DRUG QUANTITY MANAGEMENT POLICY – PER DAYS

POLICY: Inflammatory Conditions – Entyvio Subcutaneous Drug Quantity Management Policy – Per Days
- Entyvio® (vedolizumab subcutaneous injection – Takeda)

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

Entyvio subcutaneous (SC), an integrin receptor antagonist, is indicated for treatment of the following uses:[1]
- **Crohn's disease**, in adults with moderately to severely active disease.
- **Ulcerative colitis**, in adults with moderately to severely active disease.

Dosing

Therapy begins with Entyvio 300 mg IV at Weeks 0, 2, and 6, followed by every 8 weeks thereafter.[1] Alternatively, at Week 6, or at any scheduled Entyvio IV infusion in patients with a clinical response or remission, therapy can be switched to Entyvio SC. The recommended maintenance dose of Entyvio SC is 108 mg SC once every 2 weeks (Q2W).

Dose Escalation in Crohn's Disease and Ulcerative Colitis
There are data to support dose escalation of Entyvio SC from Q2W to once weekly (QW) in patients with inflammatory bowel disease who do not achieve remission with the Q2W dosing.[2] In VISIBLE OLE, an open-label extension study that enrolled patients from the pivotal studies of Entyvio, VISIBLE-1 (ulcerative colitis study) and VISIBLE-2 (Crohn's disease study), patients experiencing treatment failure with Entyvio SC Q2W could escalate to QW dosing. Treatment failure was defined as disease worsening, need for rescue medications, or need for surgical intervention. The VISIBLE OLE analysis included patients with ulcerative colitis (n = 231) or Crohn's disease (n = 344) who completed 52 weeks of treatment with Entyvio SC Q2W or placebo in VISIBLE-1 or 2 and patients without a clinical response at Week 6 in VISIBLE-1 or 2 but who responded at Week 14 to Entyvio IV. Analysis did not include patients that stopped VISIBLE-1 or 2 early due to treatment failure and subsequently enrolled in the OLE with QW dosing.

- Among patients with ulcerative colitis who escalated to QW dosing during the OLE (n = 63), 22.2% and 38.1% achieved clinical remission and response, respectively, by Week 8 after transitioning to QW dosing. This was fairly consistent through Week 48, and then steadily decreased through Week 168.
- Among patients with Crohn's disease who escalated to QW dosing during the OLE (n = 101), 38.6% and 53.5% achieved clinical remission and response, respectively, by Week 8 after transitioning to QW. This steadily decreased through Week 168.

Availability
Entyvio is available as a 108 mg/0.68 mL prefilled pens.[1] Entyvio is also available as a 300 mg vial for intravenous (IV). The 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 Entyvio SC, 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
Entyvio® (vedolizumab SC injection)	108 mg/0.68 mL prefilled pen	2 pens per 28 days	6 pens 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 per 28 days at retail or 12 pens per 84 days at home delivery if the patient meets ALL of the following (A, B, and C):
   A) Entyvio is being used to treat Crohn's disease or ulcerative colitis; AND
   B) Patient has received Entyvio 108 mg subcutaneous (SC) once every 2 weeks for 14 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 per 28 days at retail or 12 pens per 84 days at home delivery if the patient meets BOTH of the following (A and B):
   A) Entyvio is being used to treat Crohn's disease or ulcerative colitis; AND
   B) Patient has been receiving Entyvio 108 mg subcutaneous (SC) once weekly.

REFERENCES

1. Entyvio subcutaneous injection [prescribing information]. Deerfield, IL: Takeda; May 2024
2. Loftus EV, Jones S, Velazco N, et al. Persistence of treatment effect in patients with ulcerative colitis and Crohn's disease: long-term results from the VISIBLE OLE study [poster Su1859]. Presented at: the 2025 Digestive Disease Week; San Diego, CA; May 3-7, 2025.

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