Clinical Policy: Vedolizumab (Entyvio)

Reference Number: CP.PHAR.265
Effective Date: 07.16
Last Review Date: 11.21
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description

Vedolizumab (Entyvio®) is an integrin receptor antagonist.

FDA Approved Indication(s)

Entyvio is indicated in adults for the treatment of:

- Moderately to severely active ulcerative colitis (UC).
- Moderately to severely active Crohn's disease (CD).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Entyvio is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Ulcerative Colitis (must meet all)**:**

1. Diagnosis of UC;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Documentation of a Mayo Score ≥ 6 (*see Appendix F*);
5. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
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 and b):
   a. Humira® and Simponi ®;
   b. If member has failed Humira and Simponi, then failure of Zeposia®;
   **Prior authorization may be required*
7. Dose does not exceed 300 mg at weeks 0, 2, and 6, followed by maintenance dose of 300 mg every 8 weeks.

Approval duration: 6 months

B. Crohn's Disease (must meet all)**:**

1. Diagnosis of CD:
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;

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-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. Failure of a ≥ 3 consecutive month trial of adalimumab (*Humira is preferred)* AND one other TNF blocker (e.g., infliximab [*Avsola, Inflectra and Renflexis are preferred*], Cimzia®), unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for adalimumab and TNF blockers*
6. Dose does not exceed 300 mg at weeks 0, 2, and 6, followed by maintenance dose of 300 mg every 8 weeks.

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 300 mg every 8 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

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 – CP.PMN.53 for Medicaid or evidence of coverage documents

B. Combination use of biological disease-modifying antirheumatic drugs (bDMARDs), including any tumor necrosis factor (TNF) antagonists [Cimzia®, Enbrel®, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [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® (IL-23 inhibitor)], janus kinase inhibitors (JAKi) [Xeljanz®/Xeljanz® XR, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, and Rituxan Hycela®], selective co-stimulation modulators [Orencia®], or integrin receptor antagonists [Entyvio®] because of the possibility of increased immunosuppression, neutropenia and increased risk of infection.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6-MP: 6-mercaptopurine
CD: Crohn's disease
FDA: Food and Drug Administration
GI: gastrointestinal
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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum
azathioprine (Azasan®, Imuran®)	**CD*** 1.5 – 2 mg/kg/day PO	2.5 mg/kg/day
corticosteroids	**CD*** prednisone 40 mg PO QD for 2 weeks or IV 50 – 100 mg Q6H for 1 week budesonide (Entocort EC®) 6 – 9 mg PO QD	N/A
6-mercaptopurine (Purixan®)	**CD*** 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
mesalamine (Pentasa®)	**CD** 1,000 mg PO QID	4 g/day
Cimzia® (certolizumab)	**CD** Initial dose: 400 mg SC at 0, 2, and 4 weeks	400 mg every 4 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum
	Maintenance dose: 400 mg SC every 4 weeks	
Humira® (adalimumab)	**CD, UC** Initial dose: 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: 40 mg SC every other week starting on Day 29	40 mg every other week
Avsola™, Renflexis™, Inflectra® (infliximab)	**CD** Initial dose: 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg IV every 8 weeks. Some adult patients who initially respond to treatment may benefit from increasing the dose to 10 mg/kg if they later lose their response **UC** Initial dose: 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg IV every 8 weeks	CD: 10 mg/kg every 8 weeks UC: 5 mg/kg every 8 weeks
Simponi® (golimumab)	**UC** Initial dose: 200 mg SC at week 0, then 100 mg SC at week 2 Maintenance dose: 100 mg SC every 4 weeks	**UC** 100 mg every 4 weeks
Zeposia® (ozanimod)	Days 1-4: 0.23 mg PO QD Days 5-7: 0.46 mg PO QD Day 8 and thereafter: 0.92 mg PO QD If a dose of Zeposia is missed during the first 2 weeks of treatment, reinitiate treatment using the titration regimen. If a dose of Zeposia is missed after the first 2 weeks of treatment, continue with the treatment as planned.	0.92 mg/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

- Contraindication(s): patients who have had a known serious or severe hypersensitivity reaction to Entyvio or any of its excipients
- Boxed warning(s): none reported

Appendix D: General Information

- Definition of failure of MTX or 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.

Appendix E: Immunomodulator Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for Crohn's disease:
  - 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

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

- The following may be considered for medical justification supporting inability to use an immunomodulator for ulcerative colitis:

- Documentation of Mayo Score 6 – 12 indicative of moderate to severe ulcerative colitis.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
UC, CD	Initial dose: 300 mg IV at weeks 0, 2, and 6 Maintenance dose: 300 mg IV every 8 weeks	300 mg every 8 weeks

VI. Product Availability

Single-use vial: 300 mg/20 mL

VII. References

1. Entyvio Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America Inc.; March 2020. Available at: https://www.entyviohcp.com/. Accessed January 11, 2021.
2. Bernell O, Lapidus A, Hellers G. Risk Factors for Surgery and Postoperative Recurrence in Crohn's Disease. *Annals of Surgery*. 2000; 231(1): 38-45.
3. Ordas I, Feagan BG, Sandborn WJ. Early use of immunosuppressives or TNF antagonists for the treatment of Crohn's disease: time for a change. *Gut*. 2011 Dec; 60(12):1754-63.
4. Lichtenstein GR, Loftus Jr. EV, Isaacs KI, Regueiro MD, Gerson LB, and Sands BE. ACG clinical guideline: management of Crohn's disease in adults. *Am J Gastroenterol*. 2018; 113:481-517.
5. Rubin DT,Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol.* 2019;114:384-413

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, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. UC: removed Cimzia as example of second TNF for redirection as Cimzia is not indicated for UC; change required trials from immunomodulator to specifically thiopurines based on AGA and ACG guidelines and removed MTX as example of acceptable trial. Clarified immunomodulator redirection for maintenance requests for all indications. CD: modified poor prognostic indicator list to match AGA guidelines. Safety criteria revised according to the safety	07.17	07.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
guidance discussed at CPAC and endorsed by Centene Medical Affairs.		
CD: Reclassified "failure of an immunomodulator…" as one of the options to meet criteria point 1 (along with other poor prognostic indicators), instead of as an alternative to failing Humira and another TNF inhibitor in criteria point 2.	08.17	
2Q 2018 annual review: modified gastroenterologist specialty requirement to gastrointestinal specialist; modified trial and failure of all agents for all conditions to have duration of at least 3 consecutive months; added aminosalicylate as an option for trial and failure for UC;	02.27.18	05.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
specified brand names for preferred trial and failure agents in all conditions; removed specific diagnosis requirements for CD; references reviewed and updated.		
4Q 2018 annual review: modified prescriber specialist from GI specialist to gastroenterologist for CD and UC; added trial and failure of immunosuppressants, or medical necessity for use of biologics in CD; references reviewed and updated.	08.28.18	11.18
2Q 2019 annual review: no significant changes; added HIM-Medical Benefit; references reviewed and updated.	02.26.19	05.19
2Q 2020 annual review; removed HIM-Medical Benefit (see HIM.PA.SP60); for UC, revised redirection from AZA, 6-MP, and ASA to systemic corticosteroids, revised redirection from Humira and another TNFi to Humira or Simponi, and added Mayo score requirement of at least 6; references reviewed and updated.	02.28.20	05.20
2Q 2021 annual review: added combination of bDMARDs under Section III; references reviewed and updated.	02.23.21	05.21
Per June SDC and prior clinical guidance, modified Avsola to parity status with Inflectra and Renflexis.	06.02.21	08.21
Per August SDC and prior clinical guidance, modified from trial of Humira or Simponi to trial of all of the following: Humira, Simponi, and Zeposia, in a step-wise manner.	08.25.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care 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.

 Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical

policy.