EMA/706484/2010

European Medicines Agency decision

P/236/2010

of 26 November 2010

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

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/236/2010

of 26 November 2010

on the acceptance of a modification of an agreed paediatric investigation plan for etanercept (Enbrel) (EMEA-000299-PIP01-08-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/106/2009 issued on 16 June 2009, and the decision P/113/2010 issued on 07 July 2010,

Having regard to the application submitted by Wyeth Europa Limited on 27 August 2010 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 October 2010, 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 etanercept (Enbrel), Powder and solvent for solution for injection, powder for solution for injection, powder and solvent for solution for injection for paediatric use, solution for injection, subcutaneous 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 Wyeth Europa Limited, Huntercombe Lane South, Taplow, Berkshire, SL6 0PH Maidenhead, United Kingdom.

Done at London, 26 November 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/608399/2010

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

EMEA-000299-PIP01-08-M02

Scope of the application

Active substance(s):

Etanercept

Invented name:

Enbrel

Condition(s):

Plaque psoriasis

Juvenile idiopathic arthritis (JIA)

Authorised indication(s): see Annex II

Pharmaceutical form(s):

Powder and solvent for solution for injection

Powder for solution for injection

Powder and solvent for solution for injection for paediatric use

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Wyeth Europa Limited

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

Information about the authorised medicinal product: see Annex II

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 27 August 2010 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, and the decision P/113/2010 issued on 07 July 2010.
The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 15 September 2010.

Scope of the modification

Some measures of the previous Opinion 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

   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 annex(es) and appendix.

London, 08 October 2010

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. Condition(s)

Plaque psoriasis

Juvenile idiopathic arthritis

2. Waiver

2.1. Condition

Plaque psoriasis

The waiver applies to powder and solvent for solution for injection, powder for solution for injection,

powder and solvent for solution for injection for paediatric use 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

2.2. Condition

Juvenile idiopathic arthritis

The waiver applies to powder and solvent for solution for injection, powder for solution for injection,

powder and solvent for solution for injection for paediatric use and solution for injection; for subcutaneous use to:

- all subsets of paediatric population from birth to less than 18 years for systemic juvenile idiopathic arthritis on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments;
- children from birth to less than 2 years for oligoarticular juvenile idiopathic and polyarticular juvenile idiopathic arthritis on the grounds that measures would not be justified by expected therapeutic benefit as clinical trials are not feasible
- children from birth to less than 12 years for psoriatic arthritis and enthesitis related arthritis on the grounds that measures would not be justified by expected therapeutic benefit as clinical trials are not feasible

3. Paediatric Investigation Plan

3.1. Condition to be investigated

Plaque psoriasis

3.1.1. Indication targeted by the PIP

Treatment of plaque psoriasis

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

From 6 to less than 18 years.

3.1.3. Pharmaceutical form(s)

Powder and solvent for solution for injection

Powder for solution for injection

Powder and solvent for solution for injection for paediatric use

Solution for injection

3.1.4. 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).

3.2. Condition to be investigated

Juvenile idiopathic arthritis

3.2.1. Indication targeted by the PIP

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

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

- from 2 to less than 18 years (treatment of extended oligoarticular juvenile idiopathic arthritis and polyarticular juvenile idiopathic arthritis)
- from 12 to less than 18 years (treatment of psoriatic arthritis and enthesitis related arthritis)

3.2.3. Pharmaceutical form(s)

Powder and solvent for solution for injection

Powder for solution for injection

Powder and solvent for solution for injection for paediatric use

Solution for injection

3.2.4. 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 nonrandomized 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).

4. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues and efficacy in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	By October 2011
Deferral for some or all studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

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

Authorised indications:

Rheumatoid 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.

Polyarticular juvenile idiopathic arthritis

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.

Psoriatic arthritis

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.

Ankylosing spondylitis

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

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).

Paediatric plaque psoriasis

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.