Clinical Policy: Vedolizumab (Entyvio)

Reference Number: CP.PHAR.265
Effective Date: 07.16
Last Review Date: 05.24
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. Member meets both* of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a and b, *see Appendix D*):
   a. Failure of one adalimumab product (e.g. *Hadlima™, Yusimry™, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), unless the member has had history of failure of two TNF blockers;
   b. If member has had a history of failure of two TNF blockers, then failure of Zeposia®;

   **Prior authorization may be required for adalimumab products and Zeposia*
7. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);

8. Dose does not exceed one of the following (a or b):
   a. 300 mg (IV) at weeks 0, 2, and 6, followed by maintenance dose of 300 mg (IV) every 8 weeks;
   b. 300 mg (IV) at weeks 0 and 2, then 108 mg (SC) at week 6, followed by maintenance dose of 108 mg (SC) every 2 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. Member meets one of the following, unless clinically significant adverse effects are experienced or all are contraindicated (a or b, *see Appendix D*):
   a. Failure of one adalimumab product (e.g. *Hadlima™, Yusimry™, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), used for ≥ 3 consecutive months;
   b. History of failure of two TNF blockers;
   **Prior authorization may be required for adalimumab products*
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. Dose does not exceed one of the following (a or b):
   a. 300 mg (IV) at weeks 0, 2, and 6, followed by maintenance dose of 300 mg (IV) every 8 weeks;
   b. 300 mg (IV) at weeks 0 and 2, then 108 mg (SC) at week 6, followed by maintenance dose of 108 mg (SC) every 2 weeks.

Approval duration: 6 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase 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 one of the following (a or b):
   a. IV: 300 mg every 8 weeks;
   b. SC: 108 mg every 2 weeks.

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 with 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, Remicade® and its biosimilars (Avsola™, Inflectra™, Renflexis™, Zymfentra®), Simponi®], interleukin agents [e.g., Actemra® (IL-6RA), Arcalyst® (IL-1 blocker), Bimzelx® (IL-

17A and F antagonist), Cosentyx® (IL-17A inhibitor), Ilaris® (IL-1 blocker), Ilumya™ (IL-23 inhibitor), Kevzara® (IL-6RA), Kineret® (IL-1RA), Omvoh™ (IL-23 antagonist), Siliq™ (IL-17RA), Skyrizi™ (IL-23 inhibitor), Stelara® (IL-12/23 inhibitor), Taltz® (IL-17A inhibitor), Tofidence™ (IL-6), Tremfya® (IL-23 inhibitor), Wezlana™ (IL-12/23 inhibitor)], Janus kinase inhibitors (JAKi) [e.g., Cibinqo™, Olumiant™, Rinvoq™, Xeljanz®/Xeljanz® XR,], anti-CD20 monoclonal antibodies [Rituxan® and its biosimilars (Riabni™, Ruxience™, Truxima®), Rituxan Hycela®], selective co-stimulation modulators [Orencia®], integrin receptor antagonists [Entyvio®], tyrosine kinase 2 inhibitors [Sotyktu™], and sphingosine 1-phosphate receptor modulator [Velsipity™] 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

6-MP: 6-mercaptopurine
CD: Crohn's disease
FDA: Food and Drug Administration
GI: gastrointestinal
JAKi: Janus kinase inhibitors
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 Dose
azathioprine (Azasan®, Imuran®)	**CD*** 1.5 – 2.5 mg/kg/day PO	2.5 mg/kg/day
corticosteroids	**CD*** 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	Various

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Budesonide (Uceris®) 9 mg PO QAM for up to 8 weeks *Pediatric:* Prednisone 1 to 2 mg/kg/day PO QD	
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 Maintenance dose: 400 mg SC every 4 weeks	400 mg every 4 weeks
Hadlima (adalimumab-bwwd), Yusimry (adalimumab-aqvh), adalimumab-adaz (Hyrimoz®), adalimumab-fkjp (Hulio®), adalimumab-adbm (Cyltezo®)	**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	CD: 10 mg/kg every 8 weeks UC: 5 mg/kg every 8 weeks
Zeposia® (ozanimod)	**UC** 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	0.92 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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.	

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.
- 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 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

- 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

Indication	Dosing Regimen	Maximum Dose
CD, UC	Initial dose: 300 mg IV at weeks 0 and 2, followed by 300 mg IV or 108 mg SC at week 6 Maintenance dose: 300 mg IV every 8 weeks or 108 mg SC every 2 weeks	IV: 300 mg every 8 weeks SC: 108 mg every 2 weeks

VI. Product Availability

- Lyophilized powder in a single-dose vial for reconstitution for IV infusion: 300 mg
- Single-dose prefilled syringe for SC injection: 108 mg/0.68 mL
- Single-dose prefilled Entyvio Pen for SC injection: 108 mg/0.68 mL

VII. References

1. Entyvio Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America Inc.; April 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761359s000lbl.pdf. Accessed May 6, 2024.
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. 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.
4. 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.

5. 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.
6. 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, intravenous, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
2Q 2022 annual review: reiterated requirement against combination use with a bDMARD or JAKi from Section III to Sections I and II; references reviewed and updated.	02.18.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.13.22	
Per February SDC, added Amjevita as an alternative option to Humira for CD and UC.	02.13.23	
2Q 2023 annual review: for UC and CD, added TNFi criteria to allow bypass if member has had history of failure of two TNF blockers; updated off-label dosing for Appendix B; added high risk factors for postoperative occurrence to Appendix E to align with other CD policies; references reviewed and updated.	02.10.23	05.23
Per July SDC: for UC, removed criteria requiring use of Simponi,	07.25.23	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Humira, and Amjevita; for CD, removed criteria requiring use of Humira and Amjevita; added criteria requiring use of one adalimumab product and stating Yusimry, Hadlima, unbranded adalimumab-fkjp, and unbranded adalimumab-adaz as preferred; updated Appendix B with relevant therapeutic alternatives.		
RT4: added new dosage forms (prefilled syringe and Entyvio Pen) for SC injection to sections V and VI; for section VI, revised "single-use vial" to "lyophilized powder in a single-dose vial for reconstitution for IV infusion: 300 mg" per PI; for UC, updated to include SC maximum dose option in initial approval and continued therapy sections; for CD, added "request is for IV formulation" in initial approval and continued therapy sections; added Tofidence to section III.B.	10.05.23	
Per December SDC, added adalimumab-adbm to listed examples of preferred adalimumab products.	12.06.23	02.24
Revised HCPCS code [J3380] description.	02.22.24	
2Q 2024 annual review: added Bimzelx, Zymfentra, Omvoh, Wezlana, Sotyktu, and Velsipity to section III.B; references reviewed and updated.	01.22.24	05.24
RT4: for CD initial and continued therapy sections, added new dosage form (subcutaneous injection) to dosing regimen and removed "request is for IV formulation".	05.06.24	

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. 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.