Office of Therapeutic Biologics and Biosimilars
Clinical, Cross-Discipline Team Leader, and Division Memo

Date	See Electronic Stamp Date
From	Raquel Tapia, MD (Clinical Reviewer, OTBB) Thomas Herndon, MD (CTL/CDTL, OTBB) Raj Nair, MD (Division Signatory, DRTM)
Subject	Cross-Discipline Review for 351(k) BLA
Application Type	Original
BLA/Supplement Number	BLA 761498
Received Date	05/19/2025
BsUFA Goal Date	05/19/2026
Division/Office	Division of Rheumatology and Transplant Medicine (DRTM)/Office of New Drugs (OND) Office of Therapeutic Biologics and Biosimilars (OTBB)
Proprietary Name	Avtozma
Proper Name	Tocilizumab-anoh
Product Code	CT-P47
Reference Product	US-licensed Actemra (tocilizumab)
Pharmacologic Class	Interleukin-6 (IL-6) receptor antagonist
Applicant	Celltrion, Inc.
Applicant Proposed Indication (s)	• Rheumatoid arthritis in adults • Giant cell arteritis in adults • Polyarticular juvenile idiopathic arthritis, pediatric patients 2 years and older • Systemic juvenile idiopathic arthritis, pediatric patients 2 years and older
New Dosing Regimen(s)	Same dosing regimen as US-licensed Actemra
Recommendation on Regulatory Action	Approval

1. Introduction

Celltrion, Inc., (also referred to as “the Applicant” in this review) submitted a second Biologic License Application (BLA) under Section 351(k) of the Public Health Service Act (PHS Act) for Avtozma (tocilizumab-anoh, CT-P47) as a proposed biosimilar to and interchangeable with US-licensed Actemra on May 19, 2025.

Avtozma, tocilizumab-anoh, is a monoclonal antibody that binds to interleukin-6 (IL-6) receptors thereby inhibiting IL-6-mediated T-cell activation and induction of immunoglobulin secretion. Avtozma was approved on January 24, 2025, under BLA

761420, as biosimilar to and interchangeable with US-licensed Actemra (tocilizumab) for the following indications:[1]

- Rheumatoid arthritis (RA)
  - Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs)
- Giant cell arteritis (GCA)
  - Adult patients with giant cell arteritis
- Polyarticular juvenile idiopathic arthritis (PJIA)
  - Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis
- Systemic juvenile idiopathic arthritis (SJIA)
  - Patients 2 years of age and older with active systemic juvenile idiopathic arthritis
- Coronavirus Disease 2019 (COVID-19)
  - Hospitalized adult patients with coronavirus disease 2019 (COVID-19) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)

On July 29, 2025, Avtozma was approved for the following additional indication (BLA 761420/S-001).

- Cytokine Release Syndrome (CRS)
  - Adults and pediatric patients 2 years of age and older with chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome.

In BLA 761420, Avtozma is approved in the following strengths, dosage forms, routes of administration (ROA), and presentations:

Interchangeable, for intravenous (IV) use:

- 80 mg/4 mL (20 mg/mL) injection in a single-dose vial as interchangeable with US-Actemra 80 mg/4 mL (20 mg/mL) injection in a single-dose vial
- 200 mg/10 mL (20 mg/mL) injection in a single-dose vial as interchangeable with US-Actemra 200 mg/10 mL (20 mg/mL) injection in a single-dose vial
- 400 mg/20 mL (20 mg/mL) injection in single-dose vial as interchangeable with US-Actemra 400 mg/20 mL (20 mg/mL) injection in a single-dose vial

Interchangeable, for subcutaneous (SC) use:

- 162 mg/0.9 mL (180 mg/mL) injection in a single-dose pre-filled syringe (PFS) as interchangeable with US-Actemra 162 mg/0.9 mL (180 mg/mL) injection in a single-dose PFS

[1] See USPI for Avtozma (tocilizumab-anoh), sBLA 761420/S-005 approved on January 14, 2026 https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761420s005lbl.pdf

Biosimilar, for SC use:

- 162 mg/0.9 mL (180 mg/mL) injection in a single-dose pre-filled autoinjector (AI) as biosimilar to US-Actemra 162 mg/0.9 mL (180 mg/mL) injection in a single-dose pre-filled AI

The Applicant submitted BLA 761498 seeking approval of the RA, GCA, PJIA, and SJIA indications and for the following strengths, dosage form, ROAs, and presentations:

- The 162 mg/0.9 mL injection in a PFS for SC use as interchangeable with US-Actemra 162 mg/0.9 mL injection in a PFS for SC use
- The 162 mg/0.9 mL injection AI for SC use as biosimilar to US-Actemra 162 mg/0.9 mL injection in an AI for SC use

The Applicant also submitted a request to voluntarily revoke the products administered via the SC ROA from BLA 761420 once BLA 761498 is approved. The Applicant submitted BLA 761498 in order to separate the products for IV and SC use currently approved in BLA 761420 into two separate BLAs so that BLA 761420 retains the single-dose vial products for IV use and BLA 761498 contains only the PFS and AI products for SC use to align with the BLAs for US-Actemra.

The totality of the evidence contained in this BLA, which has been already reviewed in BLA 761420 and referenced in this second BLA, demonstrated that Avtozma is highly similar to US-Actemra, notwithstanding minor differences in clinically inactive components, and there are no clinically meaningful differences between Avtozma and US-Actemra in terms of the safety, purity, and potency of the product. No new clinical data are included nor required for BLA 761498.

2. Background and Regulatory History

BLA 761498 cross-references and/or includes pertinent data and information that were included, and FDA reviewed, in BLA 761420. No new data, clinical or otherwise, are included with BLA 761498. After BLA 761498 was submitted, the Applicant submitted supplements to BLA 761420 that are relevant to BLA 761498. The Applicant later amended BLA 761498 with changes that FDA approved in sBLA 761420/S-001 on July 29, 2025 (Category B to add CRS indication); sBLA 761420/S-003 on October 22, 2025 (CMC); and sBLA 761420/S-005 on January 14, 2026 (Category A).

The reference product, US-Actemra, is licensed in two BLAs (BLA 125276 and BLA 125472) with shared labeling. The Applicant's objectives align with how US-Actemra is licensed.

3. Summary of Conclusions of Other Review Disciplines

3.1. Product Quality

Relevant product quality information for drug substance (DS), drug product (DP), comparative analytical assessment, immunogenicity assay, facilities, and microbiology are provided under BLA 761420 and cross-referenced. The product quality information applicable to the SC DPs (PFS and AI) is submitted in BLA 761498. All proposed manufacturing and testing facilities are acceptable based on their current CGMP compliance status and recent relevant inspectional activity. The assessment of manufacturing information provided in this application (that is the same under the approved BLA 761420) has concluded that the methodologies and processes used for DS and DP manufacturing, release, and stability testing are sufficiently robust and controlled to ensure the consistent manufacture of a safe, pure, and potent product. The microbial control and sterility assurance strategy is sufficient to support consistent manufacture of a sterile product. The comparative analytical data support a demonstration that Avtozma is highly similar to US-licensed Actemra, notwithstanding minor differences in clinically inactive components.

OPQ recommends that this product be approved for human use under conditions specified in the package insert (see Product Quality Executive summary review dated 08/29/2025, in DARRTS).

3.2. Devices

3.2.1. Center for Devices and Radiological Health (CDRH)

The device information previously included, and assessment performed under BLA 761420 are applicable for this BLA.

3.2.2. Division of Medication Error Prevention and Analysis (DMEPA I)

DMEPA I completed a proprietary name memorandum dated April 26, 2024, and a Labeling Review dated September 13, 2024, under BLA 761420. In response to an Information Request (IR), on July 3, 2025, the Applicant submitted a Request for Proprietary Name Review for the evaluation of the proprietary name Avtozma under BLA 761498. DMEPA found the proposed proprietary name, Avtozma, conditionally acceptable under BLA 761498 in their review dated August 7, 2025.

4. Nonclinical Pharmacology/Toxicology

See BLA 761420 Nonclinical Review dated December 18, 2024, in DARRTS. No new nonclinical pharmacology/toxicology information was submitted nor required for this BLA.

5. Clinical Pharmacology

See BLA 761420 Biosimilar Multidisciplinary Evaluation and Review (BMER) Section 5, dated January 24, 2025, for details for the Clinical Pharmacology review. No new clinical pharmacology information was submitted nor required for BLA 761498.

6. Clinical Evaluation and Recommendations

6.1. Efficacy

The data and information referenced in BLA 761498 in support of licensure of Avtozma (tocilizumab-anoh, CT-P47) was previously included and reviewed in BLA 761420. Therefore, the documentation that pertains to FDA's review of BLA 761498, including all discipline reviews, relevant correspondence between FDA and the Applicant, and internal memoranda that typically would be included in BLA 761498 can be found in BLA 761420. As stated above, BLA 761420 was approved on January 24, 2025.

6.2. Safety

No new safety data were submitted with BLA 761498. Two Period Adverse Event Reports (PAER) were submitted to BLA 761420 since its January 2025 approval. The first PAER was submitted on May 23, 2025, for reporting period January 24, 2025, to April 23, 2025. No cases were received or submitted during this first reporting period. The second PAER was submitted on August 8, 2025, for reporting period April 24, 2025, to July 10, 2025; there were no cases (15-day alerts or non-15-day alerts) received or submitted during this as well. See Clinical Review dated August 11, 2025. In response to an IR on July 2, 2025, the Applicant confirmed that no new safety issues were identified that would impact safety of the SC products in BLA 761498.

6.3. Extrapolation

FDA intends to license BLA 761498 for RA and GCA in adults and PJIA and SJIA in patients ≥ 2 years of age. Section 2 of the proposed shared Prescribing Information indicates that the two products in BLA 761498 are not used for the treatment of CRS or COVID-19. During the review of the original application for CT-P47, FDA concluded that the Applicant had provided sufficient scientific justification (based on the mechanism of action, pharmacokinetics, immunogenicity and toxicity profile) for extrapolation of the data and information to support licensure of CT-P47 for each of the indications being sought and for which for which CT-P47 had not been directly studied. Additional scientific justification of extrapolation of data submitted in BLA 761420 is not required as the Applicant is not seeking licensure of any new indication(s) for BLA 761498.

7. Labeling

The labeling is compliant with Physician Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR), is consistent with labeling guidance recommendations, and conveys the essential scientific information needed for safe and effective use of the product. The prescribing information incorporated relevant data and information from

the US-Actemra prescribing information, with appropriate modifications. The version of the labeling that will be attached to the approval letter is unchanged from approved labeling for BLA 761420/S-005. The Applicant also submitted unbranded biological product labeling for Tocilizumab-anoh.

8. Pediatrics

Under the Pediatric Research Equity Act (PREA) (section 505B of the FD&C Act), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain a pediatric assessment to support dosing, safety, and effectiveness of the product for the claimed indication unless this requirement is waived, deferred, or inapplicable. Section 505B(l) of the FD&C Act provides that a biosimilar product that has not been determined to be interchangeable with the reference product is considered to have a “new active ingredient” for purposes of PREA. A pediatric assessment is generally required unless deferred or inapplicable. Under the statute, a biological product that is interchangeable with the reference product is not considered to have a “new active ingredient” for purposes of PREA.

Because one of the Avtozma approved products, specifically, the prefilled AI for SC use, is licensed as a biosimilar product, this BLA is considered to have a new active ingredient for the purposes of PREA. The Applicant addressed PREA requirements for all the approved indications during the original review of BLA 761420 based on a demonstration of biosimilarity and providing an adequate scientific justification to support the extrapolation of data and information to support licensure. Refer to the BMER dated January 24, 2025, for BLA 761420.

Avtozma has an unfulfilled PREA postmarketing requirement (PMR) for BLA 761420 for the treatment of COVID-19 in pediatric patients 1 to <18 years of age. Because Avtozma for the COVID-19 indication is only for IV treatment, the PREA PMR for COVID-19 only applies to BLA 761420 and will remain with BLA 761420 until fulfilled.

On September 23, 2025, The PeRC agreed that this application is fully assessed and that a PREA PMR is not needed because there is already a PREA PMR for the IV formulation.

9. REMS and Postmarketing Requirements and Commitments

9.1. Recommendations for Risk Evaluation and Mitigation Strategies

None.

9.2. Recommendations for Postmarketing Requirements and Commitments

BLA 761420 has a deferred pediatric assessment for the treatment of COVID-19 in pediatric patients 1 year to <18 years of age (PREA PMR 4790-1) with a final report

submission of June 2026. Since Avtozma for the COVID-19 indication is only for IV treatment, the PREA PMR for COVID-19 only applies to BLA 761420 and will remain with BLA 761420 until fulfilled.

10. Other Regulatory Issues

None.

11. Recommended Regulatory Action

Approval.

12. Recommended Comments to the Applicant

None.

13. Division Director or Designated Signatory Comments

I concur with the review team's assessment of the data and information submitted in this BLA and support the regulatory action.

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/

RAQUEL TAPIA
01/21/2026 09:59:58 AM

THOMAS M HERNDON
01/21/2026 10:03:45 AM

RAJ NAIR
01/21/2026 10:06:45 AM