Clinical Policy: Vedolizumab (Entyvio)

Reference Number: ERX.SPA.163
Effective Date: 10.01.16
Last Review Date: 05.20
Lines of Business: Commercial, Medicaid

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 for the treatment of:

- Adult ulcerative colitis (UC)
  - Adult patients with moderately to severely active 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:
    - Inducing and maintaining clinical response,
    - Inducing and maintaining clinical remission,
    - Improving the endoscopic appearance of the mucosa, and
    - Achieving corticosteroid-free remission
- Adult Crohn's disease (CD)
  - Adult patients with moderately to severely active 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:
    - Achieving clinical response,
    - Achieving clinical remission, and
    - Achieving corticosteroid-free remission

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 2 of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: adalimumab (*Humira® is preferred*), infliximab (*Remicade® is preferred*), subcutaneous Stelara®, Xeljanz®, Xeljanz XR;
   **Prior authorization is required for adalimumab, infliximab, Stelara, Xeljanz, and Xeljanz XR*

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-mercaptopurine [6-MP], 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 2 of the following, each used for ≥ 3 consecutive months unless clinically significant adverse effects are experienced or all are contraindicated: adalimumab (*Humira is preferred*), subcutaneous Stelara®, infliximab (*Remicade is preferred*), Tysabri®;
   **Prior authorization is required for adalimumab, Stelara, infliximab, and Tysabri*
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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 or evidence of coverage documents.

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 Dose
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
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
Remicade® (infliximab)	**CD, UC** Initial dose: *Adults/Pediatrics:* 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: *Adults/Pediatrics:* 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 (adults): 10 mg/kg every 8 weeks CD (pediatrics), UC: 5 mg/kg every 8 weeks
Stelara® (ustekinumab)	**CD, UC** Weight based dosing IV at initial dose, followed by 90 mg SC every 8 weeks Weight ≤ 55 kg: 260 mg Weight 55 kg to 85 kg: 390 mg Weight > 85 kg: 520 mg	90 mg every 8 weeks
Tysabri® (natalizumab)	**CD** 300 mg IV every 4 weeks	300 mg/4 weeks
Xeljanz® (tofacitinib, immediate-release)	**UC** 10 mg PO BID for 8 weeks; then 5 or 10 mg PO BID	Maintenance: 10 mg/day
Xeljanz XR® (tofacitinib, extended-release)	**UC** 22 mg PO QD for 8 weeks; then 11 mg PO QD	Maintenance: 11 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: 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.; May 2019. Available at www.entyviohcp.com. Accessed February 28, 2020.
2. 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.
3. Rubin DT,Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol 2019;114:384-413
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. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from USS.SPMN.24 Irritable Bowel Disease (IBD) Treatments and converted to new template. Removed safety criteria. Added dosing per PI. Modified approval duration to 6 months for initial and 12 months for re-auth. CD/UC: Removed criteria related to concomitant use with other biologics. Added requirement for trial and failure of PDL Humira as one of the two required TNF inhibitors, unless contraindicated. CD: Modified criteria requiring failure of immunomodulator, corticosteroids or aminosalicylate to failure of "corticosteroid, with or without immunomodulator" per 2014 AGA Clinical decision tool.	08.16	09.16
For all trial/failure requirements, indicated that member can also meet criteria if intolerant (as opposed to just contraindicated) to therapy in question. Modified the following initial criteria sets: UC: removed option for trial/failure of corticosteroid and aminosalicylate. CD: added poor prognostic indicators as alternative to trial/failure requirement. Modified trial/failure requirement to indicate an immunomodulator (as opposed to a corticosteroid with or without an immunomodulator) must be trialed.	11.16	12.16
4Q17 Annual Review Converted to new template. For all indications: diagnostic criteria modified to require verifiable information; UC: removed requirement another biologic; CD: removed poor prognostic indicators.	10.01.17	11.17
2Q 2018 annual review: modified gastroenterologist specialty requirement to gastrointestinal specialist; added aminosalicylate as an option for trial and failure for UC; modified preferencing for all indications; references reviewed and updated.	02.27.18	05.18
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 Xeljanz to list of trial options for UC; references reviewed and updated.	02.26.19	05.19
2Q 2020 annual review: for UC, revised redirection from AZA, 6-MP, and ASA to systemic corticosteroids, added Mayo score requirement of at least 6, added Xeljanz XR and SC Stelara as preferred options for redirection per formulary; references reviewed and updated.	02.28.20	05.20

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.