EMA/730065/2010

# European Medicines Agency decision

P/1/2011

of 3 January 2011

on the acceptance of a modification of an agreed paediatric investigation plan for adalimumab (Humira) (EMEA-000366-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.**

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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 726/2004[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/102/2009 issued on 18 May 2009, and the decision P/102/2010 issued on 8 June 2010,

Having regard to the application submitted by Abbott Laboratories Ltd. 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 12 November 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 adalimumab (Humira), 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 Abbott Laboratories Ltd., Abbott House, Vanwall Business Park, Vanwall Road, SL6 4XE Maidenhead, Berkshire, United Kingdom.

Done at London, 3 January 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director

(Signature on file)

EMA/PDCO/693135/2010

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

EMEA-000366-PIP01-08-M03

## Scope of the application

**Active substance(s):**

Adalimumab

**Invented name:**

Humira

**Condition(s):**

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**

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## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Abbott Laboratories Ltd. 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/102/2009 issued on 18 May 2009, the decision P/102/2010 issued on 8 June 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 latest 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 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.

   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, 12 November 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. 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.

# 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 arthriti**s**

### 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

## 3.4. Pharmaceutical form(s)

Solution for injection for subcutaneous use

## 3.5. Studies

| Area | Number of studies | Description |
|---|---|---|
| Quality | | Not applicable. |
| Non-clinical | | Not applicable. |
| Clinical | | 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<br><br>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).<br><br>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.<br><br>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).<br><br>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.<br><br>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). |

# 3. Follow-up, completion and deferral of PIP

| **Measures to address long term follow-up of potential safety or efficacy issues in relation to paediatric use:** | **Yes** |
|---|---|
| Date of completion of the paediatric investigation plan: | By July 2013 |
| Deferral for some or all 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 Rheumatoid arthritis

Authorised indications:

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.

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

2. Treatment of Polyarticular juvenile idiopathic arthritis

Authorised indications:

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.

3. Treatment of Psoriatic arthritis

Authorised indications:

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.

4. Treatment of Ankylosing spondylitis

Authorised indications:

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

5. Treatment of Crohn's disease

Authorised indications:

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. Treatment of Psoriasis

Authorised indications:

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 |