DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Drug Evaluation and Research
OND / OII / DRTM
10903 New Hampshire Ave.
Silver Spring, MD 20993

MEMO TO FILE

Application.: BLA 761071 Supplement 11

Reviewer: Anil Rajpal, M.D., M.P.H.
Clinical Team Leader
Division of Rheumatology and Transplant Medicine

Submitted: September 28, 2021

Reviewed: March 28, 2022

Product: Hyrimoz (adalimumab-adaz)

Indication: No new indications are sought with this supplement

Sponsor: Sandoz Inc.

Submission: CMC supplement for a new strength (10 mg/0.2 mL)

Synopsis:

The current sBLA (761071/11) is a CMC supplement for a 10 mg/0.2 mL pre-filled syringe (PFS) for pediatric polyarticular juvenile idiopathic arthritis (pJIA) patients who weigh 10 kg to less than 15 kg. OPQ has recommended approval of this supplement. No clinical data were submitted with this supplement. Although the Applicant did not propose to update the Dosage and Administration section with instructions for dosing with the new presentation (10 mg/0.2 mL PFS), the review team has recommended adding such instructions for pJIA patients who weigh 10 kg to less than 15 kg. This sBLA (761071/11) for the 10 mg/0.2 mL PFS (for pediatric patients who weigh 10 kg to less than 15 kg) (b) (4) with the approval of the current sBLA (761071/11), PREA PMR 3506-4 will only be partially fulfilled.

Regulatory History:

Original BLA: On October 30, 2018, BLA 761071 for adalimumab-adaz, a biosimilar to US-licensed Humira, was approved for treatment of rheumatoid arthritis, juvenile idiopathic arthritis (JIA) (4 years of age and older), psoriatic arthritis, ankylosing spondylitis, adult Crohn's disease, ulcerative colitis, and plaque psoriasis. The approved presentations were a 40 mg/0.8 mL single-use PFS and a 40 mg/0.8 mL single-use pre-filled pen. The following PREA PMR (PMR 3506-4) was issued with this

[1] https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/761071Orig1s000ltr.pdf

approval:[2]

> "Develop a presentation that can be used to accurately administer Hyrimoz (adalimumab-adaz) to pediatric patients who weigh less than 30 kg" (The final report submission milestone date was September 2021.)

(b) (4)

Review:

On September 28, 2021, the current CMC supplement (sBLA 761071/11) was submitted. This sBLA proposes a Hyrimoz 10 mg/0.2 mL PFS for pediatric pJIA patients who weigh 10 kg to less than 15 kg.

Drug Substance: The drug substance (DS) is the same for the proposed Hyrimoz 10 mg/0.2 mL PFS and the approved Hyrimoz 40 mg/0.8 mL PFS.

Drug Product: The current sBLA (sBLA 761071/11) proposes the introduction of the Sandoz GmbH Schaftenau manufacturing site for the drug product (DP). (b) (4) An Information Request (IR) was sent on January 6, 2022, for the current sBLA (sBLA 761071/11) requesting that the Applicant submit supporting information for this manufacturing site related to the Hyrimoz 10 mg/0.2 mL PFS; the response to this IR was received on January 19, 2022, and was considered a major amendment extending the BSUFA goal date by 2 months. (b) (4)

Finished Dosage Form: The current sBLA proposes the addition of the finished dosage form (FDF) site (b) (4)

The Office of Biotechnology Products (OBP) and the Office of Pharmaceutical Manufacturing Assessment (OPMA) recommended an approval action (see OBP review dated March 8, 2022 and OPMA review dated March 10, 2022). The Center for Devices and Radiological Health (CDRH) concluded that the device constituent parts of the combination product are approvable (see CDRH Review dated February 14, 2022).

PREA PMR:

The current CMC supplement (sBLA 761071/11; for the Hyrimoz 10mg/0.2 mL PFS) (b) (4) intended to fulfill PREA PMR 3506-4 ("Develop a presentation that can be used to accurately administer Hyrimoz (adalimumab-adaz) to pediatric patients who weigh less than 30 kg"; final report submission milestone date of September 2021).

Although the current sBLA (761071/11) for the Hyrimoz 10 mg/0.2 mL PFS (for pediatric patients who weigh 10 kg to less than 15 kg) will receive an approval recommendation, (b) (4) the approval of the current sBLA (761071/11), PREA PMR 3506-4 will only be partially fulfilled.

[2] https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/761071Orig1s000ltr.pdf

Labeling:

The Applicant's proposed changes to the PI included the following:

- Section 3 Dosage Forms and Strengths
  - Information about the Hyrimoz 10 mg/0.2 mL PFS including volume of pre-filled glass syringe, gauge of needle, and length of needle was added.
- Section 11 Description
  - Description of the Hyrimoz 10 mg/0.2 mL PFS including list of ingredients was added in alignment with the current description of the Hyrimoz 40 mg/0.8 mL PFS and the 40 mg/0.8 mL pre-filled pen.
- Section 16 How Supplied/Storage and Handling
  - Information about the Hyrimoz 10 mg/0.2 mL PFS including the contents of PFS cartons, number of units per carton, and NDC number was added.

The Review Team agreed with the above proposed changes, and recommended the addition of dosing instructions as described below.

- Section 2 Dosage and Administration:
  - The recommended dose of 10 mg every other week for patients with polyarticular juvenile idiopathic arthritis who weigh 10 kg to less than 15 kg was added.
  - A statement that there is no dosage form for Hyrimoz that allows weight-based dosing for pediatric patients 15 kg to less than 30 kg was added.

The Applicant's proposed changes to the Medication Guide (MG) included the addition of the Hyrimoz 10 mg/0.2 mL prefilled syringe to the section titled "What are the ingredients in HYRIMOZ". The Review Team agreed with these changes.

The Division of Medication Error Prevention and Analysis (DMEPA) provided recommendations for the PI and carton and container labeling. The final labeling will reflect their recommendations (see DMEPA Reviews dated December 28, 2021, and January 7, 2022).

Overall Conclusions:

FDA has also determined that the Applicant has provided adequate data and information to support a demonstration that Hyrimoz 10 mg/0.2 mL is highly similar to US-Humira 10 mg/0.2 mL, notwithstanding minor differences in clinically inactive components.

FDA has further determined that the data and information provided by the Applicant in the BLA, including this supplement—including the data submitted from the clinical development program and the analytical similarity and comparability data—support a demonstration of no clinically meaningful differences between Hyrimoz 10 mg/0.2 mL and US-Humira 10 mg/0.2 mL. The conditions of use for Hyrimoz 10 mg/0.2 mL have been previously approved for US-Humira 10 mg/0.2 mL, and the strength, dosage form, and route of administration of Hyrimoz 10 mg/0.2 mL are the same as those of US-Humira 10 mg/0.2 mL.

The totality of the data and information provided in the BLA, including this supplement, support licensure of Hyrimoz 10 mg/0.2 mL PFS as a biosimilar to US-Humira 10 mg/0.2 mL PFS.

Postmarketing requirements 3506-1, 3506-2, 3506-3 and 3506-4 in the October 30, 2018, approval letter, are still open.

Action:

The recommended action of this CMC supplement is approval.

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/

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