DRUG DETERMINATION POLICY

Title: DDP-20 Entyvio

Effective Date: 06/03/2020

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 (vedolizumab) 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:

A. Crohn's Disease (CD).

   1. Age: at least 18 years.

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

      a. Exceptions: skipping the requirements of "3*. Other therapies"* are allowed if patient exhibits severe or fulminant disease (see Appendix I).

   3. Other therapies: contraindication, inadequate response or significant adverse effects to two disease-modifying anti-rheumatic drugs (DMARDs) below:

      a. Short term steroids: oral or rectal glucocorticoids for two months.

      b. Oral therapies: oral mesalamine or oral sulfasalazine products.

      c. Chronic traditional DMARD therapy: azathioprine, 6-mercaptopurine and/or methotrexate for four months.

4. Dosage regimen**:**

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

    b. Discontinue: no evidence of therapeutic benefit by week 14.

5. Approval. initial: six months.

    a. Re-approval: **c**linical remission or a reduced or sustained decrease in disease activity (corticosteroid-free clinical remission by week 14).

B. Ulcerative Colitis (UC).

1. Age: at least 18 years.

2. Diagnosis and severity: moderate-severe active UC (e.g. endoscopy with marked erythema, no vascular pattern, friability, and erosions to spontaneous bleeding or ulceration).

    a. Exceptions: skipping the requirements of "3. *Other therapies"* are allowed if patient exhibits severe or fulminant disease (see Appendix I).

3. Other therapies: contraindication, inadequate response or significant adverse effects to one of each category below:

    a. Short term steroids: oral or rectal glucocorticoids for two months.

    b. Oral therapies: oral mesalamine or oral sulfasalazine for four months.

4. Dosage regimen**:**

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

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

5. Approval.

    a. Initial: four months.

    b. Re-approval: **c**linical remission or reduction or sustained decrease in disease activity (reduced rectal bleeding improved mucosa by endoscopy and corticosteroid-free clinical remission by week 14).

C. Therapeutic Drug Monitoring:

1. Indication: inadequate response or relapse of symptoms to standard dose Entyvio.

2. Criteria (meets all listed below):

    a. Patient has received three stable maintenance doses.

    b. Trough drug levels 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.

D. Administration: medication is subject to site-of-care policy (see DDP-08).

4.0 Coding:

COVERED CODES				
Code	**Brand Name**	**Generic name**	**Billing units (1u)**	**Prior Approval**
J3380	Entyvio	vedolizumab	1mg	Y

5.0 References, Citations & Resources:

1. Entyvio Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.
2. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Entyvio, accessed April 2020.
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.

6.0 Appendices:

See page 4.

7.0 Revision History:

Original Effective Date: 06/24/2015

Next Review Date: 07/22/2020

Revision Date	Reason for Revision
7/19;	Put in 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 exception to other therapies

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