EMA/804453/2013

European Medicines Agency decision

P/0324/2013

of 19 December 2013

on the acceptance of a modification of an agreed paediatric investigation plan for adalimumab (Humira) (EMEA-000366-PIP01-08-M06) 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, the decision P/102/2010 issued on 8 June 2010, the decision P/1/2011 issued on 3 January 2011, the decision P/141/2011 issued on 6 June 2011, and the decision P/0259/2012 issued on 19 November 2012,

Having regard to the application submitted by AbbVie Limited on 13 September 2013 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 6 December 2013, in accordance with Article 22 of Regulation (EC) No 1901/2006, and Article 21 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.

(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.

[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, 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 AbbVie Limited, Abbott House, Vanwall Business Park, Vanwall Road, SL6 4XE – Maidenhead, United Kingdom.

Done at London, 19 December 2013

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

EMA/PDCO/615881/2013

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

EMEA-000366-PIP01-08-M06

Scope of the application

Active substance(s):

Adalimumab

Invented name:

Humira

Condition(s):

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

Treatment of Crohn's disease

Treatment of psoriasis

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

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, AbbVie Limited submitted to the European Medicines Agency on 13 September 2013 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 decision P/1/2011 issued on 3 January 2011, the decision P/141/2011 issued on 6 June 2011, and the decision P/0259/2012 issued on 19 November 2012.

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

The procedure started on 10 October 2013.

Scope of the modification

Deferral for one study in the Paediatric Investigation Plan was granted.

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 deferral 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, 6 December 2013

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

1. Waiver

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

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.

1.2. Condition: treatment of Crohn's disease

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).

1.3. Condition: treatment of psoriasis

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.

2. Paediatric Investigation Plan

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

2.1.1. Indication(s) targeted by the PIP

Treatment of polyarticular juvenile idiopathic arthritis, treatment of enthesitis related arthritis.

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

From 2 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	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	3	**Measure 1** A multicentre, 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. **Measure 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). **Measure 3** A double-blind, placebo-controlled, multicentre study of the efficacy and safety of the human anti-TNF monoclonal antibody adalimumab in paediatric patients with enthesitis-related arthritis.

2.2. Condition: treatment of Crohn's disease

2.2.1. Indication(s) 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 of age.

2.2.3. Pharmaceutical form(s)

Solution for injection.

2.2.4. Measures

Area	Number of measures	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.

Clinical	1	**Measure 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).

2.3. Condition: treatment of psoriasis

2.3.1. Indication(s) 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 of age.

2.3.3. Pharmaceutical form(s)

Solution for injection.

2.3.4. Measures

Area	Number of measures	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	1	**Measure 5** 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

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By May 2014
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