MEDICAL MUTUAL®

Drug Policy

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

Policy:	**201423**	**Initial Effective Date: 09/05/2014** **Annual Review Date: 08/16/2018** **Last Revised Date: 08/16/2018**
Code(s):	**HCPCS J3380**	
SUBJECT:	Entyvio™ (vedolizumab injection for intravenous [IV] use–Takeda Pharmaceuticals America, Inc.)	

OVERVIEW

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 addressin cell adhesion molecule-1 (MAdCAM-1), thus inhibiting migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal (GI) parenchymal tissue.[1] It is indicated in the following conditions:

1) Ulcerative colitis (UC); and
2) Crohn's disease (CD).

POLICY STATEMENT

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 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.

The Site of Care Medical Necessity Criteria applies to initial therapy and reauthorizations.

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RECOMMENDED AUTHORIZATION CRITERIA

Food and Drug Administration (FDA)-Approved Indications

1. Crohn's Disease (CD).

Criteria. *The patient must meet the following criteria (a, b, AND c):*

a) The patient has tried at least one TNF blocker (e.g., Humira, Cimzia, or Remicade) or one immunomodulator for Crohn's disease for at least 2 months, unless intolerant or has had an inadequate response with, was intolerant to, or demonstrated dependence on corticosteroids;[2-3] AND

b) Entyvio is prescribed by or in consultation with a gastroenterologist; AND

c) Site of care medical necessity is met*

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.[1] 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.[2-3] 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].[2] 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.[3] 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).[3] 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.[1]

Initial Approval/Extended Approval.

a) *Initial Approval*: Initial approval for patients starting Entyvio is for 14 weeks

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.[1]

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

Labs/Diagnostics: None required.

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2. Ulcerative Colitis (UC).

Criteria. *The patient must meet the following criteria (a, b, AND c):*

a) The patient has tried at least one TNF blocker (e.g., Humira, Remicade, or Simponi [subcutaneous]) or one immunomodulator for UC for at least 2 months, unless intolerant or has had an inadequate response with, was intolerant to, or demonstrated dependence on corticosteroids; AND

b) Entyvio is prescribed by or in consultation with a gastroenterologist; AND

c) Site of care medical necessity is met*.

Entyvio 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.[1] 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.[4] 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.

Dosing in UC. *Dosing must meet the following*: 300 mg as an IV infusion at Weeks 0, 2, and 6, then Q8W thereafter.[1]

Initial Approval/Extended Approval.

a) *Initial Approval*: Initial approval for patients starting Entyvio is for 14 weeks

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.[1]

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. Site of care medical necessity must be met*.

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.

1. **Concurrent Use with a Biologic used for an Inflammatory Condition** (e.g., Cimzia [certolizumab pegol subcutaneous {SC} injection], Humira [adalimumab SC injection], Remicade, Renflexis, Inflectra [infliximab IV infusion], Simponi [golimumab SC injection], Tysabri® [natalizumab IV infusion]). The combination of Entyvio used simultaneously with another biologic has not been evaluated for efficacy or safety. Entyvio binds specifically to α4β7 integrin and blocks the interaction of α4β7 integrin with MAdCAM-1, thus inhibiting migration of memory T-lymphocytes; there is a Warning concerning infection in patients treated with Entyvio.[1] Therefore, co-administration of Entyvio with other biologics has the risk of added immunosuppression.
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.

REFERENCES

1. Entyvio™ for intravenous injection [prescribing information]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; May 2014.
2. Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*. 2013;369(8):711-721.
3. Sands BE, Feagan BG, Rutgeerts P, et al. Effects of vedolizumab induction therapy for patients with Crohn's disease in whom tumor necrosis factor antagonist treatment had failed. *Gastroenterology*. 2014;147(3):618-627
4. Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med*. 2013;369(8):699-710.

5. Bressler B, Marshall JK, Bernstein CN, et al. Clinical practice guidelines for the medical management of nonhospitalized ulcerative colitis: the Toronto consensus. *Gastroenterology*. 2015;148(5):1035-1058.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

***MMO Site of Care Medical Necessity Criteria:**
Medications in this policy will be administered in a place of service that identifies the location to be a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless *at least one* of the following are met[†]:

1. Age less than 21 years; or
2. Clinically unstable based upon documented medical history (e.g., patient is hemodynamically unstable); or
3. History of a severe adverse event from previous administration of the prescribed medication; or
4. Requested medication is being administered as follows:
   - part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer; or
   - administered with dialysis; or
5. Physical or cognitive impairment and caregiver is not available to assist with safe administration of prescribed medication in the home; or
6. Up to 3 doses of medication or re-initiation after at least 12 months; or
7. Experiencing adverse events that are not managed by premedication or resources available at a non-hospital facility based location.

[†]This criterion does not apply to Medicare or Medicare Advantage members.

Prior approval is required for HCPCS Code J3380

HCPCS Code(s):	
J3380	Injection, vedolizumab, 1 mg