DRUG DETERMINATION POLICY

Title: DDP-20 Entyvio

Effective Date: 8/23/23

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Entyvio intravenous (vedolizumab IV) is a specialty drug indicated for specific gastrointestinal diagnoses and is associated with adverse effects. These criteria were developed and implemented to ensure appropriate use of conventional drugs before Entyvio is used as well as, utilized for the intended diagnoses.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. General considerations.

A. Therapeutic drug monitoring [must meet all listed below]:

1. Indication: inadequate response to or relapse of symptoms while on standard dose and frequency of Entyvio.

2. Criteria [must meet both listed below]:

a. Patient has received three stable maintenance doses.

b. Trough drug levels are drawn just prior to drug infusion: verify timing.

3. Determine coverage based on drug level.

a. Drug trough level at or above 12 mcg/mL: standard frequency of every eight weeks applies.

b. Drug trough level below 12 mcg/mL: may increase dosage frequency to every four weeks.

B. Appropriate medication use [must meet one listed below]:

1. The Food and Drug Administration (FDA) approval status [must meet one listed below]:

a. FDA approved: product, indication, and/or dosage regimen.

b. Non-FDA approved: Compendium support (Lexicomp®) for use of a drug for a non-FDA approved indication or dosage regimen

2. Place in therapy: sequence of therapy supported by national or international accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

C. Administration: Medication is subject to site-of-care policy (see DDP-08 Site of Care for Administration of Parenteral Specialty Drugs).

D. Exclusions:

1. Co-administration with other biologics such as tumor necrosis factor inhibitors or Tysabri.

E. Pharmaceutical sample use: The Plan does not recognize samples as a medication trial or for continuation of therapy.

II. Crohn's Disease [must meet all listed below]:

A. Age: at least 18 years.

B. Diagnosis and severity: moderate to severe active Crohn's disease.

1. Exceptions: skipping the requirements of "C. *Other therapies"* are allowed if the patient exhibits severe or fulminant disease (see Appendix I).

C. Other therapies: Trials of two disease-modifying anti-rheumatic drugs (DMARDs) below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or a severe adverse reaction.

1. Chronic traditional DMARD therapy: azathioprine, methotrexate

D. Dosage regimen**:**

1. Entyvio intravenous (vedolizumab IV): 300 mg at zero, two, and six weeks, then every eight weeks.

2. Discontinue if no evidence of therapeutic benefit by week 14.

E. Approval

1. Initial: six months.

2. Re-approval: one year [must meet both listed below]:

a. Adherence: consistent utilization based on medical claims history or chart notes.

b. Clinical remission or a reduced or sustained decrease in disease activity (corticosteroid-free clinical remission by week 14).

III. Ulcerative Colitis [must meet all listed below]:

A. Age: at least 18 years.

B. Diagnosis and severity: moderate-severe active ulcerative colitis.

1. Endoscopy: marked erythema, no vascular pattern, friability, and erosions to spontaneous bleeding or ulceration).

2. Exceptions: skipping the requirements of "C*. Other therapies"* are allowed if patient exhibits severe or fulminant disease (see Appendix I).

C. Other therapies: Trials of one from each category below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction.

1. Oral therapies: oral mesalamine or oral sulfasalazine.

2. Disease modifying antirheumatic drugs: azathioprine.

D. Dosage regimen**:**

1. Entyvio intravenous (vedolizumab IV): 300 mg at zero, two, and six weeks, then every eight weeks.

2. Discontinue if no evidence of therapeutic benefit by week 14.

E. Approval.

1. Initial: six months.

2. Re-approval: one year [must meet both listed below]:

a. Adherence: consistent utilization (80% of days covered) based on medical claims history or chart notes.

b. Clinical remission or reduction or sustained decrease in disease activity (reduced rectal bleeding improved mucosa by endoscopy and corticosteroid-free clinical remission by week 14).

4.0 Coding:

COVERED CODES				
HCPCS Code	**Brand Name**	**Generic Name**	**Billing Units (1 Unit)**	**Prior Approval**
J3380	Entyvio	vedolizumab	1mg	Y

5.0 References, Citations, Resources & Associated Documents:

1. Entyvio Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.
2. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Entyvio, accessed July 2021.
3. Vedolizumab as induction and maintenance therapy for Crohn's Disease.N Engl J Med.2013;369(8):711-721.
4. Vedolizumab as induction and maintenance therapy for Ulcerative Colitis. *N Engl J Med*. 2013;369(8):699-710.
5. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: Part 1: Diagnosis and medical management. Journal of Crohn's and Colitis. 2017;11:3-25.
6. ACG Clinical Guideline: Management of Crohn's Disease in Adults. The American Journal of Gastroenterology.2018;113:481-517.
7. Therapeutic drug monitoring in inflammatory bowel disease: for every patient for every drug? Curr Opin Gastoenterol 2019. 35:302-310
8. Entyvio lengthen dose interval study: Lengthen vedolizumab dose interval and the risk of clinical relapse in inflammatory bowel disease. European Journal of Gastroenterology and Hepatology.2018:30(7):735-740.
9. DDP-08 Site of Care for Administration of Parenteral Specialty Medications.
10. American Gastroenterological Association Institute Clinical Guidelines Committee. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. *Gastroenterology*. 2021;160(7):2496-2508. doi:10.1053/j.gastro.2021.04.022

6.0 Appendices:

See page 5.

7.0 Revision History:

Original Effective Date: 06/24/2015

Next Review Date: 09/01/2024

Revision Date	Reason for Revision
7/19	Put in a new format, replaced abbreviations
4/20	Off-cycle review added therapeutic drug monitoring, removed prescriber type, replaced abbreviations, modified other therapies language, modified UC other therapy types, added two references., added an exception to other therapies
6/20	Annual review; revised other therapies' language and initial approval time; added exclusions; approved by P&T Committee 8/26/20.
6/21	Annual review; clarified criteria instructions, reformatting; replaced abbreviations, added appropriate use section
7/22	Annual review; clarify the treatment of UC and Crohn's disease; added reference; clarified reapproval duration
6/23	Annual review; added adherence requirement to re-approval criteria, reworded other therapies sections, added contraindication of use with other biologics, added pharmaceutical samples not accepted

Appendix I- Definitions of Disease Activity in Crohn's Disease and Ulcerative Colitis[5]

Supplementary Table 1. International Definitions of Disease Activity in Crohn's Disease and Ulcerative Colitis

Crohn's disease (international definitions based on CDAI parameters[1])					
ACG[2]	**Symptomatic remission** CDAI <150 Asymptomatic/without symptomatic inflammatory sequelae May have responded to medical or surgical therapy and have no residual active disease Does not include patients who require corticosteroids	**Mild–moderate** CDAI 150–220 Ambulatory Able to tolerate oral alimentation without manifestations of dehydration, systemic toxicity (high fevers, rigors, and prostration), abdominal tenderness, painful mass, intestinal obstruction, or >10% weight loss	**Moderate–severe** CDAI 220–450 Failed to respond to treatment for mild–moderate disease *or* Has more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia	**Severe/fulminant** CDAI >450 Persistent symptoms despite treatment with corticosteroids/biologics as outpatients *or* Has high fevers, persistent vomiting, intestinal obstruction, significant peritoneal signs, cachexia, or abscess	
ECCO[3]	**Symptomatic remission** CDAI <150	**Mild** CDAI 150–220 Ambulatory Eating and drinking <10% weight loss No obstruction, fever, dehydration, abdominal mass, or tenderness CRP increased above ULN	**Moderate** CDAI 220–450 Intermittent vomiting or weight loss >10% Treatment for mild disease ineffective or tender mass No overt obstruction CRP increased above ULN	**Severe** CDAI >450 Cachexia or evidence of obstruction/abscess Persistent symptoms despite intensive treatment CRP increased	
Ulcerative colitis (international definitions based on Truelove–Witts criteria[4])					
ACG[5]	**Symptomatic remission**	**Mild** <4 stools/d (with or without blood) No systemic signs of toxicity Normal ESR	**Moderate** ≥4 stools/d Minimal signs of toxicity	**Severe** ≥6 bloody stools/d Signs of toxicity (fever, tachycardia, anemia) Increased ESR	**Fulminant** ≥10 stools/d Continuous bleeding Toxicity Abdominal tenderness and distension Blood transfusion requirement Colonic dilation on abdominal plain films
ECCO[6]	**Symptomatic remission** <4 stools/d without bleeding or urgency	**Mild** <4 bloody stools/d Pulse <90 bmp Temperature <37.5°C Hemoglobin >11.5 g/dL ESR <20 mm/h or normal CRP	**Moderate**[a] ≥4 bloody stools/d *if* Pulse ≤90 bmp Temperature ≤37.8°C Hemoglobin ≥10.5 g/dL ESR ≤30 mm/h or CRP ≤30 mg/dL	**Severe**[b] ≥6 bloody stools/d *and* Pulse >90 bmp Temperature >37.8°C Hemoglobin <10.5 g/dL ESR >30 mm/h or CRP >30 mg/dL	

Appendix II: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Entyvio® (vedolizumab)	• Central Nervous System: headache (12%) • Gastrointestinal: nausea (9%) • Musculoskeletal: arthralgia (12%) • Respiratory: nasopharyngitis (13%), URI (7%), cough (5%) • Other: pyrexia (9%), fatigue (6%)	• During infusion patients should be monitored • Hypersensitivity medications • Signs and Symptoms of infection	None