

PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Zymfentra Prior Authorization Policy

- Zymfentra® (infliximab-dyyb subcutaneous injection – Celltrion)

REVIEW DATE: 12/17/2025; selected revision 02/11/2026

OVERVIEW

Zymfentra, a subcutaneous (SC) tumor necrosis factor (TNF) inhibitor, is indicated for the following uses:¹

- **Crohn's disease**, as maintenance treatment for moderately to severely active disease in adults who have received three induction doses with an infliximab intravenous product.
- **Ulcerative colitis**, as maintenance treatment for moderately to severely active disease in adults who have received three induction doses with an infliximab intravenous product.

Therapy (for either indication) begins with an infliximab intravenous (IV) product administered as an induction regimen at Weeks 0, 2, and 6.¹ At Week 10 or at any scheduled infliximab IV infusion in patients with a clinical response or remission, therapy can be switched to Zymfentra. The recommended dose of Zymfentra is 120 mg administered SC once every 2 weeks.

Guidelines

Guidelines for the treatment of inflammatory conditions recommend use of infliximab.

- **Crohn's Disease (CD):** The American College of Gastroenterology (ACG) [2025] and the American Gastroenterological Association (AGA) [2025] have guidelines for the management of CD in adults.^{2,3} Both guidelines recommend upfront use of advanced therapies, rather than step-up therapy after failure of corticosteroids and/or immunomodulators. Advanced therapies recommended include TNF inhibitors, Entyvio® (vedolizumab IV infusion, SC injection), interleukin (IL)-23 inhibitors, IL-12/23 inhibitors, and Rinvoq® (upadacitinib extended-release tablets).
- **Ulcerative Colitis (UC):** The AGA (2024) and the ACG (2025) have clinical practice guidelines on the management of moderate to severe UC.^{4,5} In moderate to severe disease, systemic corticosteroids or advanced therapies may be utilized for induction of remission. Advanced therapies recommended include TNF inhibitors, Entyvio, IL-23 inhibitors, IL-12/23 inhibitors, sphingosine-1-phosphate (S1P) receptor modulators, and Janus kinase (JAK) inhibitors. If steroids are utilized for induction, efforts should be made to introduce steroid-sparing agents for maintenance therapy. Of note, guidelines state corticosteroids may be avoided entirely when other effective induction strategies are planned.⁵ Both guidelines also recommend that any drug that effectively treats induction should be continued for maintenance.^{4,5}

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Zymfentra. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Zymfentra as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Zymfentra to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Zymfentra is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Crohn's Disease.** Approve for the duration noted if the patient meets ONE of the following (A or B):
 - A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
 - i. Patient is ≥ 18 years of age; AND
 - ii. According to the prescriber, the patient is currently receiving infliximab intravenous maintenance therapy or will receive induction dosing with an infliximab intravenous product within 3 months of initiating therapy with Zymfentra; AND
 - iii. The medication is prescribed by or in consultation with a gastroenterologist; OR
 - B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):
 - i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with the requested drug is reviewed under criterion A (Initial Therapy).
 - ii. Patient meets at least ONE of the following (a or b):
 - a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested product); OR
Note: Examples of objective measures include fecal markers (e.g., fecal lactoferrin, fecal calprotectin), serum markers (e.g., C-reactive protein), imaging studies (magnetic resonance enterography [MRE], computed tomography enterography [CTE]), endoscopic assessment, and/or reduced dose of corticosteroids.
 - b) Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or blood in stool.

2. **Ulcerative Colitis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
 - A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
 - i. Patient is ≥ 18 years of age; AND
 - ii. According to the prescriber, the patient is currently receiving infliximab intravenous maintenance therapy or will receive induction dosing with an infliximab intravenous product within 3 months of initiating therapy with Zymfentra; AND
 - iii. The medication is prescribed by or in consultation with a gastroenterologist; OR
 - B) Patient is Currently Receiving an Infliximab Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):
 - i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with an infliximab product is reviewed under criterion A (Initial Therapy).
 - ii. Patient meets at least ONE of the following (a or b):
 - a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating an infliximab product); OR
Note: Examples of objective measures include fecal markers (e.g., fecal calprotectin), serum markers (e.g., C-reactive protein), endoscopic assessment, and/or reduced dose of corticosteroids.
 - b) Compared with baseline (prior to initiating an infliximab product), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or rectal bleeding.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Zymfentra is not recommended in the following situations:

1. **Concurrent Use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug.** This medication should not be administered in combination with another biologic or with a targeted synthetic oral small molecule drug used for an inflammatory condition (see [Appendix](#) for examples). Combination therapy is generally not recommended due to a potentially higher rate of adverse events and lack of controlled clinical data supporting additive efficacy.
Note: This does NOT exclude the use of conventional synthetic disease-modifying antirheumatic drugs (e.g., methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine) in combination with this medication.
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Zymfentra™ subcutaneous injection [prescribing information]. Yeonsu-gu, Incheon: Celltrion; February 2024.
2. Lichtenstein, G, Loftus E, Afzali A, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2025 June;120(6):1225-1264.
3. Scott FI, Ananthakrishnan AN, Click B, et al. AGA Living Clinical Practice Guideline on the Pharmacologic Management of Moderate-to-Severe Crohn's Disease. *Gastroenterology*. 2025 Dec;169(7):1397-1448.
4. Singh S, Loftus EV Jr, Limketkai BN, et al. AGA Living Clinical Practice Guideline on Pharmacological Management of Moderate-to-Severe Ulcerative Colitis. *Gastroenterology*. 2024 Dec;167(7):1307-1343.
5. Rubin D, Ananthakrishnan A, Siegel C. ACG Clinical Guideline Update: Ulcerative Colitis in Adults. *Am J of Gastroenterol*. 2025 June;120(6):1187-1224.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	-	12/06/2023
Selected Revision	Conditions Not Recommended for Approval: Concurrent use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug was changed to as listed (previously oral small molecule drug was listed as Disease-Modifying Antirheumatic Drug).	09/11/2024
Annual Revision	No criteria changes.	12/04/2024
Selected Revision	Ulcerative Colitis: For initial therapy, removed the following options of approval: (1) the patient has tried one systemic therapy; (2) the patient has pouchitis and tried an antibiotic, probiotic, corticosteroid enema, or mesalamine enema.	07/23/2025
Annual Revision	No criteria changes. Appendix: Otezla XR (apremilast-extended release tablets) was added.	12/17/2025
Selected Revision	Crohn's Disease: For initial therapy, the following options of approval were removed: The patient has tried or is currently taking systemic corticosteroids, or corticosteroids are contraindicated; patient has tried one conventional systemic therapy for Crohn's disease along with the associated Note; patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence).	02/11/2026

APPENDIX

	Mechanism of Action	Examples of Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
Simponi®, Simponi Aria® (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC IV formulation: AS, PJIA, PsA, RA
Tocilizumab Products (Actemra® IV, biosimilar; Actemra SC, biosimilar)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA [^] , RA
Omvo® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	CD, UC
Ustekinumab Products (Stelara® IV, biosimilar; Stelara SC, biosimilar)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC IV formulation: CD, UC
Siliq® (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA IV formulation: AS, nr-axSpA, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Bimzelx® (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	PsO, AS, nr-axSpA, PsA
Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO, UC IV formulation: CD, UC
Tremfya® (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: CD, PsA, PsO, UC IV formulation: CD, UC
Entyvio® (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic Oral Small Molecule Drugs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Otezla® XR (apremilast extended-release tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA, AA
Litfulo® (ritlecitinib capsules)	Inhibition of JAK pathways	AA
Legselvi® (deuruxolitinib tablets)	Inhibition of JAK pathways	AA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, CD, UC
Rinvoq® LQ (upadacitinib oral solution)	Inhibition of JAK pathways	PsA, PJIA
Sotyktu® (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets/oral solution)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC
Zeposia® (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
Velsipity® (etrasimod tablets)	Sphingosine 1 phosphate receptor modulator	UC

* Not an all-inclusive list of indications. Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn’s disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; [^] Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.