BACKGROUND
Entyvio, an integrin receptor antagonist, is a humanized monoclonal antibody that binds specifically to α4β7 integrin and blocks the interaction of α4β7 integrin with mucosal addressing cell adhesion molecule-1 (MAdCAM-1), thus inhibiting migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal (GI) parenchymal tissue. In UC, Entyvio is indicated for inducing and maintaining clinical response, inducing and maintaining clinical remission, improving the endoscopic appearance of the mucosa, and achieving corticosteroid-free remission in adult patients who have had an inadequate response with, lost response to, or were intolerant to, a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids. In CD, Entyvio is indicated for achieving a clinical response, achieving clinical remission, and achieving corticosteroid-free remission in adult patients with moderately to severely active CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on steroids.

REQUIRED REVIEW AND APPROVALS
This policy involves the use of Entyvio. Prior authorization is recommended for medical benefit coverage of Entyvio. Coverage is recommended for those who meet the conditions of coverage in the Criteria, Dosing, Initial/Extended Approval, Duration of Therapy, and Labs/Diagnostics for the diagnosis provided. The requirement that the patient meet the Criteria and Waste Management applies for all covered conditions. Conditions Not Recommended for Approval are listed following the Recommended Authorization Criteria and Waste Management section.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Entyvio as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Entyvio to 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 required, a response to therapy is required for continuation of therapy.

CRITERIA:
Coverage Entyvio is recommended in those who meet one of the following criteria:

Food and Drug Administration (FDA)-Approved Indications
1. **Crohn’s Disease (CD).**

   **Criteria. The patient must meet the following criteria (A AND B):**
   
   A) The patient has tried at least one tumor necrosis factor (TNF) blocker for Crohn’s disease (e.g., Humira, Cimzia, or Remicade) for at least 2 months, unless intolerant; AND
   
   B) Entyvio is prescribed by or in consultation with a gastroenterologist.

   Entyvio is indicated in CD, for achieving a clinical response, achieving clinical remission, and achieving corticosteroid-free remission in adult patients with moderately to severely active CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on steroids. The efficacy and safety of Entyvio for induction and maintenance of CD were established in three studies, an integrated induction study and maintenance study, and an induction study in patients who had previously failed at least one TNF blocker. In the integrated induction and maintenance study, 62% of patients (n = 689/1,115) had previously used a TNF blocker, with patients discontinuing therapy for an inadequate response (50%; n = 320/645), loss of response (39%; n = 251/645), or unacceptable adverse event (AE) [12%; n = 74/645]. At least two TNF blockers had been tried in 36% of patients (n = 398/1,115). Overall, 51% of patients in the maintenance study had previously failed a TNF blocker. In the study evaluating Entyvio in patients with CD who had failed a TNF blocker (n = 315), there was not a statistically significant difference at Week 6 in the proportion of patients in clinical remission with Entyvio vs. placebo (15% vs. 12%, respectively). However, in an exploratory analysis significantly more patients were in clinical remission with Entyvio vs. placebo at Week 10 (27% vs. 12%, respectively; P = 0.001; relative risk, 2.2 [95% confidence interval {CI}: 1.3, 3.6]).

   **Dosing in CD.** _Dosing must meet the following:_ 300 mg as an IV infusion at Weeks 0, 2, and 6, then Q8W thereafter.

   **Initial Approval/Extended Approval.**
   
   A) **Initial Approval:** Initial approval for patients starting Entyvio is for 14 weeks (3 doses given at Weeks 0, 2, and 6).
   
   B) **Extended Approval:** Approve for an additional 12 months of therapy if the patient has responded, as determined by the prescribing physician. The patient may not have a full response by Week 14, but there should be some response.

   The recommended dose is 300 mg as a 30-minute IV infusion at Week 0, 2, and 6, and Q8W thereafter; therapy should be discontinued in patients who show no benefit by Week 14.

   **Duration of Therapy in CD.** Indefinite if the patient is responding.

   **Labs/Diagnostics:** None required.

2. **Ulcerative Colitis (UC).**

   **Criteria. The patient must meet the following criteria (A AND B):**
A) The patient has tried at least one tumor necrosis factor (TNF) blocker for ulcerative colitis (e.g., Humira, Remicade, or Simponi [subcutaneous]) for at least 2 months, unless intolerant; AND

B) Entyvio is prescribed by or in consultation with a gastroenterologist.

Enthyvio is indicated in ulcerative colitis (UC), for inducing and maintaining clinical response, inducing and maintaining clinical remission, improving the endoscopic appearance of the mucosa, and achieving corticosteroid-free remission in adult patients who have had an inadequate response with, lost response to, or were intolerant to, a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids. The efficacy of Entyvio for induction and maintenance in UC were established in two integrated randomized, double-blind, multicenter studies in adult patients with moderately to severely active disease. Approximately one-half of patients (n = 431/895) had previously used a TNF blocker, with patients discontinuing therapy for an inadequate response (48%; n = 176/895), loss of response (38%; n = 176/895), or unacceptable AE (14%; n = 50/895). In the maintenance study, concurrent treatment with glucocorticoids or immunosuppressants or previous treatment with TNF blockers did not substantially affect efficacy of Entyvio. Toronto Consensus Guidelines (2015) have been published which address use of Entyvio in UC. Entyvio is recommended for patients with primary or secondary failure of a TNF blocker. The guidelines also note that Entyvio is a treatment option for patients with moderate to severe active UC who have failed corticosteroids, thiopurines, or TNF blockers. However, there are no data regarding treatment strategies following failure of Entyvio.

Dosing in UC. Dosing must meet the following: 300 mg as an IV infusion at Weeks 0, 2, and 6, then Q8W thereafter.

Initial Approval/Extended Approval.

A) Initial Approval: Initial approval for patients starting Entyvio is for 14 weeks (3 doses given at Weeks 0, 2, and 6).

B) Extended Approval: Approve for an additional 12 months of therapy if the patient has responded (e.g., decreased stool frequency or rectal bleeding), as determined by the prescribing physician. The patient may not have a full response by Week 14, but there should be some response.

The recommended dose is 300 mg as a 30-minute IV infusion at Week 0, 2, and 6, and Q8W thereafter; therapy should be discontinued in patients who show no benefit by Week 14.

Duration of therapy in UC: Indefinite if the patient is responding.

Labs/Diagnostics: None required.

Other Uses with Supportive Evidence

3. Patient has been Established on Entyvio. Approve if the patient has been taking Entyvio AND meets the conditions for coverage required for Dosing, Extended Approval, Duration of Therapy, and Labs/Diagnostics for an approved use in this Entyvio Utilization Review policy.

Waste Management. Entyvio is supplied in a single-use 20 mL vial that contains 300 mg. Only one vial should
be needed per dose.

**CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Entyvio 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.

Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

**SPECIAL CONSIDERATIONS**

None.

**LIMITATIONS/EXCLUSIONS**

Please refer to each product line’s certificate of coverage for benefit limitations and exclusions for these services.

**REFERENCES**

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**REVISION HISTORY**

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