MEDICAL MUTUAL®

Drug Policy

Policy:	**240103**	**Initial Effective Date: 01/18/2024**
Code(s):	**HCPCS J3490, J3590, C9399**	**Annual Review Date: 01/16/2025**
SUBJECT:	**Zymfentra® (infliximab-dyyb subcutaneous injection)**	**Last Revised Date: 01/16/2025**

☒Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

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.

POLICY STATEMENT

This policy involves the use of Zymfentra. Prior authorization is recommended for pharmacy and medical benefit coverage of Zymfentra. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval,** and **Duration of Therapy** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Zymfentra as well as the monitoring required for AEs and long-term efficacy, initial approval requires Zymfrentra be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

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

1. **Crohn's Disease.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve 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 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.

Dosing in Crohn's Disease (CD). Following the first three infliximab intravenous product doses administered at Week 0 and Week 2, and Week 6, an infliximab intravenous product may be switched to Zymfentra subcutaneous injection at Week 10. Administer 120mg subcutaneously at Week 10 and every 2 weeks thereafter. If switching a patient on a maintenance intravenous infliximab product, administer the first subcutaneous dose of Zymfentra in place of the next scheduled intravenous infusion and every two weeks thereafter.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months (180 days)
B) *Extended Approval:*1 year (365 days)

2. **Ulcerative Colitis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve 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 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.

Dosing in Ulcerative Colitis (UC). Following the first three infliximab intravenous product doses administered at Week 0 and Week 2, and Week 6, an infliximab intravenous product may be switched to Zymfentra subcutaneous injection at Week 10. Administer 120mg subcutaneously at Week 10 and every 2 weeks thereafter. If switching a patient on a maintenance intravenous infliximab product, administer the first subcutaneous dose of Zymfentra in place of the next scheduled intravenous infusion and every two weeks thereafter.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months (180 days)
B) *Extended Approval:*1 year (365 days)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Zymfentra has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

Prior approval is required for HCPCS Codes J3490 and C9399

†When *unclassified drugs* (J3490) or *unclassified biologics* (J3590) or *unclassified drugs or biologics [hospital outpatient use]* (C9399) is determined to be Zymfentra

Edits and Denials:

Prior approval: Prior approval is required for Zymfentra **(HCPCS Codes J3490 , J3590, C9399)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

MEDICAL MUTUAL®

Drug Policy

Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

HCPCS Code(s):	
J3490	Unclassified drugs
J3590	Unclassified biologics
C9399	unclassified drugs or biologics [hospital outpatient use]

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
Omvoh® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	UC
Ilumya™ (tildrakizumab-asmn 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.