ENTYVIO® (VEDOLIZUMAB)

Policy Number: PHARMACY 285.10 T2 **Effective Date**: October 1, 2018

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Related Policy

- Acquired Rare Disease Drug Therapy Exception Process
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- Specialty Medication Administration - Site of Care Review Guidelines
- Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

CONDITIONS OF COVERAGE

Applicable Lines of Business/ Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	General Benefits Package
Referral Required (Does not apply to non-gatekeeper products)	No
Authorization Required (Precertification always required for inpatient admission)	Yes[1,2]
Precertification with Medical Director Review Required	Yes[1,3]
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	Office, Outpatient[3,4]
Special Considerations	[1]Precertification with review by a Medical Director or their designee through Oxford's Medical Management is required. [2]New Jersey small group plan members should refer to their Certificate of Coverage for precertification and quantity limit guidelines. [3]Additional precertification requirements apply to

Special Considerations *(continued)*	requests for hospital outpatient facility infusion of Entyvio; refer to the policy titled Specialty Medication Administration - Site of Care Review Guidelines. [4]Participating Hospitals are required to purchase Entyvio® (vedolizumab) from the BriovaRx Specialty Pharmacy when the medication is administered in an outpatient hospital setting; refer to the policy titled Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting for additional information.

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

Some Certificates of Coverage allow coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met; refer to the policy titled Acquired Rare Disease Drug Therapy Exception Process.

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

Entyvio (vedolizumab) is proven and medically necessary for the treatment of:

Crohn's disease when **all** of the following criteria are met:[1,2]

- For **initial therapy, all** of the following:
  - Diagnosis of moderately to severely active Crohn's disease (CD); **and**
  - **One** of the following:
    - History of failure, contraindication, or intolerance to at least **one** of the following conventional therapies:
      - Tumor necrosis factor (TNF) blocker [e.g., Humira (adalimumab), Cimzia (certolizumab)]
      - Immunomodulator (e.g., azathioprine, 6-mercaptopurine)
      - Corticosteroid
    - Corticosteroid dependent (e.g., unable to successfully taper corticosteroids without a return of the symptoms of CD)

    and
  - Entyvio is initiated and titrated according to US Food and Drug Administration (FDA) labeled dosing for Crohn's disease up to a maximum of 300mg every 8 weeks (or equivalent dose and interval schedule); **and**
  - Patient is **not** receiving Entyvio in combination with either of the following:
    - Tumor necrosis factor (TNF) blocker [e.g., Humira (adalimumab), Cimzia (certolizumab)]
    - Tysabri (natalizumab); **and**
  - Initial authorization will be for no more than 14 weeks
- For **continuation therapy**, **all** of the following:
  - Documentation of positive clinical response to Entyvio; **and**
  - Entyvio dosing for Crohn's disease is in accordance with the FDA labeled dosing up to a maximum of 300mg every 8 weeks (or equivalent dose and interval schedule); **and**
  - Reauthorization will be for no more than 12 months.

Ulcerative colitis when **all** of the following criteria are met:[1,2]

- For **initial therapy, all** of the following:

- Diagnosis of moderately to severely active ulcerative colitis (UC); **and**
- **One** of the following:
  - History of failure, contraindication, or intolerance to at least **one** of the following conventional therapies:
    - Tumor necrosis factor (TNF) blocker [e.g., Humira (adalimumab), Simponi (golimumab)]
    - Immunomodulator (e.g., azathioprine, 6-mercaptopurine)
    - Corticosteroid
  - Corticosteroid dependent (e.g., unable to successfully taper corticosteroids without a return of the symptoms of UC)

  and
- Entyvio is initiated and titrated according to US Food and Drug Administration labeled dosing for ulcerative colitis up to a maximum of 300mg every 8 weeks (or equivalent dose and interval schedule); **and**
- Patient is **not** receiving Entyvio in combination with either of the following:
  - Tumor necrosis factor (TNF) blocker [e.g., Humira (adalimumab), Simponi (golimumab)]
  - Tysabri (natalizumab); **and**
- Initial authorization will be for no more than 14 weeks.

- For **continuation therapy**, **all** of the following:
  - Documentation of positive clinical response to Entyvio; **and**
  - Entyvio dosing for ulcerative colitis is in accordance with the FDA labeled dosing up to a maximum of 300mg every 8 weeks (or equivalent dose and interval schedule); **and**
  - Reauthorization will be for no more than 12 months.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Entyvio is indicated for treatment of adult patients with moderately to severely active ulcerative colitis (UC) 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 for the following:[1]

- Inducing and maintaining clinical response
- Inducing and maintaining clinical remission
- Improving endoscopic appearance of the mucosa
- Achieving corticosteroid-free remission

It is also indicated for treatment of adult patients with moderately to severely active Crohn's Disease (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 corticosteroids for the following: [1]

- Achieving clinical response
- Achieving clinical remission
- Achieving corticosteroid-free remission

BACKGROUND

Entyvio is a monoclonal antibody that reduces chronically inflamed gastrointestinal parenchymal tissue associated with ulcerative colitis and Crohn's disease by binding specifically to the alpha-4-beta-7-integrin receptor and blocking its interaction with mucosal addressin cell adhesion molecule-1 which then inhibits the movement of memory T-lymphocytes across the endothelium into inflamed gastrointestinal tissue.[1,2]

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies may apply.

HCPCS Code	Description
J3380	Injection, vedolizumab, 1 mg

ICD-10 Diagnosis Code	Description
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula

ICD-10 Diagnosis Code	Description
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K51.00	Ulcerative (chronic) pancolitis without complications
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013	Ulcerative (chronic) pancolitis with fistula
K51.014	Ulcerative (chronic) pancolitis with abscess
K51.018	Ulcerative (chronic) pancolitis with other complication
K51.019	Ulcerative (chronic) pancolitis with unspecified complications
K51.20	Ulcerative (chronic) proctitis without complications
K51.211	Ulcerative (chronic) proctitis with rectal bleeding
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction
K51.213	Ulcerative (chronic) proctitis with fistula
K51.214	Ulcerative (chronic) proctitis with abscess
K51.218	Ulcerative (chronic) proctitis with other complication
K51.219	Ulcerative (chronic) proctitis with unspecified complications
K51.30	Ulcerative (chronic) rectosigmoiditis without complications
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications
K51.40	Inflammatory polyps of colon without complications
K51.411	Inflammatory polyps of colon with rectal bleeding

ICD-10 Diagnosis Code	Description
K51.412	Inflammatory polyps of colon with intestinal obstruction
K51.413	Inflammatory polyps of colon with fistula
K51.414	Inflammatory polyps of colon with abscess
K51.418	Inflammatory polyps of colon with other complication
K51.419	Inflammatory polyps of colon with unspecified complications
K51.50	Left sided colitis without complications
K51.511	Left sided colitis with rectal bleeding
K51.512	Left sided colitis with intestinal obstruction
K51.513	Left sided colitis with fistula
K51.514	Left sided colitis with abscess
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complications
K51.80	Other ulcerative colitis without complications
K51.811	Other ulcerative colitis with rectal bleeding
K51.812	Other ulcerative colitis with intestinal obstruction
K51.813	Other ulcerative colitis with fistula
K51.814	Other ulcerative colitis with abscess
K51.818	Other ulcerative colitis with other complication
K51.819	Other ulcerative colitis with unspecified complications
K51.90	Ulcerative colitis, unspecified, without complications
K51.911	Ulcerative colitis, unspecified with rectal bleeding
K51.912	Ulcerative colitis, unspecified with intestinal obstruction
K51.913	Ulcerative colitis, unspecified with fistula
K51.914	Ulcerative colitis, unspecified with abscess
K51.918	Ulcerative colitis, unspecified with other complication
K51.919	Ulcerative colitis, unspecified with unspecified complications

Maximum Dosage Requirements

HCPCS Code Based Maximum Dosage Information

This section provides information about the maximum dosage per administration for vedolizumab administered by a medical professional.

Medication Name		Maximum Dosage per Administration	HCPCS Code	Maximum Allowed
Brand	Generic			
Entyvio	vedolizumab	300 mg	J3380	300 HCPCS units (1 mg per unit)

Maximum Allowed Quantities by National Drug Code (NDC) Units

The allowed quantities in this section are calculated based upon both the maximum dosage information supplied within this policy as well as the process by which NDC claims are billed. This list may not be inclusive of all available NDC's for each drug product and is subject to change.

Medication Name		How Supplied	National Drug Code	Maximum Allowed
Brand	Generic			
Entyvio	vedolizumab	300 mg powder for reconstitution	64764-0300-20	1 Vial

CLINICAL EVIDENCE

Technology Assessments

Ulcerative Colitis

A 2014 Cochrane review was published which evaluated efficacy and safety of vedolizumab used for induction and maintenance of remission in ulcerative colitis.[7] Authors concluded that:

- Moderate to high quality data from four studies shows that vedolizumab is superior to placebo for induction of clinical remission and response and endoscopic remission in patients with moderate to severely active ulcerative colitis and prevention of relapse in patients with quiescent ulcerative colitis.

- Moderate quality data from one study suggests that vedolizumab is superior to placebo for prevention of relapse in patients with quiescent ulcerative colitis.
- Adverse events appear to be similar to placebo.
- Future trials are needed to define the optimal dose, frequency of administration and long-term efficacy and safety of vedolizumab used for induction and maintenance therapy of ulcerative colitis.
- Vedolizumab should be compared to other currently approved therapies for ulcerative colitis in these trials.

A 2015 Cochrane review was published which examined the impact of biological interventions for ulcerative colitis on health-related quality of life (HRQL).[8] The authors concluded that:
- Biologics have the potential to improve HRQL in UC patients.
- High quality evidence suggests that infliximab provides a clinically meaningful improvement in HRQL in UC patients receiving induction therapy.
- Moderate quality evidence suggests that vedolizumab provides a clinically meaningful improvement in HRQL in UC patients receiving maintenance therapy.
- These findings are important since there is a paucity of effective drugs for the treatment of UC that have the potential to both decrease disease activity and improve HRQL.
- More research is needed to assess the long-term effect of biologic therapy on HRQL in patients with UC.
- More research is needed to assess the impact of golimumab and adalimumab on HRQL in UC patients.
- Trials involving direct head to head comparisons of biologics would help determine which biologics provide optimum benefit for HRQL.

Professional Societies

Crohn's Disease

American College of Gastroenterology

According to the American College of Gastroenterology Practice Guidelines for the Management of Crohn's Disease in Adults (ACG Practice Guidelines) published in February 2009, patients with moderate-severe disease usually have a Crohn's Disease Activity Index (CDAI) of 220-450.[3] They have failed to respond to treatment for mild-moderate disease, or have more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia.

The CDAI is the sum of the following clinical or laboratory variables after multiplying by their weighting factor given in parentheses:
- Number of liquid or soft stools each day for seven days (2)
- Abdominal pain graded from 0-3 in severity each day for seven days (5)
- General well-being, subjectively assessed from 0 (well) to 4 (terrible) each day for seven days (7)
- Presence of complications where 1 point is added for each complication (20). Complications include:
  - The presence of joint pains (arthralgia) or frank arthritis
  - Inflammation of the iris or uveitis
  - Presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers
  - Anal fissures, fistulae or abscesses
  - Other fistulae (e.g., Enterocutaneous, vesicle, vaginal)
  - Fever (>37.8° C) during the previous week
- Taking diphenoxylate/atropine [Lomotil®] or opiates for diarrhea (30)
- Presence of an abdominal mass where 0 = none, 2 = questionable, 5 = definite (10)
- Absolute deviation of hematocrit from 47% in males and 42% in females (6)
- Percentage deviation from standard body weight (1)

In 2013, the AGA released an updated guideline which describes their relative positioning of immunomodulators and anti-TNF-α biologic agents in inducing and maintaining clinical remission in patients with inflammatory (luminal) Crohn's disease.[4] A summary of the recommendations along with strength of evidence are described below.

Recommendations for the Induction of Remission
- We suggest against using thiopurine monotherapy to induce remission in patients with moderately severe Crohn's disease (weak recommendation, moderate-quality evidence).
- We suggest against using methotrexate to induce remission in patients with moderately severe Crohn's disease (weak recommendation, low-quality evidence).
- We recommend using anti-TNF-α drugs to induce remission in patients with moderately severe Crohn's disease (strong recommendation, moderate-quality evidence).
- We recommend using anti-TNF-α monotherapy over thiopurine monotherapy to induce remission in patients who have moderately severe Crohn's disease (strong recommendation, moderate-quality evidence).
- We recommend using anti-TNF-α drugs in combination with thiopurines over thiopurine monotherapy to induce remission in patients who have moderately severe Crohn's disease (strong recommendation, high-quality evidence).

- We suggest using anti-TNF-α drugs in combination with thiopurines over anti-TNF-α drug monotherapy to induce remission in patients who have moderately severe Crohn's disease (weak recommendation, moderate-quality evidence).

Recommendations for Maintenance of Remission

- We recommend using thiopurines over no immunomodulator therapy to maintain a steroid-induced remission in patients with Crohn's disease (strong recommendation, moderate-quality evidence).
- We suggest using methotrexate over no immunomodulator therapy to maintain a steroid-induced remission in patients with Crohn's disease (weak recommendation, low-quality evidence).
- We recommend using anti-TNF-α drugs over no anti-TNF-α drugs to maintain a steroid or anti-TNF-α drug-induced remission in patients with Crohn's disease (strong recommendation, high-quality evidence).
- We make no recommendation for or against the combination of an anti-TNF-α drug and a thiopurine versus an anti-TNF-α drug alone to maintain remission induced by a combination of these drugs in patients with Crohn's disease (no recommendation, low-quality evidence).

REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare Pharmacy, Clinical Pharmacy Program that was researched, developed and approved by the UnitedHealth Group National Pharmacy & Therapeutics Committee. [*2018D0053G*]

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
10/01/2018	• Updated list of related policies; added reference link to the policy titled *Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting* • Revised conditions of coverage/special considerations; added language to indicate: ○ Participating hospitals are required to purchase Entyvio® (vedolizumab) from the BriovaRx Specialty Pharmacy when the medication is administered in an outpatient hospital setting; refer to the policy titled Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting for additional information • Archived previous policy version PHARMACY 285.9 T2