



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/340720/2014

## European Medicines Agency decision

P/0162/2014

of 13 June 2014

on the acceptance of a modification of an agreed paediatric investigation plan for adalimumab (Humira), (EMEA-000366-PIP02-09-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<sup>1</sup>,

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<sup>2</sup>,

Having regard to the European Medicines Agency's decision P/85/2010 issued on 1 June 2010, the decision P/63/2011 issued on 18 February 2011, and the decision P/0137/2013 issued on 21 June 2013,

Having regard to the application submitted by AbbVie Limited on 3 March 2014 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 23 May 2014, 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.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1.

<sup>2</sup> 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 agreed PIP covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/102/2009 issued on 18 May 2009, including subsequent modifications thereof.

**Article 3**

This decision is addressed to AbbVie Limited, Abbott House, Vanwall Business Park, Vanwall Road, SL6 4XE – Maidenhead, United Kingdom.

Done at London, 13 June 2014

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



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/PDCO/129550/2014 **Corr**

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

EMA-000366-PIP02-09-M03

### Scope of the application

**Active substance(s):**

Adalimumab

**Invented name:**

Humira

**Condition(s):**

Treatment of ulcerative colitis

**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:**

AbbVie Limited

**Information about the authorised medicinal product:**

See Annex II



## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, AbbVie Limited submitted to the European Medicines Agency on 3 March 2014 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 decision P/63/2011 issued on 18 February 2011, and the decision P/0137/2013 issued on 21 June 2013.

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

The procedure started on 25 March 2014.

## Scope of the modification

Some timelines 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 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, 23 May 2014

On behalf of the Paediatric Committee  
Dr Dirk Mentzer, 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 (PIP)**

# 1. Waiver

## 1.1. Condition: treatment of 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: treatment of ulcerative colitis

### 2.1.1. Indication(s) targeted by the PIP

Treatment of moderately to severely active ulcerative colitis

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

From 4 to less than 18 years of age

### 2.1.3. Pharmaceutical form(s)

Solution for injection

### 2.1.4. Measures

| Area                    | Number of measures | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-------------------------|--------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Quality-related studies | 0                  | Not applicable.                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Non-clinical studies    | 0                  | Not applicable.                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Clinical studies        | 1                  | <p><b>Studies 1-6</b> have been deleted from this Paediatric Investigation Plan (they are part of the PIP EMEA-000366-PIP-01-08).</p> <p><b>Study 8</b></p> <p>Double-blind, randomised, multi-centre placebo-controlled study to evaluate the efficacy, safety and the pharmacokinetics of adalimumab in children from 4 to less than 18 years old with moderate to-severe ulcerative colitis.</p> <p><b>Study 9</b> has been deleted from this Paediatric Investigation Plan.</p> |

|                                               |   |                                                                                                              |
|-----------------------------------------------|---|--------------------------------------------------------------------------------------------------------------|
| Extrapolation, modelling & simulation studies | 1 | <b>Study 7</b><br>Modelling and simulation study – exposure response analysis for dose selection in study 8. |
| Other studies                                 | 0 | Not applicable.                                                                                              |
| Other measures                                | 0 | Not applicable.                                                                                              |

### 3. 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 June 2019 |
| Deferral for one or more measures contained in the paediatric investigation plan:         | Yes          |

## **Annex II**

### **Information about the authorised medicinal product**

## Condition(s) and authorised indication(s):

### 1. Rheumatoid arthritis

#### Authorised indication(s):

Humira in combination with methotrexate, is indicated for:

- the treatment of moderate to severe, active rheumatoid arthritis in adult patients when the response to disease-modifying antirheumatic drugs including methotrexate has been inadequate;
- 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

#### Authorised indication(s):

Humira in combination with methotrexate is indicated for the treatment of active polyarticular juvenile idiopathic arthritis, in children and adolescents aged 2 to 17 years who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs). Humira can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate (for the efficacy in monotherapy see section 5.1). Humira has not been studied in children aged less than 2 years.

### 3. Axial spondyloarthritis

#### Ankylosing spondylitis

#### Authorised indication(s):

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

#### Axial spondyloarthritis without radiographic evidence of AS

#### Authorised indication(s):

Humira is indicated for the treatment of adults with severe axial spondyloarthritis without radiographic evidence of AS but with objective signs of inflammation by elevated C-reactive protein and / or magnetic resonance imaging, who have had an inadequate response to, or are intolerant to non-steroidal anti-inflammatory drugs.

### 4. Psoriatic arthritis

#### Authorised indication(s):

Humira is indicated for the treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying antirheumatic 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.

## 5. Psoriasis

### Authorised indication(s):

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 psoralen ultraviolet-A (PUVA).

## 6. Crohn's disease

### Authorised indication(s):

Humira is indicated for treatment of moderately to severely active Crohn's disease, in adult 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.

## 7. Paediatric Crohn's disease

### Authorised indication(s):

Humira is indicated for the treatment of severe active Crohn's disease in paediatric patients (6 to 17 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy, a corticosteroid, and an immunomodulator, or who are intolerant to or have contraindications for such therapies.

## 8. Ulcerative colitis

### Authorised indication(s):

Humira is indicated for treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies.

## **Authorised pharmaceutical form(s):**

Solution for injection

## **Authorised route(s) of administration:**

Subcutaneous use