/04/276/036	Abilify	7.5 mg/ml	Solution for injection	Intramuscular use	vial (glass)	1 vial