Clinical Policy: Vedolizumab (Entyvio®)

Reference Number: QCP.PHAR.002
Date of Last Revision: 05.24

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Vedolizumab (Entyvio®) is a monoclonal antibody medication.

Policy/Criteria
I. Initial Approval Criteria
A. Crohn's Disease (must meet all):
1. Diagnosis of CD;
2. Request is for Entyvio
3. Prescribed by or in consultation with a gastroenterologist
4. Member meets one of the following (a or b):
    a. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], methotrexate [MTX]) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
    b. Medical justification supports inability to use immunomodulators (see Appendix E);
5. Member is ≥ 18 years;
6. Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c, see Appendix D):
    a. Failure of Humira, unless the member has had a history of failure of two TNF blockers and request is not for another TNF blocker
    b. Skyrizi;
    c. Stelara;
7. Request is for IV formulation.
8. Member does not have combination use of biological disease-modifying antirheumatic drugs or JAK inhibitors (see Section III: Diagnoses/Indications for which coverage is NOT authorized);
9. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

B. Ulcerative Colitis (must meet all):
1. Diagnosis of UC;
2. Request is for Entyvio
3. Prescribed by or in consultation with a gastroenterologist;
4. Documentation of a Mayo Score ≥ 6 (see Appendix F);
5. Age ≥ 18 years

6. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
7. Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c, see Appendix D):
    a. Failure of Humira unless member has had history of failure of two TNF blockers and request is not for another TNF blocker
    b. Stelara;
    c. If member has not responded or is intolerant to one or more TNF blockers, Xeljanz/Xeljanz XR and Rinvoq, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;
8. Member does not have combination use of biological disease-modifying antirheumatic drugs or JAK inhibitors (see Section III: Diagnoses/Indications for which coverage is NOT authorized);
9. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

II. Continued Therapy

All Indications in Section I (must meet all):

1. Member currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member does not have combination use of biological disease-modifying antirheumatic drugs or JAK inhibitors (see Section III: Diagnoses/Indications for which coverage is NOT authorized);
4. If request is for a dose increase, new dose does not exceed maximum dose indicated in Section V.

Approval duration: 12 months

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – HIM.PA.154 for health insurance marketplace or evidence of coverage documents;

B. Combination use of biological disease-modifying antirheumatic drugs (bDMARDs) or potent immunosuppressants, including but not limited to any tumor necrosis factor (TNF) antagonists [e.g., Cimzia®, Enbrel®, Humira® and its biosimilars, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [e.g., Arcalyst® (IL-1 blocker), Ilaris® (IL-1 blocker), Kineret® (IL-1RA), Actemra® (IL-6RA), Kevzara® (IL-6RA), Stelara® (IL-12/23 inhibitor), Cosentyx® (IL-17A inhibitor), Taltz® (IL-17A inhibitor), Siliq™ (IL-17RA), Ilumya™ (IL-23 inhibitor), Skyrizi™ (IL-23 inhibitor), Tremfya® (IL23 inhibitor)], Janus kinase inhibitors (JAKi) [e.g., Xeljanz®/Xeljanz® XR, Cibinqo™, Olumiant™, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, Rituxan Hycela®], selective co-stimulation modulators

[Orencia®], and integrin receptor antagonists [Entyvio®] because of the additive immunosuppression, increased risk of neutropenia, as well as increased risk of serious infections

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CD: Crohn's disease
DMARDs: disease-modifying antirheumatic drugs
JAK: Janus kinase
MTX: methotrexate
TNF: tumor necrosis factor
UC: ulcerative colitis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azathioprine (Azasan®, Imuran®)	**CD*** 1.5 – 2 mg/kg/day PO	3 mg/kg/day
corticosteroids - Oral: e.g., prednisone, budesonide -Medium to very high potency topical: e.g., desoximetasone 0.05%, fluocinolone acetonide 0.025%, mometasone 0.1% cream, triamcinolone acetonide 0.1%, augmented betamethasone dipropionate 0.05%, clobetasol propionate 0.05% cream, ointment, gel, or solution, halobetasol propionate 0.05% cream, ointment	**CD*** Adult: -prednisone 40 mg – 60 mg PO QD for 1 to 2 weeks, then taper daily dose by 5 mg weekly until 20 mg PO QD, and then continue with 2.5 – 5 mg decrements weekly or IV 50 – 100 mg Q6H for 1 week - budesonide (Entocort EC□) 6 – 9 mg PO QD Pediatric: -Prednisone 1 to 2 mg/kg/day PO QD **UC** Adult: -Prednisone 40 mg – 60 mg PO QD, then taper dose by 5 to 10 mg/week -budesonide (Uceris□) 9 mg PO QD Pediatric:	Various

	-Prednisone 1 to 2 mg/kg/day PO QD	
6-mercaptopurine (Purixan®)	**CD*** 50 mg PO QD or 0.75 – 1.5 mg/kg/day PO	1.5 mg/kg/day
methotrexate (Trexall®, Otrexup™, Rasuvo®, RediTrex®, Xatmep™, Rheumatrex®)	**CD*** 15 – 25 mg/week IM or SC	30 mg/week
Pentasa® (mesalamine)	**CD** 1,000 mg PO QID	4 g/day
tacrolimus (Prograf®)	**CD*** 0.27 mg/kg/day PO in divided doses or 0.15 – 0.29 mg/kg/day PO	N/A
biologic DMARDs (e.g., Humira, Enbrel, Cosentyx, Remicade, Simponi Aria, Otezla, Xeljanz/Xeljanz XR, Kevzara)	See Section V. Dosing and Administration	See Section V. Dosing and Administration
Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azathioprine (Azasan®, Imuran®)	**CD*** 1.5 – 2 mg/kg/day PO	3 mg/kg/day
corticosteroids - Oral: e.g., prednisone, budesonide -Medium to very high potency topical: e.g., desoximetasone 0.05%, fluocinolone acetonide 0.025%, mometasone 0.1% cream, triamcinolone acetonide 0.1%, augmented betamethasone dipropionate 0.05%, clobetasol propionate 0.05% cream, ointment, gel, or solution, halobetasol propionate 0.05% cream, ointment	**CD*** Adult: -prednisone 40 mg – 60 mg PO QD for 1 to 2 weeks, then taper daily dose by 5 mg weekly until 20 mg PO QD, and then continue with 2.5 – 5 mg decrements weekly or IV 50 – 100 mg Q6H for 1 week -budesonide (Entocort EC□) 6 – 9 mg PO QD Pediatric: -Prednisone 1 to 2 mg/kg/day PO QD **UC** Adult: -Prednisone 40 mg – 60 mg PO QD, then taper dose by 5 to 10 mg/week -budesonide (Uceris□) 9 mg PO QD	Various

	Pediatric: -Prednisone 1 to 2 mg/kg/day PO QD	
6-mercaptopurine (Purixan®)	**CD*** 50 mg PO QD or 0.75 – 1.5 mg/kg/day PO	1.5 mg/kg/day
methotrexate (Trexall®, Otrexup™, Rasuvo®, RediTrex®, Xatmep™, Rheumatrex®)	**CD*** 15 – 25 mg/week IM or SC	30 mg/week
Pentasa® (mesalamine)	**CD** 1,000 mg PO QID	4 g/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
*Off-label

Appendix C: Contraindications/Boxed Warnings

Contraindications: Patients who have had a known serious or severe hypersensitivity reaction to Entyvio or any of its excipients
BBW: Risk of serious infections

Appendix D: General Information

- Definition of failure of MTX or DMARDs
- Failure of a trial of conventional DMARDs:
    - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
    - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.
- Ulcerative Colitis:
    - For Ulcerative Colitis maintenance therapy, failure is defined as having two or more exacerbations requiring steroid therapy
- Ulcerative colitis: there is insufficient evidence to support the off-label weekly dosing of adalimumab for the treatment of moderate-to-severe UC. It is the position of Centene Corporation® that the off-label weekly dosing of adalimumab for the treatment of moderate-to-severe UC is investigational and not medically necessary at this time.
    - The evidence from the post hoc study of the adalimumab pivotal trial suggests further studies are needed to confirm the benefit of weekly adalimumab dosing for the treatment of UC in patients with inadequate or

loss of therapeutic response to treatment with adalimumab every other week. No large, randomized or prospective studies have been published to support the efficacy of the higher frequency of dosing, while national and international treatment guidelines also do not strongly support dose escalation of adalimumab for UC. The current market consensus is that weekly dosing of adalimumab is not medically necessary due to lack of evidence to support its benefit

- TNF blockers:
    - Etanercept (Enbrel®), adalimumab (Humira®) and its biosimilars, infliximab (Remicade®) and its biosimilars (Avsola™, Renflexis™, Inflectra®), certolizumab pegol (Cimzia®), and golimumab (Simponi®, Simponi Aria®).

Appendix E: Immunomodulator Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for CD:
    - Inability to induce short-term symptomatic remission with a 3-month trial of systemic glucocorticoids
    - 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
    - For TNF-inhibitors, 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

Appendix F: Mayo Score

Mayo Score: evaluates ulcerative colitis stage, based on four parameters: stool frequency, rectal bleeding, endoscopic evaluation and Physician's global assessment. Each parameter of the score ranges from zero (normal or inactive disease) to 3 (severe activity) with an overall score of 12.

Score	Decoding
0-2	Remission
3-5	Mild activity
6-10	Moderate activity
>10	Severe activity

V. Dosage and Administration

- Dosing: Vedolizumab (Entyvio):
  - Initial dose: 300 mg IV at weeks 0, 2, and 6
  - Maintenance dose: 300 mg IV every 8 weeks 300 mg every 8 weeks

Maximum Dose: 300 mg every 8 weeks

VI. Product Availability

Availability: Single-use vial, 300mg/20mL

References

1. Entyvio Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America Inc.; September 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125476s057lbl.pdf. Accessed February 7, 2024

   Crohn's Disease/Ulcerative Colitis
2. Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. Gastroenterology 2021; 160:2496-2508. https://doi.org/10.1053/j.gastro.2021.04.022.
3. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology 2020;158:1450–1461. https://doi.org/10.1053/j.gastro.2020.01.006.
4. Lichtenstein GR, Loftus EV, Isaacs KL et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018 Apr;113(4):481-517. doi: 10.1038/ajg.2018.27.
5. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019 March;114(3):384-413. doi: 10.14309/ajg.0000000000000152.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3380	**Injection, vedolizumab, 1mg**

Revision Log

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy Created		05.24
2Q 2024: for Chrohn's disease, added that request is for IV formulation; reviewed and updated references.	05.24	06.24

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed healthcare professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.