DRUG QUANTITY MANAGEMENT POLICY – PER DAYS

POLICY: Inflammatory Conditions – Zymfentra Drug Quantity Management Policy – Per Days
- Zymfentra® (infliximab-dyyb subcutaneous injection – Celltrion)

REVIEW DATE: 08/27/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

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.

Dosing

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 (Q2W).

Dose Escalation in Crohn's Disease and Ulcerative Colitis
There are data to support dose escalation of Zymfentra from 120 mg Q2W to 240 mg Q2W in patients with inflammatory bowel disease.[2] In LIBERTY-OLE (n = 626 [278 with CD; 348 with UC]), an open-label extension study that enrolled patients from the LIBERTY-CD and LIBERTY-UC pivotal studies, patients with a clinical response to infliximab 5 mg/kg IV were randomized to Zymfentra 120 mg SC Q2W or placebo. From Week 22, patients in either group that demonstrated a loss of response to treatment were dose adjusted to Zymfentra 240 mg Q2W and enrolled in the OLE. Additionally, any patient that experienced loss of response during the OLE (Week 56 to Week 102) could also be dose adjusted to Zymfentra 240 mg Q2W.

- Crohn's disease results: In patients who had their dose adjusted on or after Week 22, a significant difference in the Crohn's disease activity index (CDAI) score from the dose adjusted visit to Week 102 was observed in those transitioned from standard dosing and placebo. Of the 278 patients, 86 (31%) had their dose increased to Zymfentra 240 mg Q2W (42 were increased from 120 mg Q2W and 44 were transitioned from placebo). At Week 102, clinical remission was achieved in 72% of patients that transitioned from Zymfentra 120 mg to Zymfentra 240 mg Q2W and 77% for those transitioned from placebo to Zymfentra 240 mg Q2W.
- Ulcerative colitis results: In patients who had their dose adjusted on or after Week 22, a significant difference in the modified Mayo score (MMS) and partial Mayo score from the dose adjusted visit to Week 102 was observed in those transitioned from standard dosing and placebo. Of the 348 patients, 131 (38%) had their dose increased to Zymfentra 240 mg Q2W (71 were increased from 120 mg Q2W and 60 were increased from placebo). At Week 102, clinical remission was achieved in 35% of patients that transitioned from Zymfentra 120 mg to Zymfentra 240 mg Q2W and 55% for those transitioned from placebo to Zymfentra 240 mg Q2W.

Availability
Zymfentra is available as a 120 mg/mL prefilled pens and syringes.[1] Infliximab is also available as an IV product is not targeted in this policy.

POLICY STATEMENT
This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of Zymfentra, and to manage potential premature dose escalation. If the Drug Quantity Management rule is not met at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration, unless otherwise noted below.

Drug Quantity Limits

Product	Strength and Form	Retail Maximum Quantity Limit	Home Delivery Maximum Quantity Limit
Zymfentra® (infliximab-dyyb SC injection)	120 mg/mL prefilled pen	2 pens per 28 days	6 pens per 84 days
	120 mg/mL prefilled sryinges	2 syringes per 28 days	6 syringes per 84 days

SC – Subcutaneous.

EXCEPTIONS TO THE QUANTITY LIMITS LISTED ABOVE ARE COVERED AS MEDICALLY NECESSARY WHEN THE FOLLOWING CRITERIA ARE MET. ANY OTHER EXCEPTION IS CONSIDERED NOT MEDICALLY NECESSARY.

CRITERIA

1. Approve 4 pens or syringes per 28 days at retail or 12 pens or syringes per 84 days at home delivery if the patient meets ALL of the following (A, B, and C):
   A) Zymfentra is being used to treat Crohn's disease or ulcerative colitis; AND
   B) Patient has received Zymfentra 120 mg subcutaneous (SC) once every 2 weeks for 22 weeks or longer; AND
   C) According to the prescriber, the patient has continued evidence of inflammation based on one or more of the following: elevated C-reactive protein, elevated erythrocyte sedimentation rate, elevated fecal calprotectin, or signs of inflammation on endoscopic evaluation.

2. Approve 4 pens or syringes per 28 days at retail or 12 pens or syringes per 84 days at home delivery if the patient meets BOTH of the following (A and B):
   A) Zymfentra is being used to treat Crohn's disease or ulcerative colitis; AND
   B) Patient has been receiving Zymfentra 240 mg subcutaneous (SC) once every 2 weeks.

REFERENCES

1. Zymfentra™ subcutaneous injection [prescribing information]. Yeonsu-gu, Incheon: Celltrion; May 2025.
2. Colombel JE, Sandborn WJ, Schreiber S, et al. Subcutaneous infliximab (CT-P13-SC) as maintenance therapy for Crohn's disease and ulcerative colitis: 2-year results from open-label extensions of two randomized controlled trials (LIBERTY). *J Crohns Colitis.* 2025;19(6):jjaf060.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	New Policy was created to provide overrides to existing quantity limits.	08/27/2025