CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761498Orig1s000

OTHER REVIEW(S)

LABEL AND LABELING 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:	August 7, 2025
Requesting Office or Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	BLA 761498
Product Name, Dosage Form, and Strength:	Avtozma (tocilizumab-anoh) injection, 162 mg/0.9 mL
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant Name:	Celltrion, Inc.
FDA Received Date:	May 19, 2025
TTT ID #:	2025-14755
DMEPA 1 Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA 1 Team Leader:	Damon Birkemeier, PharmD, FISMP

1 INTRODUCTION

As part of the approval process for Avtozma (tocilizumab-anoh) injection, the Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the proposed Avtozma Prescribing Information, Instructions for Use, container labels, and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 REGULATORY HISTORY

We note that Avtozma (tocilizumab-anoh) was originally approved on January 24, 2025, under BLA 761420 in single-dose vial for intravenous use and in prefilled syringe and autoinjector for subcutaneous use. BLA 761498 was submitted to separate the subcutaneous use formulations (prefilled syringe and autoinjector) from the intravenous use formulation (single-dose vial) for commercial purposes. The two BLAs share the same prescribing information that was approved under BLA 761420.

2 MATERIALS CONSIDERED

This section lists the materials considered for our review.

Table 1. Materials Considered for this Review	
Materials Considered	Appendix Section
Relevant Product Information	A
Labels and Labeling	B
Previous DMEPA Reviews	C

3 CONCLUSION

Our evaluation of the proposed Avtozma Prescribing Information, Instructions for Use, container labels, and carton labeling did not identify areas of vulnerability that may lead to medication errors. We have no recommendations at this time.

APPENDICES: MATERIALS CONSIDERED FOR THIS REVIEW

APPENDIX A. RELEVANT PRODUCT INFORMATION

Table 2 presents relevant product information for Avtozma received on May 19, 2025 from Celltrion, Inc.

Table 2. Relevant Product Information for Avtozma		
Application Type and #	BLA 761498 (proposed)	BLA 761420
Initial Approval Date	N/A	1/24/2025
Nonproprietary Name	tocilizumab-anoh	
Indication	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).	
Dosage Form	injection	
Strength	162 mg/0.9 mL	80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL)
Route of Administration	Subcutaneous injection	Intravenous infusion
Dose and Frequency	<u>Rheumatoid Arthritis</u> Recommended Adult Intravenous Dosage: When used in combination with non-biologic DMARDs or as monotherapy the recommended starting dose is 4 mg per kg every 4 weeks followed by an increase to 8 mg per kg every 4 weeks based on clinical response.	

<table>
<tr><th colspan="3">Table 2. Relevant Product Information for Avtozma</th></tr>
<tr><td>Application Type and #</td><td>BLA 761498 (proposed)</td><td>BLA 761420</td></tr>
<tr><td></td><td colspan="2">
Recommended Adult Subcutaneous Dosage:
<table>
<tr><td>Patients less than 100 kg weight</td><td>162 mg administered subcutaneously every other week, followed by an increase to every week based on clinical response</td></tr>
<tr><td>Patients at or above 100 kg weight</td><td>162 mg administered subcutaneously every week</td></tr>
</table>
<u>Giant Cell Arteritis</u>
Recommended Adult Intravenous Dosage:
The recommended dose is 6 mg per kg every 4 weeks in combination with a tapering course of glucocorticoids. AVTOZMA can be used alone following discontinuation of glucocorticoids.
Recommended Adult Subcutaneous Dosage:
The recommended dose is 162 mg given once every week as a subcutaneous injection, in combination with a tapering course of glucocorticoids.
A dose of 162 mg given once every other week as a subcutaneous injection, in combination with a tapering course of glucocorticoids, may be prescribed based on clinical considerations.
AVTOZMA can be used alone following discontinuation of glucocorticoids.
<u>Polyarticular Juvenile Idiopathic Arthritis</u>
<table>
<tr><td colspan="2">Recommended Intravenous PJIA Dosage Every 4 Weeks</td></tr>
<tr><td>Patients less than 30 kg weight</td><td>10 mg per kg</td></tr>
<tr><td>Patients at or above 30 kg weight</td><td>8 mg per kg</td></tr>
</table>
<table>
<tr><td colspan="2">Recommended Subcutaneous PJIA Dosage</td></tr>
<tr><td>Patients less than 30 kg weight</td><td>162 mg once every three weeks</td></tr>
<tr><td>Patients at or above 30 kg weight</td><td>162 mg once every two weeks</td></tr>
</table>
<u>Systemic Juvenile Idiopathic Arthritis</u>
<table>
<tr><td>Recommended Intravenous SJIA Dosage Every 2 Weeks</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th colspan="3">Table 2. Relevant Product Information for Avtozma</th></tr>
<tr><td>Application Type and #</td><td colspan="2">BLA 761498 (proposed)</td><td>BLA 761420</td></tr>
<tr><td></td><td colspan="3">
<table>
<tr><td>Patients less than 30 kg weight</td><td>12 mg per kg</td></tr>
<tr><td>Patients at or above 30 kg weight</td><td>8 mg per kg</td></tr>
</table>
<table>
<tr><th colspan="2">Recommended Subcutaneous SJIA Dosage</th></tr>
<tr><td>Patients less than 30 kg weight</td><td>162 mg every two weeks</td></tr>
<tr><td>Patients at or above 30 kg weight</td><td>162 mg every week</td></tr>
</table>
<u>Coronavirus Disease 2019</u>
The recommended dosage of AVTOZMA for adult patients with COVID-19 is 8 mg per kg administered by a 60-minute intravenous infusion.
</td></tr>
<tr><td>How Supplied</td><td colspan="2">• Each single-dose prefilled syringe delivers 162 mg/0.9 mL: carton of one syringe; carton of 4 syringes; carton of 3 packs of 4 syringes
• Each single-dose prefilled autoinjector 162 mg/0.9 mL: carton of one syringe; carton of 4 syringes; carton of 3 packs of 4 syringes</td><td>• 80 mg/ 4 mL (20 mg/mL): carton of one vial; carton of 4 vials.
• 200 mg/ 10 mL (20 mg/mL): carton of one vial; carton of 4 vials.
• 400 mg/ 20 mL (20 mg/mL): carton of one vial; carton of 4 vials</td></tr>
<tr><td>Storage</td><td colspan="3">Do not use beyond expiration date on the container, package, prefilled syringe, or autoinjector. Avtozma must be refrigerated at 36°F to 46°F (2°C to 8°C). Do not freeze. Protect the vials, syringes, and autoinjectors from light by storage in the original carton until time of use, and keep syringes and autoinjectors dry. Once removed from the refrigerator, the prefilled syringe and autoinjector can be stored at room temperature at or below 77°F (25°C) for up to 3 weeks. The prefilled syringe and autoinjector must always be kept in the carton.</td></tr>
</table>

APPENDIX B. LABELS AND LABELING

B.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[a] along with postmarket medication error data, we reviewed the following Avtozma labels and labeling submitted by Celltrion, Inc.

- Prescribing Information received on May 19, 2025, available from
  Brand: \\cdsesub1\evsprod\BLA761498\0001\m1\us\draft-labeling-text-avtozma-clean.docx
  Unbranded: \\cdsesub1\evsprod\BLA761498\0001\m1\us\draft-labeling-text-unbranded-clean.docx
- Instructions for Use received on May 19, 2025, available from
  Brand: \\cdsesub1\evsprod\BLA761498\0001\m1\us\draft-labeling-text-avtozma-clean.docx
  Unbranded: \\cdsesub1\evsprod\BLA761498\0001\m1\us\draft-labeling-text-mg-ifu-unbranded-clean.docx

- Container labels received on May 19, 2025
- Carton labeling received on May 19, 2025

B.2 Container Labels and Carton Labeling Images

Container Labels:

15 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[a] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

APPENDIX C. PREVIOUS DMEPA REVIEWS

On July 16, 2025, we searched for previous DMEPA reviews relevant to this current review using the terms, "BLA 761420" and "Avtozma". Our search identified three previous reviews[b,c,d], and we considered our previous recommendations to see if they are applicable for this current review.

[b] Vee, S. Label and Labeling Review for Avtozma (BLA 761420). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 JUL 02. TTT ID No.: 2024-8064.

[c] Vee, S. Review of Revised Label and Labeling for Avtozma (BLA 761420). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 SEP 13. TTT ID No.: 2024-8064-1.

[d] Vee, S. Review of Revised Label and Labeling for Avtozma (BLA 761420). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2025 JAN 24. TTT ID No.: 2024-8064-2.

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/s/

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