

PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Zymfentra Prior Authorization Policy

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

REVIEW DATE: 12/06/2023

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 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 subcutaneously once every 2 weeks. In the pivotal studies evaluating Zymfentra, all patients had previously tried corticosteroids and/or conventional agents for Crohn's disease and ulcerative colitis.

Guidelines

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

- **Crohn's Disease:** The American College of Gastroenterology (ACG) has guidelines for Crohn's disease (2018).² TNFis are listed as an option for disease that is resistant to corticosteroids, severely active disease, perianal fistulizing disease, and maintenance of remission. In post-operative Crohn's disease, a TNFi should be started within 4 weeks of surgery to prevent recurrence. Guidelines from the American Gastroenterological Association (AGA) [2021] include infliximab among the therapies for moderate to severe Crohn's disease, for induction and maintenance of remission.³
- **Ulcerative Colitis:** ACG guidelines for ulcerative colitis (2019) note that the following agents can be used for induction of remission in moderately to severely active disease: budesonide extended-release tablets; oral or intravenous systemic corticosteroids, Entyvio[®] (vedolizumab intravenous infusion), Xeljanz[®]/XR (tofacitinib tablets/extended-release tablets), or TNFis.⁴ Guidelines from the AGA (2020) include infliximab amongst the therapies recommended for moderate to severe ulcerative colitis.⁵

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Zymfentra. 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. 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

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, iii, and iv):
 - 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. Patient meets ONE of the following (a, b, c, or d):
 - a) Patient has tried or is currently taking systemic corticosteroids, or corticosteroids are contraindicated in this patient; OR
Note: Examples of corticosteroids are prednisone and methylprednisolone.
 - b) Patient has tried one conventional systemic therapy for Crohn's disease; OR
Note: Examples of conventional systemic therapy for Crohn's disease include azathioprine, 6-mercaptopurine, or methotrexate. An exception to the requirement for a trial of or contraindication to steroids or a trial of one other conventional systemic agent can be made if the patient has already tried at least one biologic other than the requested medication. A biosimilar of the requested biologic does not count. Refer to [Appendix](#) for examples of biologics used for Crohn's disease. A trial of mesalamine does not count as a systemic therapy for Crohn's disease.
 - c) Patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; OR
 - d) Patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence); AND
 - iv. 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, iii, and iv):
- 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. Patient meets ONE of the following (a or b):
 - a) Patient had a trial of one systemic agent or was intolerant to one of these agents for ulcerative colitis; OR
Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or methylprednisolone. A trial of a mesalamine product does not count as a systemic therapy for ulcerative colitis. A previous trial of one biologic other than the requested medication also counts as a trial of one systemic agent for ulcerative colitis. A biosimilar of the requested biologic does not count. Refer to [Appendix](#) for examples of biologics used for ulcerative colitis.
 - b) Patient meets BOTH of the following [(1) and (2)]:
 - (1) Patient has pouchitis; AND
 - (2) Patient has tried therapy with an antibiotic, probiotic, corticosteroid enema, or Rowasa[®] (mesalamine enema); AND
Note: Examples of antibiotics include metronidazole and ciprofloxacin. Examples of corticosteroid enemas include hydrocortisone enema (Cortenema, generics).
 - iv. The medication is prescribed by or in consultation with a gastroenterologist.
- 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 Disease-Modifying Antirheumatic Drug (DMARD).** Data are lacking evaluating concomitant use of an infliximab product in combination with another biologic or with a targeted synthetic DMARD used for an inflammatory condition (see [APPENDIX](#) for examples). Combination therapy with biologics and/or biologics + targeted synthetic DMARDs has a potential for a higher rate of AEs and lack controlled trial data in support of additive efficacy.
Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with an infliximab product.
-

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; October 2023.
2. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018;113(4):481-517.
3. Feuerstein JD, Ho EY, Shmidt E, et al. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. *Gastroenterology*. 2021;160(7):2496-2508.
4. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
5. Feuerstein JD, Isaac s KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. *Gastroenterology*. 2020;158:1450-1461.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	-	12/06/2023

APPENDIX

	Mechanism of Action	Examples of Inflammatory 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
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
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	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, 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
Stelara® (ustekinumab SC injection, IV infusion)	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)	Inhibition of IL-17A	AS, ERA, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Omvo® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	UC
Ilumya™ (tildrakizumab-asnm SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa IV infusion, SC injection)	Inhibition of IL-23	SC formulation: CD, PSA, PsO IV formulation: CD
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion, SC injection)	Integrin receptor antagonist	SC: UC IV: CD, UC
Oral Therapies/Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Sotyktu™ (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets)	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 (e.g., oncology indications and rare inflammatory conditions are not listed). 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; TYK2 – Tyrosine kinase 2.