Clinical Policy Title:	vedolizumab
Policy Number:	RxA.735
Drug(s) Applied:	Entyvio®
Original Policy Date:	04/18/2022
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Entyvio® is an integrin receptor antagonist indicated in adults for the treatment of:

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
vedolizumab (Entyvio®)	UC, CD	Initial dose: 300 mg intravenously at weeks 0, 2, and 6 Maintenance dose: 300 mg intravenously every 8 weeks	300 mg per dose

Dosage Forms

- Injection: 300 mg vedolizumab in a single-dose vial.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of Crohn's Disease (CD);
2. Age ≥ 18 years;
3. Prescribed by or in consultation with a gastroenterologist;
4. Member meets one of the following (a or b):
   a. Trial and failure of a ≥ 3 months of at least one (1) conventional systemic therapy (e.g., azathioprine,

6-mercaptopurine [6-MP], methotrexate [MTX]) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

b. Trial and failure of corticosteroids (e.g., prednisone, methylprednisolone, budesonide), unless contraindicated or significant adverse effects experienced;
*Exception: If one biologic DMARD that is FDA-approved for crohn's disease has been previously tried, then trial of a conventional systemic agent is not required;

5. Trial and failure of at least two (2) of the following agents: Cimzia®, Humira® or Stelara® unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 300 mg per dose.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Ulcerative Colitis (must meet all)**:**
1. Diagnosis of Ulcerative Colitis (UC);
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Trial and failure of ≥ 3 months of at least one (1) conventional agent (azathioprine, 6-mercaptopurine, aminosalicylate) unless contraindicated or clinically significant adverse effects are experienced;
   b. Trial and failure of corticosteroids (e.g., prednisone, methylprednisolone, budesonide) unless contraindicated or significant adverse effects are experienced;
   *Exception: If one biologic DMARD that is FDA-approved for ulcerative colitis has been previously tried, then trial of a conventional systemic agent is not required;
5. Trial and failure of at least two (2) of the following agents: Humira®, Simponi® or Stelara® unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 300 mg per dose.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CD: Crohn's Disease
DMARDs: Disease-Modifying Antirheumatic Drugs
MTX: Methotrexate
UC: Ulcerative Colitis

TNF: Tumor necrosis factor

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azathioprine (Azasan®, Imuran®)	**CD (off-label), UC (off-label):** 1.5 – 2 mg/kg/day orally	2.5 mg/kg/day
Corticosteroids	**CD (off-label):** prednisone 40 mg orally once daily for 2 weeks or intravenously 50 – 100 mg every 6 hour for 1 week budesonide (Entocort EC®) 6 – 9 mg orally once daily	Various
mercaptopurine (Purixan®)	**CD (off-label):** 25 mg or 50 mg orally once daily or 0.75 to 1.5 mg/kg/day **UC (off-label):** 25 mg or 50 mg orally once daily or 1.5 mg/kg/day	2.5 mg/kg or 75 mg/m^2
methotrexate	**CD (off-label):** 15 – 25 mg/week intramuscular or subcutaneously	30 mg/week
mesalamine (Pentasa®)	**CD, UC:** 1,000 mg orally four times daily	4 g/day
sulfasalazine (Azulfidine®)	**UC:** Initial dose: Adults: 3 – 4 g/day orally in divided doses (not to exceed every 8 hour) Pediatrics: 40 – 60 mg/kg/day orally in 3 –6 divided doses Maintenance dose: Adults: 2 g orally once daily Pediatrics: 30 mg/kg/day orally in 4 divided doses	UC: 4 g/day
tacrolimus (Prograf®)	**CD (off-label):** 0.27 mg/kg/day orally in divided doses or 0.15 – 0.29 mg/kg/day orally	N/A
Humira®	**CD: Initial dose:** Adults: 160 mg subcutaneously on Day 1, then 80 mg subcutaneously on Day 15 Pediatrics: Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 80 mg subcutaneously on Day 1, then 40 mg subcutaneously on Day 15 Weight ≥ 40 kg (88 lbs)160 mg subcutaneously on Day 1, then 80 mg subcutaneously on Day 15 **Maintenance dose:** Adults: 40 mg subcutaneously every other week starting on Day 29 Pediatrics: Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 20 mg subcutaneously every other week starting on Day 29 Weight ≥ 40 kg (88 lbs): 40 mg subcutaneously every other week starting on Day 29	40 mg every other week
	UC: Initial dose: Adults:160 mg subcutaneously on Day 1 (given in one day or split over two consecutive days), then 80 mg subcutaneously on Day 15	Adults:40 mg every other week Pediatrics: 80 mg

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Pediatrics: Weight 20 kg (44 lbs) to < 40 kg (88 lbs): 80 mg subcutaneously on Day 1, then 40 mg subcutaneously on Day 8, then 40 mg subcutaneously on day Day 15 Weight ≥ 40 kg(88 lbs): 160 mg subcutaneously Day 1, then 80 mg on day 8 and day 15 **Maintenance dose:** Adults:40 mg subcutaneously every other week starting on Day 29 Pediatrics: Weight 20 kg (44 lbs) to < 40 kg (88 lbs): 40 mg every other week or 20 mg every week starting on day 29 Weight ≥ 40 kg(88 lbs): 80 mg every other week or 40 mg every week starting on day 29	every other week
Cimzia®	**CD: Initial dose:** 400 mg subcutaneously at 0, 2, and 4 weeks **Maintenance dose:** 400 mg subcutaneously every 4 weeks	400 mg every 4 weeks
Simponi®	**UC: Initial dose:** 200 mg subcutaneously at week 0, then 100 mg subcutaneously at week 2 **Maintenance dose:** 100 mg subcutaneously every 4 weeks	100 mg every 4 weeks
Infliximab (Remicade®) Renflexis®, Inflectra®, Avsola®	**CD, UC: Initial dose:** 5 mg/kg intravenously at weeks 0, 2 and 6 **Maintenance dose:** 5 mg/kg intravenously every 8 weeks. Pediatric UC and CD : ≥ 6 years old For CD: 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 UC, Adults: 5 mg/kg every 8 weeks Pediatrics: 5 mg/kg every 8 weeks
Tysabri®	CD: 300 mg intravenously every 4 weeks	300 mg every 4 Weeks
Xeljanz®	UC: Induction:10 mg orally twice daily for at least 8 weeks, based on therapeutic response, may continue 10 mg twice daily for a maximum of 16 weeks or transition to maintenance dose. Discontinue after 16 weeks of 10 mg twice daily if adequate therapeutic benefit is not achieved. Maintenance: 5 mg twice daily; if loss of response on 5 mg twice daily, then use 10 mg twice daily after assessing the benefits and risks and use for the shortest duration; use lowest effective dose to maintain response.	20 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Xeljanz® XR	UC: Induction: 22 mg once daily for at least 8 weeks; may continue 22 mg once daily for a maximum of 16 weeks or transition to maintenance dose. Discontinue therapy if inadequate response achieved after 16 weeks using 22 mg once daily. Maintenance: 11 mg once daily; if loss of response on 11 mg once daily; then use 22 mg once daily for the shortest duration; use lowest effective dose to maintain response.	22 mg daily
Stelara®	UC, CD: Weight based dosing intravenous at initial dose, followed by 90 mg subcutaneous 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

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

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.

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Infusion-Related Reactions and Hypersensitivity Reactions: Discontinue Entyvio® and initiate appropriate treatment if serious reactions occur.
- Infections: Treatment with Entyvio® is not recommended in patients with active, severe infections until the infections are controlled. Consider withholding Entyvio® in patients who develop a severe infection while on treatment with Entyvio®.
- Progressive Multifocal Leukoencephalopathy (PML): Although unlikely, a risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs or symptoms.

References

1. Entyvio Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America Inc.; August 2021. Available at: www.entyviohcp.com. Accessed February 10, 2022.
2. Colombel JF, Sandborn WJ, Rutgeerts P, et.al. Adalimumab for Maintenance of Clinical Response and Remission in Patients With Crohn`s Disease: The CHARM Trial. Gastroenterology 2007; 132:52-65. Available at: https://pubmed.ncbi.nlm.nih.gov/17241859/. Accessed February 10, 2022.
3. Sandborn WJ. Crohn's Disease Evaluation and Treatment: Clinical Decision Tool. Gastroenterology 2014; 147: 702-705. Available at: https://pubmed.ncbi.nlm.nih.gov/25046160/. Accessed February 10, 2022.
4. 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. Available at: https://pubmed.ncbi.nlm.nih.gov/10636100/. Accessed February 10, 2022.
5. 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. Available at: https://pubmed.ncbi.nlm.nih.gov/29610508/. Accessed February 10, 2022.
6. Drug. Lexi-Drug. Lexicomp. Wolters Kluwer. Hudson, OH. Available at: http://online.lexi.com. Accessed February 10, 2022.
7. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2022. Available at: http://www.clinicalpharmacology-ip.com/. Accessed February 10, 2022.
8. Micromedex Solutions. Truven Health Analytics Inc. Ann Arbor, MI. Available at http://www.micromedexsolutions.com . Accessed February 10, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
RxA.592.Bilogic_DMARDs was last reviewed and updated on 01/05/2022 and archived on 04/18/2022. For details, please refer to RxA.592.Bilogics_DMARDs.	01/05/2022	04/18/2022
Drug specific policy for Entyvio was created based on RxA.592.Bilogics_DMARDs: 1. Dosing Information, Maximum Dose, vedolizumab (Entyvio®): Updated to maximum dosing information from 300 mg every 8 weeks to 300 mg per dose for indication UC, CD. 2. Dosage Forms: Updated dosage form from Vedolizumab (Entyvio®): Single-use vial: 300 mg/20 mL to Injection: 300 mg vedolizumab in a single-dose vial. 3. Initial Approval Criteria, I.A.4: Updated to remove Medical justification supports inability to use immunomodulators (see Appendix D). 4. Initial Approval Criteria, I.A.5: Updated trial and failure criteria from Failure of two (2) of the following for ≥ 3 months: Humira®, Cimzia®, Inflectra®, Renflexis™, Stelara®, unless contraindicated or clinically significant adverse effects are experienced to Trial and failure of at least one (2) of the following agents: Cimzia®, Humira® or Stelara® unless contraindicated or clinically significant adverse effects are experienced. 5. Initial Approval Criteria, I.B.5: Updated trial and failure criteria from Failure of two (2) of the following: Inflectra®, Renflexis™, Simponi®, Stelara®, Humira® or Xeljanz®/Xeljanz XR®, each used for ≥ 3 months unless contraindicated or clinically significant adverse effects are experienced to Trial and failure of at least two (2) of the following agents: Humira®, Simponi® or	02/14/2022	04/18/2022

Stelara® unless contraindicated or clinically significant adverse effects are experienced; 6. Initial Approval Criteria, I.A.6 and I.B.6: Updated dosing criteria from Dose does not exceed maximum dose indicated in background to Dose does not exceed 300 mg per dose. 7. Appendix B, Drug Name: Updated to include brand-name therapeutic alternative of other biological DMARDs. 8. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 9. Appendix D, General Information: Updated to include new information regarding Wanrings and Precautions. 10. Appendix D, General Information: Updated to remove information regarding: (a, b, c and d) a. Ulcerative Colitis; b. Medical justification supporting inability to use an immunomodulator for Crohn's disease; c. Definition of failure of MTX or DMARDs; 11. References were reviewed and updated.		