CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761262Orig1s000

PROPRIETARY NAME REVIEW(S)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

Memorandum

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Date: 2022.02.25 13:13:18 -05'00'

Subject: Evaluation of the nonproprietary name for BLA 761262

AbbVie is proposing a new indication for moderately to severely active Crohn's disease (CD) to their currently approved Skyrizi (risankizumab-rzaa) biological product pursuant to Section 351(a) of the Public Health Service Act. To that effect, AbbVie submitted a new Biologics License Application (BLA 761262) for induction treatment and a new efficacy supplement to BLA 761105/S-016 for maintenance treatment of CD.

Skyrizi (risankizumab-rzaa) (BLA 761105) is an interleukin-23 antagonist, indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. Skyrizi is currently supplied as an injection formulation as 75 mg/0.83 mL [redacted] (b) (4)) and 150 mg/mL single-dose pre-filled syringes and 150 mg/mL single-dose prefilled pens, for subcutaneous injection to be administered at Week 0, Week 4, and every 12 weeks

thereafter. AbbVie is the license holder for BLA 761105 and applicant for BLA 761262. BLA 761262 introduces a new indication, induction treatment of moderately to severely active Crohn's disease (CD), using a new injection formulation for intravenous administration. AbbVie is proposing a 600 mg/10 mL (60 mg/mL) injection formulation in single-dose vials for the induction treatment of CD, dosed at 600 mg by intravenous infusion at Weeks 0, 4, and 8. AbbVie has also submitted a supplement to BLA 761105 for the maintenance treatment of moderately to severely active Crohn's disease (CD), administered subcutaneously using an on-body injector (OBI) with 150 mg/mL pre-filled cartridge. Both the proposed intravenous formulation and the subcutaneous formulation contain comparable risankizumab drug substance and identical types and concentrations of excipients as the 150 mg/mL formulation of risankizumab-rzaa manufactured by AbbVie and approved under BLA 761105. The risankizumab drug substance process used in the manufacture of the proposed vial presentation is similar to the drug substance process used during the manufacture of the approved pre-filled syringe and proposed pre-filled cartridge, except for (b) (4) However, drug substances manufactured by these processes are alike such that additional clinical data would not be needed to support implementation of the proposed risankizumab drug substance process in the manufacture of the subcutaneous formulation. The new marketing application for the proposed intravenous formulation cross refences BLA 761105.

Under FDA's prescription drug user fee bundling policy, different formulations should be submitted in separate original applications unless the products are quantitatively and qualitatively identical (drugs) or alike (biological products) in composition[a]. After reviewing the compositions of the proposed and marketed risankizumab-rzaa formulations, the Office of Biotechnology Products (OBP) determined that these biological products are alike in composition for user fee purposes, and the proposed new formulation for intravenous administration could be managed as a sBLA submission. In addition, under the bundling policy, two different indications and routes of administration can be included under a single BLA. Although the Agency recommended submission of an sBLA, AbbVie submitted the intravenous formulation as a separate BLA.

AbbVie is proposing to have a single USPI that would include all approved indications. AbbVie is also proposing to have the same proprietary name, Skyrizi, for both BLAs.

FDA issued a final guidance entitled Nonproprietary Naming of Biological Products on January 13, 2017 stating the Agency's intention to designate proper names that include four-letter distinguishing suffixes for biological products[b]. This 351(a) application (BLA 761262) is within the scope of this guidance.

Risankizumab-rzaa was the proper name designated in the license for BLA 761105. We carefully considered whether the nonproprietary name for BLA 761262 should include a different distinguishing suffix than that designated for BLA 761105 or whether the proper name

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[a] Guidance for Industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees (Dec. 2004), available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf

[b] Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

considerations for this product warrant departing from the January 2017 final guidance and designating the same proper name (*i.e.*, risankizumab-rzaa) for BLA 761262. Among the factors we have considered are the following:

1. Based on the Office of Biotechnology Products' evaluation, the drug substance (DS) in the approved formulation and the proposed formulation is essentially unchanged with respect to product quality attributes. The same reference standard is used for the characterization, release and stability testing of the DS and drug product (DP) in the formulations.
2. AbbVie is proposing to have a single USPI that includes all indications and the same proprietary name. The naming convention of using the same proprietary name for different indications, different formulations or routes of administration is not uncommon and has been found acceptable in the past. We have not identified any safety or misbranding concerns that would render the proprietary name, Skyrizi, unacceptable for BLA 761262.
3. We noted above that this new formulation could also be managed under a supplement to the current BLA, which would have not resulted in a change to the proper name under the approach to nonproprietary naming described in the final guidance.
4. As noted in the final Nonproprietary Naming of Biological Products guidance, distinguishing nonproprietary names will facilitate pharmacovigilance when other means to track a specific dispensed product are not readily accessible or available; facilitate accurate identification of these biological products by health care practitioners and patients; and help prevent inadvertent substitution that may lead to medication errors. As the guidance explains, a distinguishing suffix supports the tracking of product-specific events over time, our ability to track adverse events to a specific manufacturer (and as appropriate, to a manufacturing lot or manufacturing site for a particular biological product), and our ability to detect safety signals throughout the life cycle of a product so that the Agency and the manufacturer can act swiftly and in a targeted manner to identify and address a problem. As noted above, AbbVie is the license holder for BLA 761105 and applicant for BLA 761262.

Given the above factors, a different nonproprietary name for BLA 761262 will not be designated in this particular case. The addition of a different suffix to the nonproprietary name for BLA 761262, could create confusion and would not further the goals of the naming convention.

This memorandum documents the justification for and supervisory concurrence with the decision to depart from the recommendations in the January 2017 final Nonproprietary Naming of Biological Products guidance in approving the same nonproprietary name for BLA 761262[a]. We based this determination upon consideration of all the factors outlined above. If any of the

[a] See 21 C.F.R. § 10.115(d)(3) ("Although guidance documents do not legally bind FDA, they represent the agency's current thinking. Therefore, FDA employees may depart from guidance documents only with appropriate justification and supervisory concurrence.").

factors enumerated above were to change, we may reconsider the appropriate proper name format for this BLA. The following comments will be communicated to AbbVie in an advice letter.

Comments for AbbVie for BLA 761262

We have determined that risankizumab-rzaa will be the proper name designated in the license should your 351(a) BLA be approved during this review cycle.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

CARLOS M MENA-GRILLASCA
02/25/2022 01:21:29 PM

IRENE Z CHAN
02/25/2022 03:25:01 PM

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)

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:	January 3, 2022
Application Type and Number:	BLA 761262
Product Name and Strength:	Skyrizi (risankizumab-rzaa) injection, 600 mg/10 mL (60 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	AbbVie Inc. (AbbVie)
PNR ID #:	2021-1044724185
DMEPA 1 Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA 1 Team Leader:	Idalia E. Rychlik, PharmD
DMEPA 1 Associate Director for Nomenclature and Labeling:	Mishale Mistry, PharmD, MPH

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Skyrizi, 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. AbbVie did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Skyrizi (risankizumab-rzaa) injection was approved on April 23, 2019 under BLA 761105 for the treatment of moderate-to-severe plaque psoriasis (PsO) in adults who are candidates for systemic therapy or phototherapy. Supplemental BLAs (sBLAs) for a 150 mg/mL formulation of Risankizumab-rzaa in a prefilled syringe (PFS) and an autoinjector (AI) were approved on April 26, 2021.

On September 16, 2021, AbbVie submitted the name, Skyrizi*** for review under BLA 761262 for the proposed indication of for the treatment of moderately to severely active Crohn's Disease (CD) in patients aged 16 years and older and a proposed new formulation of 600 mg/10 mL vial for the intravenous induction dosing regimen for CD.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on September 16, 2021.

Table 1. Relevant Product Information for Skyrizi		
Product Name	Skyrizi (BLA 761262)	Skyrizi (BLA 761105)
Intended Pronunciation	sky-RIZZ-ee	
Initial Approval Date	N/A	April 23, 2019
Active Ingredient	Risankizumab-rzaa	
Indication	for the treatment of moderately to severely active Crohn's disease in patients 16 years of age and older.	for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.
Route of Administration	Intravenous infusion	Subcutaneous injection
Dosage Form	injection	
Strength	600 mg/10 mL (60 mg/mL)	150 mg/mL, 75 mg/0.83 mL
Dose and Frequency	600 mg at week 0, 4, and 8 followed by 360 mg at week 12 and every 8 weeks thereafter	150 mg at week 0, 4, and every 12 weeks thereafter

How Supplied	Carton of 1 single-dose vial	150 mg/mL: Carton of 1 single-dose pen or PFS 75 mg/0.83 mL: Carton of 2 single-dose PFS
Storage	Store in a refrigerator at 2°C to 8°C (36°F to 46° F). Do not freeze. Do not shake. Keep prefilled pens and prefilled syringes in the original cartons to protect from light.	

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Skyrizi would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 1 (DMEPA 1) and the Division of Gastroenterology (DG) concurred with the findings of OPDP's assessment for Skyrizi.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

AbbVie did not provide a derivation or intended meaning for the proposed proprietary name, Skyrizi, in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e., a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On October 4, 2021, the Division of Gastroenterology (DG) did not forward any comments or concerns relating to Skyrizi at the initial phase of the review.

[a] USAN stem search conducted on November 15, 2021.

2.2.4 Medication Error Data Selection of Cases

On December 1, 2021, 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 Skyrizi that would be relevant for this review.

Table 2. FAERS Search Strategy	
Product Name	RISANKIZUMAB, RISANKIZUMAB-RZAA (Product Active Ingredient)
Date Limit	N/A
Event	DMEPA Official PNR Name Confusion Search Terms
Country (derived)	USA

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 cases of name confusion with the proprietary name Skyrizi.

2.2.5 Multiple Dosage Forms Under a Single Proprietary Name

Under BLA 761262 AbbVie proposes to introduce a single dose vial presentation of risankizumab-rzaa injection, to be marketed under the same name as the currently approved product, Skyrizi, in a strength of 600 mg/10 mL (60 mg/mL) for intravenous administration. Skyrizi is currently available for the treatment of plaque psoriasis as a single dose prefilled syringe in strengths of 75 mg/0.83 mL and 150 mg/mL and a single dose prefilled pen in a strength of 150 mg/mL.

We note that the proposed Crohn's Disease (CD) induction dose of 600 mg could be inadvertently achieved using the subcutaneous formulation (four 150 mg/mL prefilled syringe (PFS) or four 150 mg/mL autoinjector (AI)). We also note that the plaque psoriasis dose of 150 mg could be achieved using the proposed intravenous formulation (i.e., 2.5 mL of the 600 mg/10 mL formulation). Thus, we have concerns that the subcutaneous and intravenous formulations may be confused for one another. For example, if a prescriber ordered the 600 mg induction dose for CD, four 150 mg/mL PFS could be administered intravenously or subcutaneously (wrong formulation and wrong route of administration errors).

DMEPA shared the above concerns with the Applicant via an information request (IR) dated December 17, 2021 and requested that Abbvie 1) describe the clinical consequences of medication errors associated with inadvertent formulation substitution and 2) provide their plans to mitigate such errors. In response to the Agency's IR, Abbvie stated the following:

"While the same risankizumab active substance is used in both the 600 mg vial and 150 mg/mL pre-filled syringe (PFS), and the formulations include the same excipients, these product

presentations are not intended to be used in an interchangeable manner. The BLA 761262 application includes data demonstrating the analytical and pharmacokinetic (PK) comparability between the 90 mg/mL and 60 mg/mL formulations, and between the 300 mg vial and 600 mg vial presentations, for the purposes of bridging between the Phase 3 clinical and to-be-commercialized presentations." Furthermore, "*The likelihood of the specific medication error scenarios described by the Agency is considered very low based on package labeling (i.e., dose, strength, and route of administration) and logistical considerations. Regarding package labeling, the subcutaneous (SC) presentations are described and labeled indicating they are "FOR SUBCUTANENEOUS USE ONLY." The intravenous (IV) presentation's package and labeling contains wording "FOR INTRAVENOUS USE ONLY," "Must be diluted prior to use," and "Single dose vial."* We note that the Applicant intends to distribute the 600 mg/10 mL (60 mg/mL) vial presentation directly to physicians, infusion centers, and hospital pharmacies, thus mitigating any confusion at the patient level.

It is a common and accepted practice to have a product line with multiple dosage forms and presentations managed under one proprietary name. The differences in dose and maintenance dose frequency (600 mg at week 0, 4, and 8 followed by 360 mg at week 12 and every 8 weeks thereafter versus 150 mg at week 0, 4, and every 12 weeks thereafter) and route of administration (intravenous infusion vs. subcutaneous) will help to differentiate between the presentations. Additionally, the proposed intravenous formulation requires preparation and administration by a healthcare provider for the induction phase of the treatment. In the case of Skyrizi, the residual risk of confusion between the different presentations of the product may be mitigated through labels and labeling intervention.

Furthermore, we note that through our routine monitoring we have not identified any medication errors involving name confusion with the proprietary name Skyrizi. Based on the totality of the information provided, we find that label and labeling mitigations can adequately address any risk of product confusion as described above. Our review of product labeling and packaging will be conducted under a separate cover. Therefore, in this case, we find that the multiple formulations/dosage forms and strengths can be managed under one proprietary name and we do not have concerns with extending the use of Skyrizi as a proprietary name for the intravenous infusion formulation.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

On January 3, 2022, DMEPA 1 communicated our determination to the Division of Gastroenterology.

3 CONCLUSION

The proposed proprietary name, Skyrizi, is acceptable.

If you have any questions or need clarifications, please contact Alvis Dunson, OSE project manager, at 301-796-6400.

3.1 COMMENTS TO ABBVIE INC.

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

If any of the proposed product characteristics as stated in your submission, received on September 16, 2021, 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.

2. *Drugs@FDA*

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. Misbranding Assessment: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. Safety Assessment: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [b]

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.

[b] National Coordinating Council for Medication Error Reporting and Prevention. https://www.nccmerp.org/about-medication-errors Last accessed 10/05/2020.

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/s/

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