Collaborative Clinical, Cross-Discipline Team Leader, and Division Summary Memo of BLA 761024/S-017

Date	See Electronic Stamp Date
From	Carol Kim, PharmD, Clinical Reviewer (OTBB) Thomas Herndon, MD, CDTL (OTBB) Wiley A. Chambers, MD, Division Director (DO)
Subject	351(k) BLA Category B supplement to add the Uveitis indication
BLA # and Supplement#	761024/S-017
Applicant	Amgen
Date of Submission	March 14, 2023
BsUFA Goal Date	July 14, 2023
Product Code Name	ABP 501
Nonproprietary Name	adalimumab-atto
Proprietary Name	Amjevita
Reference Product	Humira (adalimumab) (U.S.-licensed Humira, US-Humira)
Applicant Proposed Indication(s)/Population(s)	Uveitis: Treatment of non-infectious intermediate, posterior, and panuveitis in adults
Applicant Proposed Dosing Regimen(s)	Same as US-Humira dosing for the respective indications
Recommended Indication(s)/Population(s)	Uveitis: Treatment of non-infectious intermediate, posterior, and panuveitis in adults
Recommended Dosing Regimen(s)	Same as US-Humira dosing for the respective indications
Recommendation on Regulatory Action	Approval

1. Introduction

The Applicant, Amgen Inc., submitted a supplemental biologics license application for BLA 761024 (sBLA-017) to expand the indication for Amjevita (adalimumab-atto) to include Uveitis (UV): Treatment of non-infectious intermediate, posterior, and panuveitis in adults. US-Humira's orphan-drug exclusivity for this indication expired on June 30, 2023. Subsequent to the approval of the UV indication in adults, Humira was approved to treat pediatric patients 2 years of age and older with UV. The term of orphan-drug exclusivity for US-Humira for "the treatment of non-infectious intermediate, posterior, and panuveitis in pediatric patients 2 years of age and older" expires on September 28, 2025.

No new clinical information is included nor required for the Applicant's submission. The Applicant has provided a scientific justification for extrapolation to the UV indication and updated labeling to include the additional indication sought for licensure.

2. Background

Amjevita (adalimumab-atto) is a recombinant human immunoglobulin (Ig) G1 monoclonal antibody (mAb) that binds tumor necrosis factor (TNF)-alpha. Amjevita was approved as a biosimilar to US-Humira on September 23, 2016, under section 351(k) of the Public Health Service Act. According to current label dated April 6, 2023, Amjevita is approved for the treatment of:

1. Rheumatoid Arthritis (RA): Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA.
2. Juvenile Idiopathic Arthritis (JIA): Reducing signs and symptoms of moderately to severely active polyarticular JIA in patients 2 years of age and older.
3. Psoriatic Arthritis (PsA): Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA.
4. Ankylosing Spondylitis (AS): Reducing signs and symptoms in adult patients with active AS.
5. Crohn's Disease (CD): Treatment of moderately to severely active Crohn's disease in adults and pediatric patients 6 years of age and older.
6. Ulcerative Colitis (UC): Moderately to severely active ulcerative colitis in adult patients. Limitations of Use: Effectiveness has not been established in patients who have lost response to or were intolerant to TNF-blockers.
7. Plaque Psoriasis (Ps): The treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.
8. Hidradenitis Suppurativa (HS): Moderate to severe hidradenitis suppurativa (HS) in adult patients.

In considering the totality of the evidence for the original BLA submission, review of the data submitted by the Applicant showed that Amjevita is highly similar to US-Humira, notwithstanding minor differences in clinically inactive components, and that there are no clinically meaningful differences between Amjevita and US-Humira in terms of the safety, purity, and potency of the product. The Applicant also provided adequate scientific justification for extrapolation of data and information to support licensure of Amjevita for the non-studied indications sought for approval.

Amjevita is approved in the following strengths and presentations:

- 40 mg/0.8 mL single-dose prefilled SureClick autoinjector
- 40 mg/0.8 mL single-dose prefilled glass syringe
- 20 mg/0.4 mL single-dose prefilled glass syringe
- 10 mg/0.2 mL single-dose prefilled glass syringe

3. CMC/Product Quality

No new product quality information was submitted nor required for this sBLA. There are no CMC or product quality issues that would preclude approval of the indications sought for licensure. According to the Office of Biotechnology Products review dated May 9, 2023, the Applicant's claim for categorical exclusion from the preparation of an environmental assessment under 21 CFR Part 25 is considered appropriate and acceptable.

4. Nonclinical Pharmacology/Toxicology

No new nonclinical pharmacology/toxicology information was submitted nor required for this sBLA. There are no nonclinical pharmacology/toxicology issues that would preclude approval of the indications sought for licensure.

5. Clinical Pharmacology

No new clinical pharmacology information was submitted nor required for this sBLA. There are no clinical pharmacology issues that would preclude approval of the indications sought for licensure.

6. Clinical/Statistical-Efficacy

Amjevita was previously evaluated in comparative clinical studies in subjects with RA (20120262) and Ps (20120263). The data were previously reviewed and summarized in the clinical and statistical reviews of the original BLA by the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP), dated September 7, 2016, and September 15, 2016. No new clinical/statistical efficacy information was submitted nor required for the current sBLA. There are no clinical/statistical efficacy issues that would preclude approval of the indication sought for licensure.

7. Safety

Amjevita was previously evaluated in comparative clinical studies in subjects with RA (20120262) and Ps (20120263), and in healthy subjects in a PK similarity study (20110217). The data were previously reviewed and summarized in the clinical review dated September 7, 2016, of the original BLA by DPARP. No new safety data were submitted nor required for this sBLA. There are no clinical safety issues that would preclude approval of the indication sought for licensure.

8. Considerations for Extrapolation of Biosimilarity in Other Conditions of Use

Amjevita is approved for the treatment of RA, PsA, AS, CD in patients 6 years of age and older, UC, JIA in patients 2 years of age and older, Ps, and HS in adult patients. In this supplement, the applicant submitted justification for extrapolation of the data and information in support of licensure of Amjevita for the treatment of UV in adults and pediatric patients 2 years of age and older (Also, see Section 9 Pediatrics).

Scientific considerations for the extrapolation of data and information to support licensure for UV in adults and pediatric patients 2 years of age and older are outlined below:

1. Biosimilarity has previously been established between Amjevita and US-Humira. The data supporting its approval included extensive comparative analytical characterization data, and comparative PK, efficacy, safety and immunogenicity data.
2. Adequate scientific justification supporting extrapolation of data and information from the original BLA submission that addressed the mechanism of action, PK, immunogenicity, and safety for each non-studied indication for which the applicant previously sought licensure and for which the reference product has been approved.
3. Similar extrapolation of data and information from the original BLA submission applies to the indication that is subject of this supplement. Therefore, in adult and pediatric patients 2 years of age and older with UV between Amjevita and US-Humira:
    a. Similar PK profile would be expected.
    b. Similar immunogenicity would be expected.
    c. Similar safety profile would be expected.
    d. Amgen addressed each of the known and potential mechanisms of action of US-Humira and submitted data to support the conclusion of having the same mechanism for UV, to the extent that the mechanisms of action are known and can reasonably be determined.

In conclusion, the totality of evidence and scientific justification discussed above is adequate to justify extrapolating data and information submitted to this BLA to support licensure of Amjevita for the indication of UV: Treatment of non-infectious intermediate, posterior, and panuveitis in adults.

Note that while the Applicant has also submitted acceptable extrapolation justification for pediatric UV patients 2 years of age and older, FDA has determined that US-Humira is eligible for orphan drug exclusivity for pediatric UV 2 years of age and older. FDA therefore cannot license Amjevita for this indication prior to the expiration of the orphan drug exclusivity on September 28, 2025.

In conclusion, the totality of evidence and scientific justification discussed above is adequate to justify extrapolating data and information submitted to this BLA to support

licensure of Amjevita for the indication of UV: Treatment of non-infectious intermediate, posterior, and panuveitis in adults.

9. Pediatrics

The submission included an Agreed Pediatric Study Plan that included the Applicant's plan for addressing Pediatric Research Equity Act (PREA) requirements for the UV indication.

A term of orphan-drug exclusivity for US-Humira for the "treatment of non-infectious intermediate, posterior, and panuveitis in pediatric patients 2 years of age and older" expires on September 28, 2025. The Applicant proposes to fulfill PREA requirements for pediatric patients 2 years of age and older for this indication with extrapolation of data and information to support licensure of Amjevita for this population; however, FDA cannot license Amjevita for this indication in this age group until US-Humira's orphan-drug exclusivity for it expires on September 28, 2025. The labeling for US-Humira does not contain adequate pediatric information for the UV indication in pediatric patients less than 2 years of age, and no pediatric assessment will be required of the Applicant under PREA for the UV indication in pediatric patients less than 2 years of age.

The Applicant refers to the following guidance for industry: "Questions and Answers on Biosimilar Development and the BPCI Act".

On May 2, 2023, the Pediatric Review Committee (PeRC) reviewed the agreed PSP and agreed with the Applicant's proposal.

10. Other Relevant Regulatory Issues

None at this time.

11. Labeling

The proposed Amjevita prescribing information incorporated relevant data and information from the US-Humira prescribing information, with appropriate modifications. It was determined that the proposed labeling is consistent with the current FDA labeling practice. The labeling has been agreed upon with the Applicant.

12. Postmarketing Recommendations

There are no new safety or efficacy issues identified in this review that warrant further assessment with a postmarketing requirement or commitment.

13. Risk Evaluation and Mitigation Strategies

The review team did not identify a need for Risk Evaluation and Mitigation Strategies (REMS) to ensure the safe use of Amjevita.

14. Recommended Regulatory Action

Approval

15. Division Director Comments

I concur with the team's assessment of the data and information submitted in this supplemental BLA.

No additional data, new PMRs, PMCs, or REMS are required for this supplement.

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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