

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

**Summary Minutes of the Arthritis Advisory Committee Meeting
August 3, 2017**

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

Topic: The committee discussed supplemental new drug applications (sNDAs) 203214 supplement 17, for XELJANZ (tofacitinib) tablets and 208246 supplement 3, for XELJANZ XR (tofacitinib) extended release tablets submitted by Pfizer Inc., for the treatment of adult patients with active psoriatic arthritis. The committee discussed the efficacy and safety data and benefit-risk considerations.

These summary minutes for the August 3, 2017, meeting of the Arthritis Advisory Committee of the Food and Drug Administration were approved on August 22, 2017.

I certify that I attended the August 3, 2017, meeting of the Arthritis Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/
Philip A. Bautista, PharmD
Acting Designated Federal Officer, AAC

/s/
Daniel H. Solomon, MD, MPH
Chairperson, AAC

Summary Minutes of the Arthritis Advisory Committee Meeting August 3, 2017

The following is the final report of the Arthritis Advisory Committee meeting, held on August 3, 2017. 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: <https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/ucm564748.htm>

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

The Arthritis Advisory Committee met on August 3, 2017, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Pfizer, Inc. The meeting was called to order by Daniel H. Solomon, MD, MPH (Chairperson). The conflict of interest statement was read into the record by Philip A. Bautista, PharmD (Acting Designated Federal Officer). There were approximately 160 people in attendance. There were two Open Public Hearing (OPH) speaker presentations.

Issue: The committee discussed supplemental new drug applications (sNDAs) 203214 supplement 17, for XELJANZ (tofacitinib) tablets and 208246 supplement 3, for XELJANZ XR (tofacitinib) extended release tablets submitted by Pfizer Inc., for the treatment of adult patients with active psoriatic arthritis. The committee discussed the efficacy and safety data and benefit-risk considerations.

Attendance:

Arthritis Advisory Committee Members Present (Voting): Mara L. Becker, MD, MSCE; Jennifer Horonjeff, PhD (Consumer Representative); Beth L. Jonas, MD; Alyce M. Oliver, PhD, MD; Daniel H. Solomon, MD, MPH (Chairperson)

Arthritis Advisory Committee Members Present (Non-Voting): James B. Chung, MD, PhD (Industry Representative)

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

Temporary Members (Voting): Diane Aronson (Patient Representative); Erica Brittain, PhD; James Katz, MD; Steven B. Meisel, PharmD; Maria E. Suarez-Almazor, MD, PhD; Michael H. Weisman, MD

FDA Participants (Non-Voting): Badrul Chowdhury, MD, PhD; Gregory Levin, PhD; Janet Maynard, MD, MHS; Raj Nair, MD; Rebecca Rothwell, PhD

Acting Designated Federal Officer (Non-Voting): Philip A. Bautista, PharmD

OPH Speakers: Stephen Marmaras (Global Health Living Foundation and Creaky Joints); Richard Howard (Spondylitis Association of America)

The agenda was as follows:

Call to Order and Introduction of Committee	Daniel H. Solomon, MD, MPH Chairperson, AAC
Conflict of Interest Statement	Philip A. Bautista, PharmD Acting Designated Federal Officer, AAC
FDA Introductory Remarks	Janet Maynard, MD, MHS Clinical Team Leader, Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) Office of Drug Evaluation II (ODE II) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	Pfizer, Inc.
Introduction	Nancy McKay Director, Regulatory Affairs Pfizer, Inc.
Psoriatic Arthritis: A Physician's Perspective/Unmet Medical Need	Philip Mease, MD, MACR Director, Rheumatology Research Swedish-Providence-St. Joseph Health Systems Clinical Professor University of Washington, School of Medicine
Tofacitinib PsA Development Program and Efficacy	Keith Kanik, MD, FACR Senior Director, Global Clinical Lead PsA Inflammation and Immunology Pfizer, Inc.
Tofacitinib PsA Safety	Daniela Graham, MD Clinician, PsA Development Program Inflammation and Immunology Pfizer, Inc.
Risk Management	Thomas Jones, MD Senior Director, Safety Risk Management Pfizer, Inc.

APPLICANT PRESENTATIONS (CONT.)

Benefit: Risk and Conclusions

Michael Corbo, PhD
Senior VP
Chief Development Officer, Inflammation and
Immunology
Pfizer, Inc.

Clarifying Questions

FDA PRESENTATIONS

Introduction and Clinical Overview

Raj Nair, MD
Medical Officer
DPARP, ODE II, OND, CDER, FDA

Statistical Considerations on Efficacy

Rebecca Rothwell, PhD
Mathematical Statistician
Division of Biometrics II (DB II)
Office of Biostatistics (OB)
Office of Translational Sciences (OTS), CDER, FDA

Summary of Safety and Risk/Benefit
Considerations

Raj Nair, MD

Clarifying Questions

BREAK

OPEN PUBLIC HEARING

Charge to the Committee

Janet Maynard, MD, MHS

Questions to the
Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Discuss the efficacy of the proposed dose of tofacitinib for adult patients with active psoriatic arthritis. In your discussion, comment on the following:
 - a. The overall efficacy of tofacitinib with respect to signs and symptoms and physical function for adult patients with psoriatic arthritis.
 - b. The evaluation of the effect of tofacitinib on radiographic progression in psoriatic arthritis.

Committee Discussion: Overall, the committee agreed that the results of the studies demonstrate the efficacy of tofacitinib for adult patients with active psoriatic arthritis with respect to signs and symptoms and physical function. In regards to the evaluation of the effect of the tofacitinib on radiographic progression in psoriatic arthritis, the committee members noted that the totality of the data does not provide substantial evidence that tofacitinib has an effect on radiographic progression in this patient population. The committee commented that due to the design of the study, including the small patient sample size and the shortened time on placebo, the evidence was insufficient to draw definitive conclusions on radiographic benefit. Based on this, the committee members concluded that no claim or implied claim should be made in the labeling to suggest that tofacitinib has a positive effect on radiographic progression in psoriatic arthritis patients, if the product were to be approved. Please see the transcript for details of the committee discussion.

2. **DISCUSSION:** Discuss the safety of tofacitinib for the treatment of adult patients with active psoriatic arthritis.

Committee Discussion: The committee agreed that the results of the studies demonstrate the safety of tofacitinib for the treatment of adult patients with active psoriatic arthritis. The committee noted that the safety profile was consistent with the known safety in rheumatoid arthritis. The committee members added that the risk for herpes zoster infection with this drug product was clear and that a more aggressive risk mitigation strategy should be implemented to prevent infection given the availability of a vaccine. Please see the transcript for details of the committee discussion.

3. **VOTE:** Overall, do the data provide substantial evidence of the efficacy of tofacitinib for the treatment of adult patients with active psoriatic arthritis?
 - a. If not, what data are needed?

Vote Result: Yes: 10 No: 1 Abstain: 0

Committee Discussion: The majority of the committee (10 to 1) agreed that the data provide substantial evidence of the efficacy of tofacitinib for the treatment of adult patients with active psoriatic arthritis. The one committee member who voted "No" noted concerns with regards to lack of evidence for reducing radiographic progression. Please see the transcript for details of the committee discussion.

4. **VOTE:** Is the safety profile of tofacitinib adequate to support approval of tofacitinib for the treatment of adult patients with active psoriatic arthritis?
 - a. If not, what further data should be obtained?

Vote Result: Yes: 10 No: 1 Abstain: 0

Committee Discussion: The majority of the committee (10 to 1) agreed that the safety profile of tofacitinib is adequate to support the approval of tofacitinib for the treatment of

adult patients with active psoriatic arthritis. The committee members agreed that the safety profile was consistent with the known safety in rheumatoid arthritis, and reiterated the need for more aggressive risk mitigation strategies to prevent herpes zoster infection. The one member who voted “No” noted concerns regarding the risk of infection with tofacitinib. Please see the transcript for details of the committee discussion.

5. **VOTE:** Do you recommend approval of the proposed dose of tofacitinib for the treatment of adult patients with active psoriatic arthritis?

Vote Result: Yes: 10 No: 1 Abstain: 0

***Committee Discussion:** The majority of the committee (10 to 1) recommended the approval of the proposed dose of tofacitinib for the treatment of adult patients with active psoriatic arthritis. One committee member noted that there is not enough evidence to conclude a positive effect on radiographic progression outcomes, but acknowledged that the study was not designed to demonstrate this statistically. Committee members reiterated that if approved, the label should not include any claim or implied claim regarding a positive effect on radiological progression. The one member who voted “No” noted concerns with the efficacy and safety. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 12:30 p.m.