Neighborhood Health Plan OF RHODE ISLAND™

Effective Date: 03/01/2025
Reviewed: 12/24, 7/26 Pharmacy Scope: Medicaid Medical Scope: Medicaid, Commercial, Medicare

Infliximab SC Products: ZYMFENTRA (infliximab-dyyb)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the patient has no exclusions to the prescribed therapy.

FDA-Approved Indications

Zymfentra

1. Maintenance treatment of moderately to severely active ulcerative colitis (UC) in adults following treatment with an infliximab product administered intravenously
2. Maintenance treatment of moderately to severely active Crohn's disease (CD) in adults following treatment with an infliximab product administered intravenously

All other indications are considered experimental/investigational and are not a covered benefit.

II. SUMMARY OF EVIDENCE

The efficacy of Zymfentra SC for use in UC and CD was established in a two randomized, double-blind, placebo-controlled clinical trials, LIBERTY-UC and LIBERTY-CD, in adults with moderately to severely active UC or moderately to severely active CD, respectively, that previously had an inadequate response or intolerance to treatment with corticosteroids alone or in combination with 6-mercaptopurine or azathioprine. All subjects received three IV induction doses of infliximab-dyyb at weeks 0, 2, and 6. In the LIBERTY-UC trial, subjects that achieved clinical response, defined as a decrease from baseline in the modified Mayo score (mMS) of at least 2 points and at least 30%, with an accompanying decrease in the rectal bleeding score (RBS) of at least 1 point or an absolute RBS of 0 or 1 point, at week 10 after induction therapy (N=438) were then randomized (2:1) to receive either Zymfentra 120mg SC or placebo every 2 weeks. The primary endpoint, the proportion of subjects in clinical remission at week 54, was achieved in 43% participants treated with Zymfentra and 21% participants treated with placebo ($p < 0.0001$). In the LIBERTY-CD trial, subjects that achieved clinical response, defined as a decrease from baseline in Crohn's Disease Activity Index (CDAI) of at least 100 points, at week 10 after induction therapy (N=323) were then randomized (2:1) to receive either Zymfentra 120mg SC or placebo every 2 weeks. The co-primary endpoints were clinical remission (defined as an absolute CDAI score of <150 points) and endoscopic response (defined as a >50% decrease in Simplified Endoscopic Activity Score for Crohn's Disease [SES-CD] from the baseline value) at week 54. The results showed that 63% of participants treated with Zymfentra and 30% of participants treated with placebo achieved clinical remission ($p < 0.0001$). In addition, endoscopic response was observed in 50% of Zymfentra-treated patients and 18% of placebo-treated patients ($p < 0.0001$).

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III. CRITERIA FOR INITIAL APPROVAL

For all indications:

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Authorization of 6 months may be granted for treatment of moderately to severely active ulcerative colitis (UC) or Crohn's disease (CD) when all of the following criteria are met:

1. Submission of the member's chart or medical record is required, documenting medical necessity based on the criteria corresponding to the applicable indication; AND
2. Physician has assessed baseline disease severity utilizing an objective measure/tool; AND
3. Member is free of any clinically important active infection, including clinically important localized infections; AND
4. Member will not receive live vaccines during therapy; AND
5. Member has been evaluated and screened for the presence of latent TB (tuberculosis) infection prior to initiating treatment and will receive ongoing monitoring for presence of TB during treatment; AND
6. Member is 18 years of age or older; AND
7. Zymfentra is prescribed by, or in consultation with, a specialist in gastroenterology; AND
8. Only one formulation of infliximab will be used (intravenous or subcutaneous); AND
9. Documentation has been submitted that the member has received at least 10 weeks of IV infliximab therapy (3 induction doses), is in clinical remission, and cannot continue receiving maintenance IV infliximab therapy (e.g., Inflectra or Avsola) due to intolerable side effects with medical rationale provided; AND
10. Member has moderate to severe disease (e.g., Mayo Clinical Score 6-12, with Mayo Endoscopic Subscore 2 or 3 for UC and Crohn's Disease Activity Index (CDAI) score ≥220 for CD); AND
11. Zymfentra will not be used concomitantly with an injectable biologic response modifier including TNF-inhibitors (e.g., adalimumab (e.g., Hadlima), Enbrel (etanercept), Simponi (golimumab), etc.) and IL-inhibitors (e.g., Cosentyx (secukinumab), ustekinumab (e.g., Stelara, Otulfi, Selarsdi, Steqeyma, and Yesintek, etc.), Tremfya (guselkumab), Ilumya (tildrakizumab), Skyrizi (risankizumab), Bimzelx (bimekizumab), Omvoh (mirikizumab), etc.) or other oral non-biologic agent (e.g., Otezla (apremilast), tofacitinib (Xeljanz), Olumiant (baricitinib), Rinvoq (upadacitinib), Velsipity (etrasimod), etc.); AND

IV. CONTINUATION OF THERAPY

For all indications:

Authorization of 6 months may be granted for treatment of moderately to severely active ulcerative colitis (UC) or Crohn's disease (CD) in adults when all of the following criteria are met:

1. Member continues to meet all initial criteria; AND
2. Member is tolerating medication; AND
3. Member meets either of the following criteria:
    A. For members using the requested medication for moderately to severely active Crohn's disease, documentation is submitted indicating one of the following:
        - Member has achieved or maintained remission; OR

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- Member has achieved or maintained a positive clinical response to therapy, as indicated by low disease activity or improvement in signs and symptoms compared to baseline such as number of liquid stools, presence and severity of abdominal pain, presence of abdominal mass, body weight compared to IBW, hematocrit, presence of extra-intestinal complications, tapering or discontinuation of corticosteroid therapy, use of anti-diarrheal drugs, appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound and/or an improvement on a disease activity scoring tool [e.g., an improvement on the Crohn's Disease Activity Index (CDAI) score or the Harvey-Bradshaw Index score].

B. For members using the requested medication for moderately to severely active ulcerative colitis, documentation is submitted indicating one of the following:
   - Member has achieved or maintained remission; OR
   - Member has achieved or maintained a positive clinical response to therapy, as indicated by improvement in signs and symptoms compared to baseline such as stool frequency, rectal bleeding, urgency of defecation, C-reactive protein (CRP), fecal calprotectin (FC), appearance of the mucosa on endoscopy, computed tomography enterography (CTE),magnetic resonance enterography (MRE), or intestinal ultrasound, tapering or discontinuation of corticosteroid therapy, and/or an improvement on a disease activity scoring tool [e.g., an improvement on the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) score or the Mayo Score].

V. DOSAGE AND ADMINISTRATION

Indication	Recommended Dosage
Ulcerative Colitis and Crohn's Disease (maintenance treatment only)	<u>Maintenance Dose Starting at Week 10 and thereafter:</u> • 120 mg subcutaneously once every two weeks • To switch patients who are responding to maintenance therapy with an infliximab product administered intravenously, administer the first subcutaneous dose of Zymfentra in place of the next scheduled intravenous infusion and every two weeks thereafter. *Note: All patients must complete an intravenous induction regimen (5 mg/kg at Weeks 0, 2 and 6) with an infliximab product (e.g., Inflectra, Avsola, Remicade) before starting Zymfentra.*

VI. DOSING LIMITS

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

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A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

Drug Name	GPI	NDC	Quantity Limit	Daily Dose Limit
ZYMFENTRA 1-PEN	5250504020F530	72606-0025-01	2 pens per 28 days	0.072
ZYMFENTRA 2-PEN	5250504020F530	72606-0025-02	1 box (2 pens) per 28 days	0.036
ZYMFENTRA 2-SYRINGE	5250504020F830	72606-0025-10	1 box (2 syringes) per 28 days	0.036

B. Max Units (per dose and over time) [Medical Benefit]:

- Crohn's Disease and Ulcerative Colitis: 12 billable units (120 mg) every 2 weeks

VII. BILLING CODE

HCPCS Code	Description
J1748	Injection, infliximab-dyyb (zymfentra), 10 mg

Per §§ 42 CFR 422.101, this clinical medical policy only applies to Medicare in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Zymfentra was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its patients use Zymfentra according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its patients are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

VIII. REFERENCES

1. Zymfentra [package insert]. Jersey City, NJ: Celltrion USA, Inc.; February 2024. Accessed April 2026.
2. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol.* 2011;106(Suppl 1):S2-S25.
3. Lichtenstein GR, Loftus Jr EV, Isaacs KI, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol.* 2018;113:481-517.
4. Rubin DT, Ananthakrishnan AN, et al. 2019 ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol.* 2019;114:384-413.

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