EMA/409344/2012

European Medicines Agency decision

P/0112/2012

of 22 June 2012

on the acceptance of a modification of an agreed paediatric investigation plan for voriconazole (Vfend), (EMEA-000191-PIP01-08-M04) 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 voriconazole (Vfend), (EMEA-000191-PIP01-08-M04) 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/42/2010 issued on 31 March 2010, the decision P/198/2010 issued on 27 October 2010 and the decision P/74/2011 issued on 5 April 2011.

Having regard to the application submitted by Pfizer Limited on 26 March 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 8 June 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 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for voriconazole (Vfend), film-coated tablets, powder for oral suspension, powder for solution for infusion, oral use, intravenous 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 Pfizer Limited, Ramsgate Road, Sandwich, CT13 9NJ, United Kingdom.

Done at London, 22 June 2012

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

EMA/PDCO/220617/2012

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

EMEA-000191-PIP01-08-M04

Scope of the application

Active substance(s):

Voriconazole

Invented name:

Vfend

Condition(s):

Treatment of invasive aspergillosis

Treatment of candidaemia in non-neutropenic patients

Treatment of fluconazole-resistant serious invasive candida infections (including C. krusei)

Treatment of serious fungal infections caused by Scedosporium spp. and Fusarium spp.

Prevention of invasive fungal infections

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablets

Powder for oral suspension

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Oral use

Name/corporate name of the PIP applicant:

Pfizer Limited

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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 Limited submitted to the European Medicines Agency on 26 March 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/42/2010 issued on 31 March 2010, the decision P/198/2010 issued on 27 October 2010 and the decision P/74/2011 issued on 5 April 2011.

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

The procedure started on 16 April 2012.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. Amendment of the scope of the Paediatric Investigation Plan to include another condition.

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 Icelandic and the Norwegian Paediatric Committee members agree 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.

London, 8 June 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 invasive aspergillosis

The waiver applies to:

- The paediatric population from birth to less than 24 months of age on the grounds that the specific medicinal product is likely to be unsafe;
- for
  - film-coated tablets, oral use,
  - powder for oral suspension, oral use,
  - powder for solution for infusion, intravenous use.

1.2. Condition: treatment of candidaemia in non-neutropenic patients

The waiver applies to:

- the paediatric population from birth to less than 24 months of age on the grounds that the specific medicinal product is likely to be unsafe;
- the paediatric population from 2 years to less than 18 years on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered;
- for
  - film-coated tablets, oral use,
  - powder for oral suspension, oral use,
  - powder for solution for infusion, intravenous use.

1.3. Condition: treatment of Fluconazole-resistant serious invasive Candida infections (including C. krusei)

The waiver applies to:

- the paediatric population from birth to less than 24 months of age on the grounds that the specific medicinal product is likely to be unsafe;
- the paediatric population from 2 years to less than 18 years on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered;
- for
  - film-coated tablets, oral use,
  - powder for oral suspension, oral use,
  - powder for solution for infusion, intravenous use.

1.4. Condition: treatment of serious fungal infections caused by Scedosporium spp. and Fusarium spp.

The waiver applies to:

- the paediatric population from birth to less than 24 months of age on the grounds that the specific medicinal product is likely to be unsafe;
- the paediatric population from 2 years to less than 18 years on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered;
- for
  - film-coated tablets, oral use,
  - powder for oral suspension, oral use,
  - powder for solution for infusion, intravenous use.

1.5. Condition: prevention of invasive fungal infections

The waiver applies to:

- the paediatric population from birth to less than 24 months of age on the grounds that the specific medicinal product is likely to be unsafe;
- for
  - film-coated tablets, oral use,
  - powder for oral suspension, oral use,
  - powder for solution for infusion, intravenous use.

2. Paediatric Investigation Plan

2.1. Condition to be investigated:

Invasive aspergillosis.

2.1.1. Indication targeted by the PIP

Voriconazole in combination with anidulafungin for the treatment of invasive aspergillosis in children from 2 to less than 18 years and (in adults).

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

From 2 years to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

- Film-coated tablets
- Powder for Oral Suspension
- Powder for Solution for Infusion

2.1.4. Studies

Area	Number of studies	Description
Quality		Not applicable
Non-clinical	1	1. 5 week single compound and combination toxicology study in juvenile rats with a 4 week recovery period.
Clinical	5	2. Open-label, intravenous to oral switch, multiple dose study to evaluate the pharmacokinetics, safety and tolerability of voriconazole in immunocompromised adolescents aged 12 years to less than 17 years who are at high risk for systemic infection. 3. Open-label, intravenous to oral switch, multiple dose study to evaluate the pharmacokinetics, safety and tolerability of voriconazole in immunocompromised children aged 2 years to less than 12 years who are at high risk for systemic infection. 4. Open label, non-comparative, multi-centre trial to investigate the safety, tolerability, and efficacy of voriconazole monotherapy as treatment of invasive aspergillosis and rare mold infections such as Scedosporium or Fusarium species in paediatric patients 2 years to less than 18 years of age. 5. Open-label, non-comparative study of voriconazole for the treatment of paediatric patients 2 years to less than 18 years of age with invasive candidiasis, including candidaemia, and oesophageal candidiasis. 6. Randomized, multi-centre trial to assess the safety, tolerability, and efficacy of voriconazole plus anidulafungin in combination to that of voriconazole monotherapy for treatment of invasive aspergillosis in patients 2 years to less than 18 years of age.

2.2. Condition to be investigated:

Prevention of invasive fungal infections

2.2.1. Indication targeted by the PIP

Prophylaxis in paediatric (and in adults) patients patients who are at high risk of developing invasive fungal infections, such as haematopoietic stem cell transplant (HSCT) recipients

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

From 2 years to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

- Film-coated tablets
- Powder for Oral Suspension
- Powder for Solution for Infusion

2.2.4. Studies

Area	Number of studies	Description
Quality		Not applicable
Non-clinical		Not applicable
Clinical	6	7. Open-label, multiple intravenous dose, multi-centre study to investigate the pharmacokinetics, safety and toleration of voriconazole in children aged 2 to less than 12 years who required treatment for the prevention of systemic fungal infection (A1501007) 8. Open-label, multi-centre study to investigate the pharmacokinetics, safety and tolerability of increasing intravenous doses and following a switch to oral voriconazole in immunocompromised subjects aged 2 to < 12 years who required treatment for the prevention of systemic fungal infection (A1501037) 9. Open-label, intravenous to oral switch, multiple dose study to evaluate the pharmacokinetics, safety and tolerability of voriconazole in immunocompromised adolescents aged 12 to <17 years who are at high risk for systemic fungal infection (A1501081) 10. Open-label, intravenous to oral switch, multiple dose study to evaluate the pharmacokinetics, safety and tolerability of voriconazole in immunocompromised children aged 2 to <12 years who are at high risk for systemic fungal infection (A1501088) 11. Population Pharmacokinetic Analysis of Voriconazole in Children, Adolescents and Adults based on the results of the 4 above mentioned studies A1501037, A1501007, A1501081, and A1501088 12. Extrapolation of the efficacy and safety data from the adults studies A1501038 and A1501073, to the subset of patients 24 months to less than 18 years of age.

3. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By September 2012
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 invasive aspergillosis.

Treatment of candidemia in non-neutropenic patients.

Treatment of fluconazole-resistant serious invasive *Candida* infections (including *C. krusei*).

Treatment of serious fungal infections caused by *Scedosporium* spp. and *Fusarium* spp.

Authorised indications:

Treatment of invasive aspergillosis.

Treatment of candidemia in non-neutropenic patients.

Treatment of fluconazole-resistant serious invasive Candida infections (including C. krusei).

Treatment of serious fungal infections caused by Scedosporium spp. and Fusarium spp.

VFEND should be administered primarily to patients with progressive, possibly life-threatening infections.

EU Number	Invented name	Strength	Pharmaceutical form	Route of administration	Packaging	Content	Package size
EU/1/02/212/001	Vfend	50 mg	Tablet	Oral use	blister (PVC/alu)		2 tablets
EU/1/02/212/002	Vfend	50 mg	Tablet	Oral use	blister (PVC/alu)		10 tablets
EU/1/02/212/003	Vfend	50 mg	Tablet	Oral use	blister (PVC/alu)		14 tablets
EU/1/02/212/004	Vfend	50 mg	Tablet	Oral use	blister (PVC/alu)		20 tablets
EU/1/02/212/005	Vfend	50 mg	Tablet	Oral use	blister (PVC/alu)		28 tablets
EU/1/02/212/006	Vfend	50 mg	Tablet	Oral use	blister (PVC/alu)		30 tablets
EU/1/02/212/007	Vfend	50 mg	Tablet	Oral use	blister (PVC/alu)		50 tablets
EU/1/02/212/008	Vfend	50 mg	Tablet	Oral use	blister (PVC/alu)		56 tablets
EU/1/02/212/009	Vfend	50 mg	Tablet	Oral use	blister (PVC/alu)		100 tablets
EU/1/02/212/010	Vfend	50 mg	Tablet	Oral use	bottle (HDPE)		2 tablets
EU/1/02/212/011	Vfend	50 mg	Tablet	Oral use	bottle (HDPE)		30 tablets
EU/1/02/212/012	Vfend	50 mg	Tablet	Oral use	bottle (HDPE)		100 tablets
EU/1/02/212/013	Vfend	200 mg	Tablet	Oral use	blister (PVC/alu)		2 tablets
EU/1/02/212/014	Vfend	200 mg	Tablet	Oral use	blister (PVC/alu)		10 tablets
EU/1/02/212/015	Vfend	200 mg	Tablet	Oral use	blister (PVC/alu)		14 tablets
EU/1/02/212/016	Vfend	200 mg	Tablet	Oral use	blister (PVC/alu)		20 tablets
EU/1/02/212/017	Vfend	200 mg	Tablet	Oral use	blister (PVC/alu)		28 tablets
EU/1/02/212/018	Vfend	200 mg	Tablet	Oral use	blister (PVC/alu)		30 tablets
EU/1/02/212/019	Vfend	200 mg	Tablet	Oral use	blister (PVC/alu)		50 tablets
EU/1/02/212/020	Vfend	200 mg	Tablet	Oral use	blister (PVC/alu)		56 tablets
EU/1/02/212/021	Vfend	200 mg	Tablet	Oral use	blister (PVC/alu)		100 tablets

EU/1/02/212/022	Vfend	200 mg	Tablet	Oral use	bottle (HDPE)		2 tablets
EU/1/02/212/023	Vfend	200 mg	Tablet	Oral use	bottle (HDPE)		30 tablets
EU/1/02/212/024	Vfend	200 mg	Tablet	Oral use	bottle (HDPE)		100 tablets
EU/1/02/212/025	Vfend	200 mg	Powder for solution for infusion	Intravenous use	vial (glass)	10 mg/ml	1 vial
EU/1/02/212/026	Vfend	40 mg/ml	Powder for oral suspension	Oral use	bottle (HDPE)	45 g	1 bottle