

EMA/140284/2011

European Medicines Agency decision

P/63/2011

of 18 February 2011

on the acceptance of a modification of an agreed paediatric investigation plan for adalimumab (Humira) (EMA-000366-PIP02-09-M01) 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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/85/2010 issued on 1 June 2010,

Having regard to the application submitted by Abbott Laboratories Ltd on 15 February 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 16 February 2011, in accordance with Article 22 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 acceptance of changes to the agreed paediatric investigation plan and to the deferral 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 deferral and 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 adalimumab (Humira), solution for injection, subcutaneous use, including changes to the deferral and 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 Abbott Laboratories Ltd, Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead SL6 4XE, United Kingdom.

Done at London, 18 February 2011

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

EMA/PDCO/135226/2011

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

EMA-000366-PIP02-09-M01

Scope of the application

Active substance(s):

Adalimumab

Invented name:

Humira

Condition(s):

Ulcerative colitis

Rheumatoid Arthritis

Juvenile Idiopathic Arthritis

Crohn's Disease

Psoriasis

Psoriatic Arthritis

Ankylosing Spondylitis

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Abbott Laboratories 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, Abbott Laboratories Limited submitted to the European Medicines Agency on 15 February 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/85/2010 issued on 1 June 2010.

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

The procedure started on 16 February 2011.

Scope of the modification

The measures, waivers and deferrals for already authorised indications have been added.

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, to the deferral 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 annex(es) and appendix.

London, 16 February 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:

Rheumatoid arthritis

Indications:

- Treatment of moderate to severe, active rheumatoid arthritis in adult patients when the response to disease-modifying anti-rheumatic drugs including methotrexate has been inadequate.
- Treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with methotrexate.

The waiver applies to:

All subsets of the paediatric population from birth to less than 18 years for solution for injection for subcutaneous use

on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adults.

1.2. Condition

Juvenile idiopathic arthritis

Indications:

- Treatment of active polyarticular juvenile idiopathic arthritis who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs).

The waiver applies to:

Paediatric population from birth to less than 2 years of age for solution for injection for subcutaneous 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

- Treatment of enthesitis-related arthritis

The waiver applies to:

Paediatric population from birth to less than 12 years of age for solution for injection for subcutaneous 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

1.3. Condition

Crohn's disease

Indication:

Treatment of severe, active Crohn's disease, in patients who have not responded despite a full and adequate course of therapy with a corticosteroid and/or an immunosuppressant; or who are intolerant to or have medical contraindications for such therapies.

The waiver applies to:

Paediatric population from birth to less than 6 years of age for solution for injection for subcutaneous 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)

1.4. Condition

Psoriasis

Indication:

Treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or PUVA.

The waiver applies to:

Paediatric population from birth to less than 4 years of age for solution for injection for subcutaneous use

on the grounds that the specific medicinal product is likely to be unsafe

1.5. Condition

Psoriatic arthritis

Indication:

Treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying anti rheumatic drug therapy has been inadequate.

The waiver applies to:

All subsets of the paediatric population from birth to less than 18 years of age for solution for injection for subcutaneous use

on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adults. (Paediatric psoriatic arthritis is a subtype of juvenile idiopathic arthritis).

1.6. Condition

Ankylosing spondylitis

Indication:

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

The waiver applies to:

All subsets of the paediatric population from birth to less than 18 years of age for solution for injection for subcutaneous use

on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adults.

1.7. Condition

Ulcerative colitis

The waiver applies to:

- children from birth to less than 4 years
- for solution for injection in pre-filled syringe, subcutaneous 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).

2. Paediatric Investigation Plan

2.1. Condition to be investigated

Juvenile idiopathic arthritis

2.1.1. Indication targeted by the PIP

Treatment of polyarticular juvenile idiopathic arthritis

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

From 2 to less than 18 years.

2.1.3. Indication targeted by the PIP

Treatment of enthesitis-related arthritis

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

From 12 to less than 18 years.

2.2. Condition to be investigated

Crohn's disease

2.2.1. Indication targeted by the PIP

Treatment of Crohn's disease

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

From 6 to less than 18 years.

2.3. Condition to be investigated

Psoriasis

2.3.1. Indication targeted by the PIP

Treatment of severe chronic plaque psoriasis

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

From 4 to less than 18 years

2.4. Condition to be investigated

Ulcerative colitis

2.4.1. Indication targeted by the PIP

Treatment of moderately to severely active ulcerative colitis

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

From 4 to less than 18 years of age.

2.5. Pharmaceutical form(s)

Solution for injection

3. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	9	1. A Multicenter, Randomised, Double-Blind, Placebo-Controlled Study of the Safety, Efficacy, and Pharmacokinetics of the Human Anti-TNF Monoclonal Antibody Adalimumab in Children With Polyarticular Juvenile Idiopathic Arthritis 2. Compassionate Use Study of Adalimumab in Children from 2 to less than 4 Years Old or Age 4 and Above Weighing Less Than 15 kg with Active Juvenile Idiopathic Arthritis (JIA). 3. A double-blind, placebo-controlled, multicenter study of the efficacy and safety of the human anti-TNF monoclonal antibody adalimumab in paediatric patients with enthesitis-related arthritis. 4. A Multi-centre, Double-blind (DB) Study to Evaluate the Safety, Efficacy and Pharmacokinetics (PK) of the Human Anti-TNF Monoclonal Antibody Adalimumab in Paediatric Patients with Moderate to Severe Crohn's Disease (CD). 5. A Multi-centre, Open-label (OL) Study of the Human Anti-TNF Monoclonal Antibody Adalimumab to Evaluate the Efficacy and the Long-term Safety and Tolerability of Repeated Administration of Adalimumab in Paediatric Patients with Crohn's Disease (CD) Who Have Demonstrated a Clinical Response in a Controlled Double-blind Study. 6. A multi-centre, randomised, double-dummy, double-blind study evaluating two doses of adalimumab versus methotrexate (MTX) in

		paediatric patients with chronic plaque psoriasis (Ps). 7. Modelling and simulation study – exposure response analysis for dose selection in study 8. 8. Multicentre, randomised, double-blind, three arm, lower and higher dose, placebo-controlled trial to evaluate the efficacy, safety and pharmacokinetics of adalimumab in children from 4 to less than 18 years of age with moderately to severely active ulcerative colitis 9. Multi-centre, open-label study to evaluate the efficacy and the long-term safety and tolerability of adalimumab in children from 4 to less than 18 years of age with moderately to severely active ulcerative colitis
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4. 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:	Yes
Date of completion of the paediatric investigation plan:	By December 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. Rheumatoid arthritis**

Humira in combination with methotrexate, is indicated for:

- 1.1. the treatment of moderate to severe, active rheumatoid arthritis in adult patients when the response to disease-modifying anti-rheumatic drugs including methotrexate has been inadequate.
- 1.2. the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with methotrexate.

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

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

2. Polyarticular juvenile idiopathic arthritis

Humira in combination with methotrexate is indicated for the treatment of active polyarticular juvenile idiopathic arthritis, in adolescents aged 13 to 17 years who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs). Humira can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate (see section 5.1).

3. Psoriatic arthritis

Humira is indicated for the treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying anti-rheumatic drug therapy has been inadequate. Humira has been shown to reduce the rate of progression of peripheral joint damage as measured by X-ray in patients with polyarticular symmetrical subtypes of the disease (see Section 5.1) and to improve physical function.

4. Ankylosing spondylitis

Humira is indicated for the treatment of adults with severe active ankylosing spondylitis who have had an inadequate response to conventional therapy.

5. Crohn's disease

Humira is indicated for treatment of severe, active Crohn's disease, in patients who have not responded despite a full and adequate course of therapy with a corticosteroid and/or an immunosuppressant; or who are intolerant to or have medical contraindications for such therapies.

6. Psoriasis

Humira is indicated for the treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or PUVA.

EU Number	(Invented) name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content (concentration)	Package size
EU/1/03/256/001	Humira	40 mg	Solution for injection	Subcutaneous use	vial (glass)	0.8 ml	1 vial + 1 syringe + 2 alcohol pads
EU/1/03/256/002	Humira	40 mg	Solution for injection	Subcutaneous use	pre-filled syringe (glass)	0.8 ml	1 pre-filled syringe + 1 alcohol pad
EU/1/03/256/003	Humira	40 mg	Solution for injection	Subcutaneous use	pre-filled syringe (glass)	0.8 ml	2 pre-filled syringes + 2 alcohol pads
EU/1/03/256/004	Humira	40 mg	Solution for injection	Subcutaneous use	pre-filled syringe (glass)	0.8 ml	4 pre-filled syringes + 4 alcohol pads
EU/1/03/256/005	Humira	40 mg	Solution for injection	Subcutaneous use	pre-filled syringe (glass)	0.8 ml	6 pre-filled syringes + 6 alcohol pads
EU/1/03/256/006	Humira	40 mg	Solution for injection	Subcutaneous use	pre-filled syringe (glass)	0.8 ml	1 pre-filled syringe with needleguard + 1 alcohol pad
EU/1/03/256/007	Humira	40 mg	Solution for injection	Subcutaneous use	pre-filled pen (glass)	0.8 ml	1 pre-filled pen + 1 alcohol pad in a blister
EU/1/03/256/008	Humira	40 mg	Solution for injection	Subcutaneous use	pre-filled pen (glass)	0.8 ml	2 pre-filled pens + 2 alcohol pads in a blister
EU/1/03/256/009	Humira	40 mg	Solution for injection	Subcutaneous use	pre-filled pen (glass)	0.8 ml	4 pre-filled pens + 4 alcohol pads in a blister
EU/1/03/256/010	Humira	40 mg	Solution for injection	Subcutaneous use	pre-filled pen (glass)	0.8 ml	6 pre-filled pens + 6 alcohol pads in a blister