EMA/764025/2011

European Medicines Agency decision

P/241/2011

of 29 September 2011

on the acceptance of a modification of an agreed paediatric investigation plan for etanercept (Enbrel) (EMEA-000299-PIP01-08-M03) 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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8409
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

European Medicines Agency decision

P/241/2011

of 29 September 2011

on the acceptance of a modification of an agreed paediatric investigation plan for etanercept (Enbrel) (EMEA-000299-PIP01-08-M03) 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/106/2009 issued on 16 June 2009, the decision P/113/2010 issued on 7 July 2010 and the decision P/236/2010 issued on 26 November 2010,

Having regard to the application submitted by Pfizer Limited on 4 July 2011 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 9 September 2011, 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 waiver.

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

Changes to the agreed paediatric investigation plan for etanercept (Enbrel), powder and solvent for solution for injection, powder for solution for injection, solution for injection, subcutaneous use, including changes to the waiver, 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 Kent, United Kingdom.

Done at London, 29 September 2011

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

EMA/PDCO/530631/2011

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

EMEA-000299-PIP01-08-M03

Scope of the application

Active substance(s):

Etanercept

Invented name:

Enbrel

Condition(s):

Treatment of plaque psoriasis

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder and solvent for solution for injection

Powder for solution for injection

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Pfizer Limited

Information about the authorised medicinal product:

See Annex II

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Wyeth Europa Limited submitted to the European Medicines Agency on 4 July 2011 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/106/2009 issued on 16 June 2009, the decision P/113/2010 issued on 07 July 2010, and the decision P/236/2010 issued on 26 November 2010.

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

The procedure started on 13 July 2011.

Scope of the modification

Some measures 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 waiver 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, 9 September 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 plaque psoriasis

The waiver applies to powder and solvent for solution for injection, powder for solution for injection, and solution for injection; for subcutaneous use to:

- children from birth to less than 6 years on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments

1.2. Condition: Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis)

The waiver applies to powder and solvent for solution for injection, powder for solution for injection and solution for injection; for subcutaneous use to:

- children from birth to less than 2 years on the grounds that measures would not be justified by expected therapeutic benefit as clinical trials are not feasible

2. Paediatric Investigation Plan

2.1. Condition: Treatment of plaque psoriasis

2.1.1. Indication(s) targeted by the PIP

Treatment of plaque psoriasis

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

From 6 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder and solvent for solution for injection

Powder for solution for injection

Solution for injection

2.1.4. Studies

Area	Number of studies	Description
Quality	1	Powder and solvent for solution for injection 10mg vial.
Non-clinical	0	Not applicable.
Clinical	1	Multicentre, open-label extension study to evaluate safety and efficacy in children from 4 to less than 18 years (age range determined before the PDCO review).

2.2. Condition: Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis)

2.2.1. Indication targeted by the PIP

Treatment of extended oligoarticular juvenile idiopathic arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis and enthesitis related arthritis.

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

- from 2 to less than 18 years

2.2.3. Pharmaceutical form(s)

Powder and solvent for solution for injection

Powder for solution for injection

Solution for injection

2.2.4. Studies

Area	Number of studies	Description
Quality	1	Powder and solvent for solution for injection 10mg vial.
Non-clinical	0	Not applicable.
Clinical	3	Open-label nonrandomised multicentre registry study of children with polyarticular course or systemic onset JIA from 1 year to less than 18 years for evaluation of long-term safety of etanercept compared to patients receiving methotrexate (Study 20021626). Open-label multicentre extension study for evaluation of long-term efficacy and safety in patients with RA and JIA involved in previous studies (Study 20021618). Single-treatment open-label multicentre study of patients with oligoarticular JIA from 2 years to less than 18 years and psoriatic arthritis or enthesitis related arthritis from 12 to less than 18 years to evaluate efficacy and safety of etanercept in comparison with historical control cohort of placebo treated patients (Study 0881A1-3338-WW).

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 October 2011
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 chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis)

Enbrel in combination with methotrexate is indicated for the treatment of moderate to severe active rheumatoid arthritis in adults when the response to disease-modifying antirheumatic drugs, including methotrexate (unless contraindicated), has been inadequate.

Enbrel can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.

Enbrel is also indicated in the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with methotrexate.

Enbrel, alone or in combination with methotrexate, has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function.

Treatment of active polyarticular juvenile idiopathic arthritis in children and adolescents from the age of 4 years who have had an inadequate response to, or who have proved intolerant of, methotrexate. Enbrel has not been studied in children aged less than 4 years.

Treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying antirheumatic drug therapy has been inadequate. Enbrel has been shown to improve physical function in patients with psoriatic arthritis, and to reduce the rate of progression of peripheral joint damage as measured by X ray in patients with polyarticular symmetrical subtypes of the disease.

Treatment of adults with severe active ankylosing spondylitis who have had an inadequate response to conventional therapy.

Treatment of plaque psoriasis

Treatment of adults with moderate to severe plaque psoriasis who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapy, including ciclosporin, methotrexate or psoralen and ultraviolet-A light (PUVA) (see section 5.1).

Treatment of chronic severe plaque psoriasis in children and adolescents from the age of 8 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.

EU Number	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of Administration**	**Packaging**	**Content**	**Package size**
EU/1/99/126/001	Enbrel	25 mg	Powder and solvent for solution for injection	Subcutaneous use	powder: vial (glass); solvent: syringe (glass)	solvent: 1 ml (25 mg/ml)	4 vials + 4 pre-filled syringes + 8 swabs

EU/1/99/126/002	Enbrel	25 mg	Powder for solution for injection	Subcutaneous use	powder: vial (glass)		4 vials + 8 swabs
EU/1/99/126/003	Enbrel	25 mg	Powder and solvent for solution for injection	Subcutaneous use	powder: vial (glass); solvent: syringe (glass)	solvent: 1 ml (25 mg/ml)	4 vials + 4 pre-filled syringes + 4 needles + 4 vial adaptors + 8 swabs
EU/1/99/126/004	Enbrel	25 mg	Powder and solvent for solution for injection	Subcutaneous use	powder: vial (glass); solvent: syringe (glass)	solvent: 1 ml (25 mg/ml)	8 vials + 8 pre-filled syringes + 8 needles + 8 vial adaptors + 16 swabs
EU/1/99/126/005	Enbrel	25 mg	Powder and solvent for solution for injection	Subcutaneous use	powder: vial (glass); solvent: syringe (glass)	solvent: 1 ml (25 mg/ml)	24 vials + 24 pre-filled syringes + 24 needles + 24 vial adaptors + 48 swabs

EU/1/99/126/006	Enbrel	50 mg	Powder for solution for injection	Subcutaneous use	powder: vial (glass)		2 vials + 4 swabs
EU/1/99/126/007	Enbrel	50 mg	Powder for solution for injection	Subcutaneous use	powder: vial (glass)		4 vials + 8 swabs
EU/1/99/126/008	Enbrel	50 mg	Powder for solution for injection	Subcutaneous use	powder: vial (glass)		12 vials + 24 swabs
EU/1/99/126/009	Enbrel	50 mg	Powder and solvent for solution for injection	Subcutaneous use	powder: vial (glass); solvent: syringe (glass)	solvent: 1 ml (50 mg/ml)	2 vials + 2 pre-filled syringes + 2 needles + 2 vial adaptors + 4 swabs
EU/1/99/126/010	Enbrel	50 mg	Powder and solvent for solution for injection	Subcutaneous use	powder: vial (glass); solvent: syringe (glass)	solvent: 1 ml (50 mg/ml)	4 vials + 4 pre-filled syringes + 4 needles + 4 vial adaptors + 8 swabs

EU/1/99/126/011	Enbrel	50 mg	Powder and solvent for solution for injection	Subcutaneous use	powder: vial (glass); solvent: syringe (glass)	solvent: 1 ml (50 mg/ml)	12 vials + 12 pre-filled syringes + 12 needles + 12 vial adaptors + 24 swabs
EU/1/99/126/012	Enbrel	25 mg	powder and solvent for solution for injection for paediatric use	Subcutaneous use	powder: vial (glass); solvent: syringe (glass)	solvent: 1 ml (25 mg/ml)	4 vials + 4 pre-filled syringes + 8 empty syringes + 20 needles + 24 alcohol swabs
EU/1/99/126/013	Enbrel	25 mg	Solution for injection in a pre-filled syringe	Subcutaneous use	syringe (glass)	0.5 ml (50 mg/ml)	4 pre-filled syringes + 8 alcohol swabs
EU/1/99/126/014	Enbrel	25 mg	Solution for injection in a pre-filled syringe	Subcutaneous use	syringe (glass)	0.5 ml (50 mg/ml)	8 pre-filled syringes + 16 alcohol swabs
EU/1/99/126/015	Enbrel	25 mg	Solution for injection in a pre-filled syringe	Subcutaneous use	syringe (glass)	0.5 ml (50 mg/ml)	24 pre-filled syringes + 48 alcohol swabs

EU/1/99/126/016	Enbrel	50 mg	Solution for injection in a pre-filled syringe	Subcutaneous use	syringe (glass)	1 ml (50 mg/ml)	2 pre-filled syringes + 4 alcohol swabs
EU/1/99/126/017	Enbrel	50 mg	Solution for injection in a pre-filled syringe	Subcutaneous use	syringe (glass)	1 ml (50 mg/ml)	4 pre-filled syringes + 8 alcohol swabs
EU/1/99/126/018	Enbrel	50 mg	Solution for injection in a pre-filled syringe	Subcutaneous use	syringe (glass)	1 ml (50 mg/ml)	12 pre-filled syringes + 24 alcohol swabs
EU/1/99/126/019	Enbrel	50 mg	Solution for injection in a pre-filled pen	Subcutaneous use	Pre-filled pen	1 ml (50 mg/ml)	2 pre-filled pens + 4 alcohol swabs
EU/1/99/126/020	Enbrel	50 mg	Solution for injection in a pre-filled pen	Subcutaneous use	Pre-filled pen	1 ml (50 mg/ml)	4 pre-filled pens + 8 alcohol swabs
EU/1/99/126/021	Enbrel	50 mg	Solution for injection in a pre-filled pen	Subcutaneous use	Pre-filled pen	1 ml (50 mg/ml)	12 pre-filled pens + 24 alcohol swabs

EU/1/99/126/022	Enbrel	10 mg	Powder and solvent for solution for injection	Subcutaneous use	powder: vial (glass); solvent: syringe (glass)	solvent: 1 ml (10 mg/ml)	4 vials + 4 pre-filled syringes + 4 needles + 4 vial adaptors + 8 swabs