



NDA 203214/S-008

**SUPPLEMENT APPROVAL  
REMOVE REMS ELEMENT  
REMS ASSESSMENT PLAN REVISION**

PF PRISM C.V.  
c/o Pfizer, Inc.  
445 Eastern Road  
Groton, CT 06340

Attention: James T. Mayne, PhD, DABT  
Senior Director, Worldwide Safety and Regulatory

Dear Dr. Mayne:

Please refer to your Supplemental New Drug Application (sNDA) dated and received November 7, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Xeljanz (tofacitinib) 5 mg tablets.

We also refer to our REMS Modification Notification letter, dated September 9, 2014, in which we notified you that the Medication Guide should be removed as an element of the REMS to decrease the burden on the healthcare delivery system of complying with the REMS. We also notified you that the REMS assessment plan should be revised.

This Prior Approval Supplemental New Drug Application proposes to eliminate the requirement for the approved Medication Guide as an element of the approved Xeljanz REMS.

We have completed our review of this supplemental application. It is approved, effective on the date of this letter.

**RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

The REMS for Xeljanz (tofacitinib) was originally approved on November 6, 2012, and REMS modifications were approved on November 8, 2013 and March 26, 2014. The REMS consists of a Medication Guide, communication plan, and timetable for submission of assessment of the REMS.

Your proposed modification to the REMS consists of eliminating the requirement for the Medication Guide as an element of the REMS.

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in

21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of Xeljanz (tofacitinib) outweigh the risks.

Therefore, we agree with your proposal, and a Medication Guide is no longer required as part of the REMS for Xeljanz (tofacitinib).

Your proposed modified REMS submitted on November 7, 2014 and appended to this letter is approved.

The modified REMS consists of a communication plan and a timetable for submission of assessments for the REMS.

We remind you that the Medication Guide will continue to be part of the approved labeling for Xeljanz (tofacitinib) in accordance with 21 CFR 208.

The timetable for submission of assessments of the REMS will remain the same as that approved on November 6, 2012.

### **REMS ASSESSMENT PLAN**

Our March 26, 2014, Supplement Approval/REMS Modification Approval, letter described the REMS assessment plan. As described in our September 9, 2014, letter, the REMS assessment plan should be revised to remove the Survey of Patient Knowledge and Understanding since the REMS goals will be revised to only include healthcare providers.

The revised REMS assessment plan should include, but is not limited to the following:

- i. A survey of physicians' knowledge and understanding of the serious risks of tofacitinib will be made.
- ii. A survey of pharmacists' knowledge and understanding of the serious risks of tofacitinib will be made.
- iii. An assessment and conclusions regarding the success of the REMS in meeting the stated goals will be made.
- iv. An assessment of the communication plan including:
  - o The source(s) of the list of healthcare professionals to whom the Dear Healthcare Provider Letter, Dear Pharmacist Letter are distributed
  - o Journal information pieces published, including date and journal name, volume, and issue
  - o The date of launch of the communication plan (Dear Healthcare Provider Letter, Dear Pharmacist Letter, website, and journal information pieces)

- The number of recipients of the Dear Healthcare Provider and Dear Pharmacist Letters
- Date(s) of distribution of the Dear Healthcare Provider and Dear Pharmacist Letters
- The number of returned and refused letters

The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

**NDA 203214 REMS CORRESPONDENCE  
(insert concise description of content in bold capital letters, e.g.,  
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT  
METHODOLOGY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**NDA 203214 REMS ASSESSMENT  
  
NEW SUPPLEMENT FOR NDA 203214  
PROPOSED REMS MODIFICATION  
  
NEW SUPPLEMENT (NEW INDICATION FOR USE)**

**FOR NDA 203214  
REMS ASSESSMENT  
PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

**REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

**REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Carol F. Hill, Safety Regulatory Health Project Manager, at (301) 796-1226.

Sincerely,

*{See appended electronic signature page}*

Sally Seymour, MD  
Deputy Director for Safety  
Division of Pulmonary, Allergy, and Rheumatology  
Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

ENCLOSURES:  
REMS

-----  
**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
-----

/s/  
-----

CAROL F HILL  
02/11/2015

SALLY M SEYMOUR  
02/11/2015