Effective Date: 09/1/2014
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Next Review Due By: 10/2022
Policy Number: C6773-A

Entyvio (vedolizumab)

PRODUCTS AFFECTED

Entyvio (vedolizumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Crohn's Disease, Ulcerative Colitis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. FOR ALL INDICATIONS
1. (a) Prescriber attests member has had a negative TB screening or TB test result within the last 12 months for initial and continuation of therapy requests

OR

(b) For members who have a positive test for latent TB, provider documents member has completed a treatment course (a negative chest x-ray is also required every 12 months)

OR that member has been cleared by an infectious disease specialist to begin treatment
AND

2. Member is not on concurrent treatment or will be used in combination with other TNF-inhibitor, biologic response modifier or other biologic DMARDs, Janus kinase Inhibitors, or Phosphodiesterase 4 inhibitor (i.e., apremilast, tofacitinib, baricitinib) as verified by prescriber attestation, member medication fill history, or submitteddocumentation
AND
3. Prescriber attests member does not have an active, severe infection
AND
4. IF THIS IS A NON-FORMULARY PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. If yes, please submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s)

B. MODERATE TO SEVERE CROHNSDISEASE

1. Documentation of a diagnosis of currently ACTIVE moderate to severely active Crohn's Disease (Crohn's disease activity index-CDAI score of 221-450)
AND
2. (a) Member has had a trial (>3 months) and inadequate response to ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine, methotrexate) up to maximally indicated doses unless contraindicated or significant adverse reactions are experienced

OR

(b) Prescriber provides documented medical justification that supports the inability to use immunomodulators

i. Inability to induce short-term symptomatic remission with a 3-month trial of systemic glucocorticoids

ii. High-risk factors for intestinal complications may include: Initial extensive ileal, ileocolonic, or proximal GI involvement, Initial extensive perianal/severe rectal disease, Fistulizing disease (e.g., perianal, enterocutaneous, and rectovaginal fistulas), Deep ulcerations, Penetrating, stricturing or stenosis disease and/or phenotype, Intestinal obstruction or abscess

iii. High risk factors for postoperative recurrence may include: Less than 10 years duration between time of diagnosis and surgery, Disease location in the ileum and colon, Perianal fistula, Prior history of surgical resection, Use of corticosteroids prior to surgery

AND

3. Member has had a trial (>3 months) and inadequate response to ONE FORMULARY OR PREFERREDTNF-inhibitor unless contraindicated or significant adverse reactions experienced
AND
4. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal

C. ULCERATIVE COLITIS

1. Documentation of ulcerative colitis diagnosis with evidence of moderate to severe disease activity
AND

2. (a) Member has had a 2-month trial of one systemic agent (e.g., 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone, methylprednisolone) or was intolerant to one of these agents for ulcerative colitis or will continue to take concurrently.
   NOTE: A previous trial of a biologic (e.g., an adalimumab product [e.g., Humira], Simponi SC [golimumab SC injection], or Entyvio [vedolizumab IV infusion] also counts as a trial of one systemic agent for UC)
   OR
   b) The member has pouchitis AND has tried therapy with an antibiotic (e.g., metronidazole, ciprofloxacin), probiotic, corticosteroid enema [for example, Cortenema® {hydrocortisone enema, generics}], or Rowasa® (mesalamine)
   enema AND
3. Member has had a trial (>3 months) and inadequate response to ONE FORMULARY OR PREFERREDTNF-inhibitor unless contraindicated or significant adverse reactions experienced
   AND
4. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy atrenewal

CONTINUATION OF THERAPY:

A. ALLINDICATIONS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required) AND
2. Documentation of no intolerable adverse effects or drug toxicity AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs andsymptoms.
   AND
4. (a) Prescriber attests member has had a negative TB screening or TB test result within the last 12 months for initial and continuation of therapy requests
   OR
   (b) For members who have a positive test for latent TB, provider documents member has completed a treatment course (a negative chest x-ray is also required every 12 months)
   OR
   that member has been cleared by an infectious disease specialist to begin treatment

DURATION OF APPROVAL:

Initial authorization: 5 months [4 doses (zero, two, six weeks and one every eight- week dose)]
*Discontinue therapy if no evidence of therapeutic benefit by week 14, Continuation authorization: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with, a board-certified gastroenterologist or colorectal surgeon. [If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age or older

QUANTITY:

300 mg IV at weeks 0, 2 and 6 and then every 8 weeks thereafter

When requests for off-label dosing, dose escalation, or dose intensification are received, requests will be reviewed for evidence that current or standard dosing is not adequate to produce a therapeutic level of drug (e.g., pharmacokinetic failure), clinical failure or significant loss of response is present, and the requested dosing is established as safe and effective for the condition. There are certain situations where no additional amount of drug is likely to produce or recapture clinical effect because the condition is no longer responsive to the drug (e.g., pharmacodynamic failure) or the drug cannot reach the site of activity at sufficient levels. The following items will assist reviewers in determining if the requested dosing is medically necessary:

- *FDA or compendium-supported dosing and therapeutic monitoring recommendations for the drug*
- *Member claims/adherence history*
- *Clinical documentation of the member's response to current or standard dosing regimens (disease activity indices if commonly used in clinical practice or documentation to approximate them may be necessary to demonstrate the response)*
- *In conjunction with documented clinical failure or loss of response or wearing off of effect, test results that demonstrate failure of current or standard dosing to reach established treatment thresholds (e.g., established therapeutic monitoring recommendations)*
- *If applicable, documentation showing the member does not have conditions which make achieving a therapeutic level of drug unlikely even with dose intensification (e.g., dose intensification may be futile due to the presence of anti-drug antibodies, protein losing enteropathy, nephrotic syndrome, severe drug excretion or malabsorption issues, etc.)*
- *In certain situations, documentation or peer-to-peer determination that re-induction cannot be tried to recapture response as an alternative to long term dose escalation or intensification*

PLACE OF ADMINISTRATION:

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Entyvio (vedolizumab). For information on site of care, see "place holder for hyperlink for Specialty Medication Administration Site of Care coverage criteria policy"

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Intravenous

DRUG CLASS:

Integrin Receptor Antagonists

FDA-APPROVED USES:

Crohn Disease: Treatment of moderately to severely active Crohn disease in patients who have had an inadequate response with lost response to or were intolerant to a tumor necrosis factor-alpha (TNF-alpha) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

Ulcerative Colitis: Treatment of moderately to severely active ulcerative colitis in patients who have had

an inadequate response with lost response to, were intolerant to a tumor necrosis factor alpha (TNF-alpha) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

Crohn's Disease Activity Index (CDAI): frequently used to assess disease severity; scores ranging from 0 to over 600, based on a diary of symptoms kept by the member for 7 days, general well-being, deviation of weight, features of extraintestinal disease, use of antidiarrheal medications, presence of
abdominal mass, and hematocrit levels.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of the gastrointestinal tract of unknown etiology and characterized by a chronic idiopathic inflammation of the intestine and consists of two main forms, ulcerative colitis (UC) and Crohn's disease (CD). While UC and CD have similar clinical presentations, they differ in the body areas affected. CD is characterized by deeper and more erratic inflammation that can occur throughout the entire digestive tract. In UC, inflammation is continuous and widespread and disturbs the superficial mucosal layer of the large intestine or the colon.
Crohn's disease (CD) is a chronic, inflammatory, multisystem disorder of unknown etiology with genetic, immunologic, and environmental influences. CD involves any area of the gastrointestinal tract(GIT) from the oral cavity to the anus, but it is limited primarily to the colon with or without small- intestine disease. Moreover, the inflammation in CD is often described as transmural, damaging each mucosal layer of the GIT, and noncontinuous. Therapy for CD includes medical therapy with pharmacologic agents consisting of 5-aminosalicylates (5-ASA), antibiotics, corticosteroids, immunomodulators, and biologics. Surgery is reserved for patients who are refractory to medical therapy. The key symptoms of CD include abdominal pain, diarrhea, and fatigue. Weight loss, fever, growth failure, anemia, recurrent fistulas, or extraintestinal manifestations (e.g., arthritis, iritis) can also occur. There is no single laboratory test that can make an unequivocal diagnosis of CD.
Ulcerative colitis (UC) is a chronic inflammatory condition characterized by relapsing and remitting episodes of inflammation that involves the rectum and colon. The definitive etiology of ulcerative colitis is unknown, but suspected causes are similar to those of CD. Inflammation can be mild, moderate, or severe. UC is limited to the superficial mucosa of the colon. UC more commonly involves the entire colon in children than in adults, who more commonly will have limited left-sided disease. The goals of treatment are to control the acute attacks, prevent recurrent attacks and promote healing of the colon. Severe attacks may require hospitalization. Generally, first-line treatment of UC include as corticosteroids, 6-mercaptoprine and azathioprine.

The anti-tumor necrosis factor (anti-TNF) agents (infliximab, adalimumab, and certolizumab pegol) are effective for treatment of patients with CD who respond inadequately to treatment with corticosteroids,

thiopurines, and methotrexate. Anti-TNF agents have rapid onset of effect, with benefit often noted within 2 weeks of initiating therapy. Anti–TNF) agents are reserved for moderate to severe disease refractory to corticosteroids and immunomodulators in both CD and UC. Infliximab and adalimumab carry approvals for both CD and UC, though certolizumab pegol is approved only for CD.

Other monoclonal antibodies approved for IBD are the integrin inhibitors. Vedolizumab, an α4 β7integrin inhibitor, is approved for both CD and UC, and natalizumab, an α4 integrin inhibitor, is approved for use in CD. These drugs are reserved for patients nonresponsive to conventional therapies, including TNF inhibitors, and carry a risk of PML.

Vedolizumab (Entyvio), a humanized monoclonal antibody, works as an antagonist of the α4β7 integrin receptor that ultimately blocks T cell migration within the gastrointestinal tract. Vedolizumab is a gut-selective immunosuppressive biologic and humanized monoclonal antibody that is being developed to specifically antagonize the α4β7 integrin. With this target, the drug is designed to inhibit the binding of alpha4beta7 ingegrin to intestinal mucosal addressing cell adhesion molecule 1 (MAdCAM-1) and fibronectin, but not vascular cell adhesion molecule 1 (VCAM-1). By inhibiting alpha4beta7 integrin, vedolizumab has the potential to limit the ability of some white blood cells to permeate gut tissues.

American College of Gastroenterology (ACG)

In March 2018, the ACG released an updated guideline on managing CD in adult patients. It includes preferable approaches on diagnosis, disease modifiers, and medical therapy for the various disease severities.

Nonsteroidal anti-inflammatory drugs (NSAIDs) may exacerbate disease activity and should be avoided when possible in patients with Crohn disease.

Sulfasalazine is effective for treating symptoms of colonic Crohn disease that is mild to moderately active and can be used as treatment for this member population.

For patients with low risk of progression, treatment of active symptoms with antidiarrheals, other nonspecific medications, and dietary manipulation, along with careful observation for inadequate symptom relief, worsening inflammation, or disease progression, is acceptable.

Oral corticosteroids are effective and can be employed for short-term use in alleviating signs and symptoms of moderately to severely active Crohn disease. Thiopurines (azathioprine, 6- mercaptopurine) are effective and should be considered for use for steroid sparing in Crohn disease. Azathioprine and 6-mercaptopurine are effective therapies and should be considered for treatment of patients with Crohn disease for maintenance of remission

Methotrexate (up to 25 mg once weekly intramuscularly [IM] or subcutaneously [SC]) is effective and should be considered for use in alleviating signs and symptoms in patients with steroid- dependent Crohn disease and for maintaining remission.

Anti–tumor necrosis factor (anti-TNF) agents (infliximab, adalimumab, certolizumab pegol) should be used to treat Crohn disease that is resistant to treatment with corticosteroids.

Anti-TNF agents should be given for Crohn disease refractory to thiopurines or methotrexate. Combination therapy of infliximab with immunomodulators (thiopurines) is more effective than treatment with either immunomodulators alone or infliximab alone in patients who are naive to those agents.

For patients with moderately to severely active Crohn disease and objective evidence of active disease, anti-integrin therapy (with vedolizumab) with or without an immunomodulator is more effective than

placebo and should be considered for use in induction of symptomatic remission inpatients with Crohn disease.

Natalizumab is more effective than placebo and should be considered for use in induction of symptomatic response and remission in patients with active Crohn disease.

Natalizumab should be used for maintenance of natalizumab-induced remission of Crohn disease only if serum antibody to John Cunningham (JC) virus is negative. Testing for anti-JC virus antibody should be repeated every 6 months and treatment stopped if the result is positive. Ustekinumab should be given for moderate to severe Crohn disease patients who failed previous treatment with corticosteroids, thiopurines, methotrexate, or anti-TNF inhibitors or who have had no prior exposure to anti-TNF inhibitors.

Intravenous corticosteroids should be used to treat severe or fulminant Crohn disease.

Anti-TNF agents (infliximab, adalimumab, certolizumab pegol) can be considered to treat severely active Crohn disease.

Infliximab may be administered to treat fulminant Crohn disease. Infliximab is effective and should be considered in treating perianal fistulas in Crohn disease. Infliximab may be effective and should be considered in treating enterocutaneous and rectovaginal fistulas in Crohn disease.

Adalimumab and certolizumab pegol may be effective and should be considered in treating perianal fistulasin Crohn disease.

Thiopurines (azathioprine, 6-mercaptopurine) may be effective and should be considered intreating fistulizing Crohn disease.

Once remission is induced with corticosteroids, a thiopurine or methotrexate should be considered. Anti-TNF therapy, specifically infliximab, adalimumab, and certolizumab pegol, should be used to maintain remission of anti-TNF–induced remission.

Anti-TNF monotherapy is effective at maintaining anti-TNF–induced remission, but because of the potential for immunogenicity and loss of response, combination with azathioprine/6- mercaptopurine or methotrexate should be considered.

Imidazole antibiotics (metronidazole and ornidazole) at doses between 1 and 2 g/day can be used after small intestinal resection in Crohn disease patients to prevent recurrence.

ACG Clinical Guideline: Ulcerative Colitis in Adults

The management of ulcerative colitis (UC) has changed since the last guideline was published in 2010. The recommendations in the current update are based on the quality of evidence using GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodology. An updated clinical guideline on the management of UC shifts the focus from symptom-based treatment to both symptom management and mucosal healing. New tests, including those based on serum drug levels and fecal calprotectin, as well as newer FDA-approved therapies, including budesonide, vedolizumab, and tofacitinib. Key recommendations include:

Treat patients with UC to achieve mucosal healing, increase the likelihood of sustained steroid- free remission, and prevent hospitalizations and surgery.

In patients with moderately active UC, use non-systemic corticosteroids, such as budesonide MMX, before systemic therapy.

In patients with moderately to severely active UC, use vedolizumab to induce remission.

In patients with moderately to severely active UC, use tofacitinib (10 mg orally twice daily for 8 weeks)to induce remission.

Do not defer colectomy because of exposure to infliximab and cyclosporine, as these agents do not increase the risk for postoperative complications.

In patients with acute severe UC and concomitant *Clostridium difficile* infection, use vancomycin instead

of metronidazole.

Perform surveillance colonoscopies in patients with UC at 1- to 3-year intervals, based on the combined risk factors for colorectal cancer in UC and the findings on previous colonoscopy.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Entyvio (vedolizumab) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy.

Contraindications to Entyvio (vedolizumab) include: Severe hypersensitivity to vedolizumab or any component of the formulation including L-histidine, L-arginine, sucrose, or polysorbate 80.
Exclusions for coverage include, but are not limited to: Combination with another biologic agent for an inflammatory condition [e.g., Actemra (tocilizumab), Enbrel (etanercept), Kineret (anakinra), Orencia (abatacept), Remicade (infliximab), Rituxan (rituximab), Simponi (golimumab)]; Currently diagnosed with, or history of, progressive multifocal leukoencephalopathy (PML)

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J3380	Injection, vedolizumab, 1mg

AVAILABLE DOSAGE FORMS:

Entyvio SOLR 300MG (1 vial) single use 20ml

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