CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213082Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	July 2, 2020
Application Type and Number:	NDA 213082
Product Name and Strength:	Xeljanz (tofacitinib) oral solution, 1 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Pfizer
Panorama #:	2020-39102189
DMEPA Safety Evaluator:	Teresa McMillan, PharmD
DMEPA Team Leader:	Idalia Rychlik, PharmD
DMEPA Associate Director of Nomenclature and Labeling:	Mishale Mistry, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Xeljanz, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A respectively. Pfizer did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Xeljanz (tofacitinib) immediate-release tablets and Xeljanz XR (tofacitinib) extended-release tablets were approved on November 6, 2012 and February 23, 2016, respectively. Pfizer submitted the name Xeljanz, for the proposed new dosage form of an oral solution and proposed indication of Polyarticular Course Juvenile Idiopathic Arthritis for review under NDA 213082 on April 10, 2020.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on April 10, 2020.

Table 1. Relevant Product Information for Xeljanz

Product Name	**Xeljanz (NDA 203214)**	**Xeljanz XR (NDA 208246)**	**Xeljanz (NDA 213082)**
Initial Approval Date	November 6, 2012	February 23, 2016	N/A – proposed
Intended Pronunciation	zell-jans		
Active Ingredient	tofacitinib		
Indication	• Rheumatoid Arthritis • Psoriatic Arthritis • Ulcerative Colitis • Polyarticular Course Juvenile Idiopathic Arthritis*		
Route of Administration	oral		
Dosage Form	immediate-release tablets	extended-release tablets	oral solution
Strength	5 mg, 10 mg	11 mg, 22 mg	1 mg/mL*
Dose and Frequency	*Rheumatoid Arthritis* • XELJANZ 5 mg twice daily or XELJANZ XR 11 mg once daily. • Recommended dosage in patients with moderate and severe renal impairment or moderate hepatic impairment is XELJANZ 5 mg once daily. *Psoriatic Arthritis (in combination with nonbiologic DMARDs)* • XELJANZ 5 mg twice daily or XELJANZ XR 11 mg once daily		

<table>
<tr><th>Product Name</th><th>Xeljanz
(NDA 203214)</th><th>Xeljanz XR
(NDA 208246)</th><th>Xeljanz
(NDA 213082)</th></tr>
<tr><td></td><td colspan="3">

Recommended dosage in patients with moderate and severe renal impairment or moderate hepatic impairment is XELJANZ 5 mg once daily.

Ulcerative Colitis

Induction: XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily for 8 weeks; evaluate patients and transition to maintenance therapy depending on therapeutic response. If needed, continue XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily for a maximum of 16 weeks. Discontinue XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily after 16 weeks if adequate therapeutic response is not achieved.
Maintenance: XELJANZ 5 mg twice daily or XELJANZ XR 11 mg once daily. For patients with loss of response during maintenance treatment, XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily may be considered and limited to the shortest duration, with careful consideration of the benefits and risks for the individual patient. Use the lowest effective dose needed to maintain response.
Dosage adjustment is needed in patients with moderate and severe renal impairment or moderate hepatic impairment: see full prescribing information.

Polyarticular Course Juvenile Idiopathic Arthritis*

XELJANZ/XELJANZ Oral Solution 5 mg twice daily or weight-based equivalent twice daily
Recommended Tofacitinib Dosing for Pediatric Subjects with pJIA

<table>
<tr><th>Body Weight (kg)</th><th>Dosage Regimen</th></tr>
<tr><td>10 to <20</td><td>3.2 mg (3.2 mL oral solution) BID</td></tr>
<tr><td>20 to <40</td><td>4 mg (4 mL oral solution) BID</td></tr>
<tr><td>≥40</td><td>5 mg (one 5 mg tablet or 5 mL oral solution*) BID</td></tr>
</table>
Abbreviations: BID = twice daily.
*Patients treated with 5 mL XELJANZ Oral Solution may be switched to a XELJANZ 5 mg tablet.
Dosage adjustment is needed in patients with moderate and severe renal impairment or moderate hepatic impairment: see full prescribing information.
</td></tr>
<tr><td>How Supplied</td><td>Immediate-release 5 mg: White, round, immediate-release film-coated tablets,</td><td>Extended-release 11 mg: Pink, oval, extended-release film-coated tablets</td><td>Clear, colorless solution:
Bottle fill volume-240 mL</td></tr>
</table>

Product Name	Xeljanz (NDA 203214)	Xeljanz XR (NDA 208246)	Xeljanz (NDA 213082)
	debossed with "Pfizer" on one side, and "JKI 5" on the other side: Bottle sizes 28 and 60 count *Immediate-release 10 mg:* Blue, round, immediate-release film-coated tablets, debossed with "Pfizer" on one side, and "JKI 10" on the other side: Bottle sizes 28, 60, 180 count	with a drilled hole at one end of the tablet band and "JKI 11" printed on one side of the tablet: Bottles sizes 14, 30 count *Extended-release 22 mg:* Beige, oval, extended-release film-coated tablets with a drilled hole at one end of the tablet band and "JKI 22" printed on one side of the tablet: Bottle size 30	It is packaged in HDPE bottles as follows: Each bottle is packaged with one press-in bottle adapter and one 5 mL oral dosing syringe with 3.2 mL, 4 mL, and 5 mL gradations. The press-in bottle adapter and oral dosing syringe are not made with natural rubber latex
Storage	20°C to 25°C (68°F to 77°F). [See USP Controlled Room Temperature	20°C to 25°C (68°F to 77°F). [See USP Controlled Room Temperature	Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C and 30°C (between 59°F and 86°F). [See USP Controlled Room Temperature]. Store in the original bottle and carton to protect from light. Use contents of bottle within 60 days of opening. Discard remaining oral solution after 60 days.

*new proposed indication and strength

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Xeljanz.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Xeljanz would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Rheumatology and Transplant Medicine (DRTM) concurred with the findings of OPDP's assessment for Xeljanz.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Xeljanz.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[a].

2.2.2 Comments from Other Review Disciplines at Initial Review

In response to the OSE, April 28, 2020 e-mail, the Division of Rheumatology and Transplant Medicine (DRTM) did not forward any comments or concerns relating to Xeljanz at the initial phase of the review.

2.2.3 Medication Error Data Selection of Cases

On May 11, 2020, we searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving ***Xeljanz*** that would be relevant for this review.

Table 2. FAERS Search Strategy

FAERS Field	Search Terms
Initial FDA Receive Dates	11/06/2012* to 05/01/2020
Product Name	Xeljanz
Verbatim Name(s)	---
Product Active Ingredient	---
Drug Role	Primary Suspect
Event	DMEPA Official PNR Name Confusion Search Terms
Country (derived)	USA

*Xeljanz approval date

Each report was reviewed for relevancy and duplication. Duplicates were merged into a single case. The NCC MERP Taxonomy of Medication Errors was used to code the case outcome and error root causes when provided by the reporter.

The search yielded no relevant cases of name confusion with the proprietary name, Xeljanz.

[a] USAN stem search conducted on April 30, 2020.

2.2.4 Safety Analysis of Multiple Dose Forms Under the Same Proprietary Name

Xeljanz (tofacitinib) immediate release tablets (NDA 203214) and Xeljanz XR (tofacitinib) extended release tablets (NDA 208246) were approved on November 6, 2012 and February 23, 2016, respectively. The immediate release formulation is available in strengths of 5 mg and 10 mg and the extended release formulation is available in strengths of 11 mg and 22 mg. Under NDA 213082, Pfizer proposes a new dosage form, a 1 mg/mL oral solution, to be marketed under the same proprietary name, Xeljanz. Xeljanz (tofacitinib) oral solution is intended for the proposed indication Polyarticular Course Juvenile Idiopathic Arthritis. The newly proposed pediatric indication utilizes weight-based doses of 3.2 mg, 4 mg or 5 mg; therefore an age appropriate oral solution was developed.

We considered the appropriateness of using the proprietary name, Xeljanz, for the oral solution formulation proposed under NDA 213082, which would represent a product line extension. We note that the proposed oral solution, currently approved immediate release and extended release tablets share the same active ingredient, indications, route of administration, and there is some overlap in dose and frequency of administration. However, we considered instances where the dosage form is not provided and the prescription is written for either a 5 mg or 10 mg dose as we note that either the immediate release tablet formulation or the oral solution may be dispensed to achieve that dose. Per the clinical and clinical pharmacology team, the immediate release 5 mg and 10 mg tablets and the proposed oral formulation are equivalent in on a milligram per milligram basis when switching between the formulations and have no clinically significant differences. Additionally, we also considered that if Xeljanz XR was prescribed, there is a risk that the modifier 'XR' is omitted or overlooked[b], and therefore, Xeljanz oral solution may be dispensed. In this instance, a patient may receive Xeljanz 11 mL once daily of the oral solution instead of 11 mg once daily of the extended release tablet formulation. Per the clinical and clinical pharmacology team, Pfizer did not provide a "*head to head comparison for the extended release tablet and [oral] solution*". However, it is noted that "*the [oral] solution is bioequivalent to the immediate release tablet, i.e., a daily dose of 10 mg/10 mL solution is equivalent to 10 mg immediate release tablet and therefore 11 mg extended release tablet*". If a patient receives Xeljanz 11 mL once daily of the oral solution instead of 11 mg once daily of the extended release tablet formulation, per clinical pharmacology "*the patient will have 10% more daily dose"*; however, "*there would not be a grave impact on efficacy or safety with short term use*".

We note that it is common and accepted practice to have a product line with multiple dosage forms share one proprietary name. An alternative option to distinguish the proposed oral solution from the currently marketed formulations is to use a different root name. However, marketing the new product under a unique proprietary name also carries risk of medication errors, such as therapeutic duplication and over doses. These errors may have greater associated safety risks than the risks discussed above. Another option would be to use the same root name, Xeljanz, with a modifier to distinguish between the formulations. However, as stated above, omission and oversight of a modifier is cited in literature as a common cause of medication error[c] and therefore, the risks in this approach would be same as the proposed approach of using the same proprietary

[b] Lesar TS. Prescribing Errors Involving Medication Dosage Forms. J Gen Intern Med. 2002; 17(8): 579-587.

[c] Lesar TS. Prescribing Errors Involving Medication Dosage Forms. J Gen Intern Med. 2002; 17(8): 579-587.

name. Furthermore, we have not retrieved any medication error name confusion reports involving Xeljanz (see Section 2.2.4).

Therefore, for the aforementioned reasons and given the precedent for using a single proprietary name to market multiple dosage forms, DMEPA finds that the proprietary name, Xeljanz, for the oral solution, although not free from the risk of error, offers a safer approach to naming this product. In addition, the residual risk of confusion between the oral solution, immediate release tablets, and extended release tablets may be mitigated through labels and labeling interventions.

2.2.5 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Rheumatology and Transplant Medicine (DRTM) via e-mail on June 29, 2020. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Rheumatology and Transplant Medicine (DRTM) on July 1, 2020, they stated no additional concerns with the proposed proprietary name, Xeljanz.

3 CONCLUSION

The proposed proprietary name, Xeljanz, is acceptable.

If you have any questions or need clarifications, please contact Mathew Davis, OSE project manager, at 240-402-4559.

3.1 COMMENTS TO PFIZER

We have completed our review of the proposed proprietary name, Xeljanz, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your submission, received on April 10, 2020, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. ***USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)***

   USAN Stems List contains all the recognized USAN stems.

APPENDICES

Appendix A1: Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

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