

**Food and Drug Administration  
Center for Drug Evaluation and Research**

**Summary Minutes of the Arthritis Advisory Committee Meeting  
July 12, 2016**

**Location:** The FDA White Oak Campus, Building 31, The Great Room (Rm. 1503), White Oak Conference Center, Silver Spring, Maryland.

**Topic:** The committee discussed biologics license application 761024, for ABP 501, a proposed biosimilar to AbbVie Inc.'s HUMIRA (adalimumab), submitted by Amgen, Inc. The proposed indications (uses) for this product are: (1) Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis (alone or in combination with methotrexate or other non-biologic disease-modifying anti-rheumatic drugs (DMARDs)); (2) reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 4 years of age and older (alone or in combination with methotrexate); (3) reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis (alone or in combination with non-biologic DMARDs); (4) reducing signs and symptoms in adult patients with active ankylosing spondylitis; (5) reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy (ABP 501 would be indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab); (6) inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP) (the effectiveness of ABP-501 would not be established in patients who have lost response to or were intolerant to TNF blockers); and (7) treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate (only to be administered to patients who will be closely monitored and have regular follow-up visits with a physician).

These summary minutes for the July 12, 2016 meeting of the Arthritis Advisory Committee of the Food and Drug Administration were approved on September 6, 2016.

I certify that I attended the July 12, 2016 meeting of the Arthritis Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

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/s/  
Moon Hee V. Choi, PharmD  
Acting Designated Federal Officer, AAC

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/s/  
Daniel Solomon, MD, MPH  
Acting Chairperson, AAC

## Summary Minutes of the Arthritis Advisory Committee Meeting July 12, 2016

The following is an internal report (which has not been reviewed) of the Arthritis Advisory Committee meeting held on July 12, 2016. A verbatim transcript will be available in approximately six weeks, sent to the Division of Pulmonary, Allergy, and Rheumatology Products and posted on the FDA website at:  
<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/ucm481975.htm>.

All external requests for the meeting transcripts should be submitted to the CDER Freedom of Information Office.

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The Arthritis Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on July 12, 2016, at the FDA White Oak Campus, 10903 New Hampshire Avenue, Building 31 Conference Center, The Great Room (Rm. 1503), Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Amgen, Inc. The meeting was called to order by Daniel Solomon, MD, MPH (Acting Chairperson). The conflict of interest statement was read into the record by Moon Hee V. Choi, PharmD (Acting Designated Federal Officer). There were approximately 280 people in attendance. There were 20 Open Public Hearing (OPH) presentations.

**Issue:** The committee discussed biologics license application (BLA) 761024, for ABP 501, a proposed biosimilar to AbbVie Inc.'s HUMIRA (adalimumab), submitted by Amgen, Inc. The proposed indications (uses) for this product are: (1) Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis (alone or in combination with methotrexate or other non-biologic disease-modifying anti-rheumatic drugs (DMARDs)); (2) reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 4 years of age and older (alone or in combination with methotrexate); (3) reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis (alone or in combination with non-biologic DMARDs); (4) reducing signs and symptoms in adult patients with active ankylosing spondylitis; (5) reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy (ABP 501 would be indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab); (6) inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP) (the effectiveness of ABP 501 would not be established in patients who have lost response to or were intolerant to TNF blockers); and (7) treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate (only to be

administered to patients who will be closely monitored and have regular follow-up visits with a physician).

**Attendance:**

**Arthritis Advisory Committee Members Present (Voting):** Mara L. Becker, MD, MSCE; Jennifer Horonjeff, PhD (Consumer Representative); Beth L. Jonas, MD; Donald R. Miller, PharmD, FASHP; Andreas M. Reimold, MD; Therese M. Wolpaw, MD, MHPE

**Arthritis Advisory Committee Members Not Present (Voting):** Liron Caplan, MD, PhD; Jeffrey Curtis, MD, MPH; Veena K. Ranganath, MD, MS; Eric J. Tchetgen Tchetgen, BS, PhD

**Arthritis Advisory Committee Members Not Present (Non-Voting):** James B. Chung, MD, PhD

**Temporary Members (Voting):** Jeremy Adler, MD, MSc; Diane Aronson, BS in Ed (Patient Representative); Wilma F. Bergfeld, MD, FAAD; Warren B. Bilker, PhD; Erica Brittain, PhD; Linda A. Feagins, MD; Nancy L. Geller, PhD; William Hancock, PhD, DSc; Robert J. Hohman, PhD; Donald E. Mager, PharmD, PhD; David J. Margolis, MD, PhD; Jeffrey W. Nathanson, MD; Alyce M. Oliver, PhD, MD; June K. Robinson, MD; Jose U. Scher, MD; Richard Siegel, MD, PhD; Steven F. Solga, MD; Daniel Solomon, MD, MPH (Acting Chairperson); Sarah E. Streett, MD; Scott A. Waldman, MD, PhD, FCP, FAHA

**Acting Industry Representative to the Committee (Non-Voting):** Sean P. Curtis, MD

**FDA Participants (Non-Voting):** Leah Christl, PhD; Badrul Chowdhury, MD, PhD; Nikolay P. Nikolov, MD; Steven Kozlowski, MD; Joel Welch, PhD

**Acting Designated Federal Officer (Non-Voting):** Moon Hee V. Choi, PharmD

**Open Public Hearing Speakers:** Seth Ginsberg (Global Healthy Living Foundation and CreakyJoints); Wendy B. Foster (US Pain Foundation); Andrew Spiegel, Esquire on behalf of Harry Gewanter, MD, FACR, FAAP (Alliance for Safe Biologic Medicines); Robert Salcedo (Biosciences Corp.), Andrew Spiegel, Esquire (Digestive Disease National Coalition); Emily Lemiska on behalf of Casey Cashman (US Pain Foundation); Jasey Cardenas on behalf of Lawrence A. La Motte (Patients for Biologic Safety and Access); Peter Pitts (Center for Medicine in the Public Interest); Cindy Becker (Crohn's and Colitis Foundation of America); Jochen G. Salfeld, PhD (AbbVie, Inc.); Joshua B. Stolow, MD (Coalition of State Rheumatology Organizations); Madelaine Feldman, MD (Alliance for Patient Access); Dennis R. Cryer, MD (Biologics Prescribers Collaborative); Kathleen A. Arntsen (Lupus and Allied Diseases Association); Christine Simmon (The Biosimilars Council); Thair Phillips (RetireSafe); Susan Loretta Behen, MD, FACS; Sarah Buchanan (Crohn's and Colitis Foundation of America); Jasey Cardenas (United Spinal Association); Tiffany McCaslin (National Business Group on Health)

***The agenda proceeded as follows:***

Call to Order and Introduction of  
Committee

**Daniel Solomon, MD, MPH**  
Acting Chairperson, AAC

Conflict of Interest Statement

**Moon Hee Choi, PharmD**  
Acting Designated Federal Officer, AAC

FDA Opening Remarks

**Janet Woodcock, MD**  
Director  
CDER, FDA

Overview of the Regulatory Pathway and  
FDA's Guidance for the Development and  
Approval of Biosimilar Products in the US

**Leah Christl, PhD**  
Associate Director, Therapeutic Biologics  
Therapeutic Biologics and Biosimilars Staff  
Office of New Drugs (OND), CDER, FDA

Clarifying Questions to the FDA

FDA Introductory Remarks

**Nikolay P. Nikolov, MD**  
Clinical Team Leader  
Division of Pulmonary, Allergy & Rheumatology  
Products (DPARP)  
Office of Drug Evaluation II (ODE-II)  
OND, CDER, FDA

**APPLICANT PRESENTATIONS**

**Amgen, Inc.**

Introduction

**Richard Markus, MD, PhD**  
Vice President, Global Biosimilars Development  
Amgen, Inc.

Analytical and Nonclinical Similarity to  
Adalimumab

**Simon Hotchin**  
Executive Director, Global Biosimilars Regulatory  
Affairs  
Amgen, Inc.

ABP 501 Clinical Similarity

**Richard Markus, MD, PhD**

Conclusions

**Steven Galson, MD, MPH**  
Senior Vice President, Global Regulatory Affairs &  
Safety  
Amgen, Inc.

Clarifying Questions to Applicant

**BREAK**

**FDA PRESENTATIONS**

Product Quality Review

**Joel Welch, PhD**  
Product Quality Team Leader  
Division of Biotechnology Review and Research II  
Office of Biotechnology Products  
Office of Pharmaceutical Quality, CDER, FDA

ABP 501 Statistical Equivalence Testing  
for Bioactivity

**Meiyu Shen, PhD**  
Lead Mathematical Statistician  
Division of Biometrics VI  
Office of Biostatistics (OB)  
Office of Translational Sciences (OTS), CDER, FDA

Clinical Pharmacology Review

**Jianmeng Chen, MD, PhD**  
Clinical Pharmacology Reviewer  
Division of Clinical Pharmacology II  
Office of Clinical Pharmacology, OTS, CDER, FDA

Clinical Efficacy Review

**Yongman Kim, PhD**  
Mathematical Statistician  
Division of Biometrics II, OB, OTS, CDER, FDA

**Kathleen Fritsch, PhD**  
Mathematical Statistician  
Division of Biometrics III, OB, OTS, CDER, FDA

Safety and Immunogenicity Review

**Keith M. Hull, MD, PhD**  
Medical Officer  
DPARP, ODE-II, OND, CDER, FDA

Considerations for Extrapolation and  
Summary

**Nikolay P. Nikolov, MD**

Clarifying Questions to FDA

**LUNCH**

**OPEN PUBLIC HEARING**

Charge to the Committee

**Nikolay P. Nikolov, MD**

Questions to the Committee/Committee Discussion

**BREAK**

Questions to the Committee/Committee Discussion

**ADJOURNMENT**

***Questions to the Committee:***

FDA has requested additional data from Amgen regarding reverse signaling activity and this request is still pending. FDA will evaluate these additional data after they are submitted. To maximize the utility of the Committee's voting results, FDA requests that the Committee evaluate the discussion and voting questions based on the premise that the additional data provided by the sponsor would not preclude a demonstration that ABP 501 is biosimilar to US-licensed Humira.

- 1. DISCUSSION:** Please discuss whether the evidence from analytical studies supports a demonstration that ABP 501 is highly similar to US-licensed Humira, notwithstanding minor differences in clinically inactive components.

*Committee Discussion:* Most committee members agreed that the evidence from analytical studies supports a demonstration that ABP 501 is highly similar to US-licensed Humira, notwithstanding minor differences in clinically inactive components. One committee member noted that they accepted the similarity of the *in vitro* Fc binding and Fc-mediated assays to reflect functional *in vivo* similarity to support the extrapolation to inflammatory bowel disease indications. One committee member noted that differences in post-translational modifications, such as glycosylation, could result in differences in immunogenicity. However, another member noted that in the clinical program similar immunogenicity was observed between ABP 501 and the reference product. Please see the transcript for details of the committee discussion.

- 2. DISCUSSION:** Please discuss whether the evidence supports a demonstration that there are no clinically meaningful differences between ABP 501 and US-licensed Humira in the studied conditions of use (rheumatoid arthritis (RA) and plaque psoriasis (PsO)).

*Committee Discussion:* Most committee members agreed that the evidence supports a demonstration that there are no clinically meaningful differences between ABP 501 and US-licensed Humira in the studied conditions of use (rheumatoid arthritis (RA) and plaque psoriasis (PsO)). One committee member stated that the comparative clinical studies in RA and PsO have statistically demonstrated a high degree of similarity in efficacy between ABP 501 and the comparator products. One committee member noted that the study sample was small to detect differences in safety. Some committee members recommended the need for post marketing surveillance to assess long-term safety. Please see the transcript for details of the committee discussion.

- 3. DISCUSSION:** Please discuss whether the data provides adequate scientific justification to support a demonstration of no clinically meaningful differences between ABP 501 and US-licensed Humira for the following additional indications for which US-licensed Humira is licensed:

- Juvenile Idiopathic Arthritis (JIA) in patients 4 years of age and older

- Psoriatic Arthritis (PsA)
- Ankylosing Spondylitis (AS)
- Adult Crohn's Disease (CD)
- Adult Ulcerative Colitis (UC)

If not, please state the specific concerns and what additional information would be needed to support such a demonstration. Please discuss by indication if relevant.

**Committee Discussion:** *The committee members did not come to a consensus on whether the data provides adequate scientific justification to support a demonstration of no clinically meaningful differences between ABP 501 and US-licensed Humira for the following additional indications for which US-licensed Humira is licensed (JIA in patients 4 years of age and older, PsA, AS, CD and UC). One committee member noted that one can extrapolate by mechanism of action to the rheumatology indications. However, because the mechanism of action in inflammatory bowel disease indications was unclear, this leaves residual uncertainty for the extrapolation to those indications. The committee members who agreed that the data provided adequate justification, added that they were comfortable with the extrapolation to the pediatric population as well. Please see the transcript for details of the committee discussion.*

4. **VOTE:** Does the totality of the evidence support licensure of ABP 501 as a biosimilar product to US-licensed Humira for the following indications for which US-licensed Humira is currently licensed and for which Amgen is seeking licensure (RA, JIA in patients 4 years of age and older, PsA, AS, adult CD, adult UC, and PsO)?

Please explain the reason for your vote.

**Vote Result:** YES: 26 NO: 0 ABSTAIN: 0

**Committee Discussion:** *The committee members unanimously agreed that the evidence support licensure of ABP 501 as a biosimilar product to US-licensed Humira for the following indications for which US-licensed Humira is currently licensed and for which Amgen is seeking licensure (RA, JIA in patients 4 years of age and older, PsA, AS, adult CD, adult UC, and PsO). Some committee members expressed concerns with the potential for market-place non-medical switching of biosimilars. Some committee members recommended mandatory postmarketing surveillance to assess long-term safety, in addition to the data presented. Some committee members also stressed the importance of patient education on biosimilars and interchangeability. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 4:42 p.m.