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Section:	Prescription Drugs	**Effective Date:**	October 1, 2024
Subsection:	Gastrointestinal Agents	**Original Policy Date:**	October 1, 2014
Subject:	Entyvio	**Page:**	1 of 9

Last Review Date: September 6, 2024

Entyvio

Description

Entyvio (vedolizumab)

Background
Entyvio (vedolizumab) is a humanized monoclonal antibody that specifically binds to the α4β7 integrin and blocks the interaction of α4β7 integrin with mucosal addressing cell adhesion molecule-1 (MAdCAM-1) and inhibits the migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal parenchymal tissue. The α4β7 integrin is expressed on the surface of a discrete subset of memory T-lymphocytes that preferentially migrate into the gastrointestinal tract. MAdCAM-1 is mainly expressed on gut endothelial cells and plays a critical role in the homing of T-lymphocytes to gut lymph tissue. The interaction of the α4β7 integrin with MAdCAM-1 has been implicated as an important contributor to the chronic inflammation that is a hallmark of ulcerative colitis and Crohn's disease (1).

Regulatory Status
FDA-approved indications: Entyvio is an integrin receptor antagonist indicated for adults in the treatment of: (1)

1. Moderately to severely active ulcerative colitis (UC)
2. Moderately to severely active Crohn's disease (CD)

Entyvio has warnings for infusion-related reactions and hypersensitivity reactions, infections, and progressive multifocal leukoencephalopathy (PML). Entyvio is not recommended in patients with active, severe infections until the infections are controlled. Patients who develop a severe infection while on treatment with Entyvio should have treatment withheld. Although unlikely, a risk of PML cannot be ruled out. Patients should be monitored for any new or worsening neurological signs or symptoms (1).

Entyvio should be administered intravenously by a healthcare provider on weeks 0 and 2 over approximately 30 minutes. On week 6, the patient may remain on intravenous therapy or switch to subcutaneous injection. Intravenous therapy may be given every eight weeks, while subcutaneous injection may be given every two weeks thereafter. Physicians will need to discontinue therapy in patients who show no evidence of therapeutic benefit by week 14 (1).

The safety and effectiveness of Entyvio in pediatric patients have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Entyvio may be considered **medically necessary** if the conditions indicated below are met.

Entyvio may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Moderate to severely active Ulcerative Colitis (UC)
2. Moderate to severely active Crohn's Disease (CD)

AND ALL of the following for **ALL** indications:

a. Inadequate treatment response, intolerance, or contraindication to at least **ONE** conventional therapy option (see Appendix 1)
b. Inadequate treatment response, intolerance, or contraindication to a biologic DMARD or targeted synthetic DMARD (see Appendix 2) if adjudicated through the pharmacy benefit
c. Patient's condition will be re-evaluated at week 14 to confirm if therapy with Entyvio may continue

d. Prescriber will initiate dosing via IV infusion on weeks 0 and 2
e. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
    i. IV infusion: 300 mg every 8 weeks
    ii. Subcutaneous administration: 108 mg every 2 weeks
f. Patient **MUST** have tried the preferred product(s) (see Appendix 3), if adjudicated through the pharmacy benefit, unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)
g. **NOT** to be used in combination with any other biologic DMARD or targeted synthetic DMARD (see Appendix 2)

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Ulcerative Colitis (UC)
2. Crohn's Disease (CD)

AND ALL of the following for **ALL** indications:

a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
    i. IV infusion: 300 mg every 8 weeks
    ii. Subcutaneous administration: 108 mg every 2 weeks
b. Patient **MUST** have tried the preferred product(s) (see Appendix 3), if adjudicated through the pharmacy benefit, unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)
c. **NOT** to be used in combination with any other biologic DMARD or targeted synthetic DMARD (see Appendix 2)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Diagnosis	Dosage Form	Strength	Quantity
Crohn's disease (CD)	IV	300 mg IV vial	9 IV vials per 365 days **OR**
Crohn's disease (CD)	IV then switch to SC	300 mg IV vial 108 mg SC pen/syringe	2 IV vials + 6 SC pens/syringes per 84 days **OR**
Ulcerative colitis (UC)	IV	300 mg IV vial	9 IV vials per 365 days **OR**
Ulcerative colitis (UC)	IV then switch to SC	300 mg IV vial 108 mg SC pen/syringe	2 IV vials + 6 SC pens/syringes per 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Quantity

Diagnosis	Dosage Form	Strength	Quantity
Crohn's disease (CD)	IV	300 mg IV vial	1 IV vial per 56 days
Crohn's disease (CD)	SC	108 mg SC pen/syringe	6 SC pens/syringes per 84 days
Ulcerative colitis (UC)	IV	300 mg IV vial	1 IV vial per 56 days
Ulcerative colitis (UC)	SC	108 mg SC pen/syringe	6 SC pens/syringes per 84 days

Duration 18 months

Rationale

Summary

Entyvio (vedolizumab) is an integrin receptor antagonist indicated for adults in the treatment of moderate to severely active ulcerative colitis and moderate to severely active Crohn's disease. Entyvio has warnings for infusion-related reactions and hypersensitivity reactions, infections, and progressive multifocal leukoencephalopathy (PML). Therapy should be discontinued in

patients who show no evidence of therapeutic benefit after the first 14 weeks of treatment. The safety and effectiveness of Entyvio in pediatric patients have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Entyvio while maintaining optimal therapeutic outcomes.

References

1. Entyvio [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; April 2024.

Policy History

Date	Action
June 2014	New policy addition
September 2014	Addition of no concurrent use with Kineret from SME
March 2015	Annual editorial review and reference update
September 2015	Annual review
December 2016	Annual editorial review Addition of age to renewal requirements, removal of examples of TNF blocker and interleukin antagonists from criteria Policy number change from 5.18.09 to 5.50.12
March 2017	Annual editorial review and reference update Addition of no concurrent use with TNF blockers, Kineret and Tysabri to renewal criteria and prior PA initiation duration changed from 3 months to 4 months
March 2018	Annual editorial review Addition of Appendix 1 - List of Conventional Therapies
June 2018	Addition of dosage limit requirements Addition of Appendix 2 - List of DMARDs Removal of inadequate response with, or lost response to or was not able to tolerate an immunomodulator and inadequate response with, or lost response to or demonstrated dependence on corticosteroids and changed to inadequate response, intolerance, or contraindication to at least ONE conventional therapy option (see Appendix 1)
September 2018	Annual editorial review
March 2019	Annual review
December 2019	Annual review and reference update. Addition of requirement to trial preferred product
March 2020	Annual review
August 2020	Clarifying language added to pharmacy benefit
December 2020	Annual review and reference update. Removed requirement to t/f preferred product Humira. Moved requirement to reevaluate condition at week 14

	from continuation to initiation. Changed approval durations to 12 months and 18 months. Added PA quantity limits. Added initiation requirement to t/f a biologic or targeted synthetic DMARD per FEP. Changed policy name from Entyvio to Entyvio (IV) per FEP.
March 2021	Annual editorial review. Clarification added to the t/f, intolerance, C/I to a biologic or targeted synthetic DMARD requirement indicating that it only applies to claims adjudicated through the pharmacy benefit. Updated Appendix 2.
June 2021	Annual editorial review
March 2022	Annual review and reference update
September 2022	Annual review and reference update
December 2022	Annual review
March 2023	Annual review
November 2023	Addition of non-preferred subcutaneous dosage form. Revised IV formulation to also be non-preferred as part of the MedEx program if adjudicated through the pharmacy benefit for all indications
March 2024	Annual review
June 2024	Per FEP, added dosing information in regulatory section. Per PI update, allowed subcutaneous dosage form for Crohn's disease
September 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.

APPENDIX 1 – List of Conventional Therapies

Conventional Therapy Options for CD
1. Mild to moderate disease – induction of remission: a. Oral budesonide, oral mesalamine b. Alternatives: metronidazole, ciprofloxacin
2. Mild to moderate disease – maintenance of remission: a. Azathioprine, mercaptopurine b. Alternatives: oral budesonide, methotrexate intramuscularly (IM)
3. Moderate to severe disease – induction of remission: a. Prednisone, methylprednisolone intravenously (IV) b. Alternatives: methotrexate IM
4. Moderate to severe disease – maintenance of remission: a. Azathioprine, mercaptopurine b. Alternative: methotrexate IM
5. Perianal and fistulizing disease – induction of remission c. Metronidazole ± ciprofloxacin
6. Perianal and fistulizing disease – maintenance of remission d. Azathioprine, mercaptopurine e. Alternative: methotrexate IM

Conventional Therapy Options for UC
1. Mild to moderate disease – induction of remission: a. Oral mesalamine (e.g., Asacol, Lialda, Pentasa), balsalazide, olsalazine b. Rectal mesalamine (e.g., Canasa, Rowasa) c. Rectal hydrocortisone (e.g., Colocort, Cortifoam) d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission: a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission: a. Prednisone, hydrocortisone IV, methylprednisolone IV b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission: a. Azathioprine, mercaptopurine b. Alternative: sulfasalazine
5. Pouchitis: a. Metronidazole, ciprofloxacin b. Alternative: rectal mesalamine

Appendix 2 – List of DMARDs

Biological disease-modifying drugs (DMARDs)

Generic Name	Brand Name
abatacept	Orencia
adalimumab	Humira
anakinra	Kineret
brodalumab	Siliq
certolizumab	Cimzia
etanercept	Enbrel
golimumab	Simponi/Simponi Aria
guselkumab	Tremfya
infliximab	Remicade/Avsola/Inflectra/Renflexis
ixekizumab	Taltz
risankizumab-rzaa	Skyrizi
rituximab	Rituxan/Riabni/Ruxience/Truxima
sarilumab	Kevzara
secukinumab	Cosentyx
spesolimab-sbzo	Spevigo
tildrakizumab-asmn	Ilumya
tocilizumab	Actemra
ustekinumab	Stelara
vedolizumab	Entyvio

Targeted synthetic disease-modifying drugs (DMARDs)

Generic Name	Brand Name
apremilast	Otezla
baricitinib	Olumiant
deucravacitinib	Sotyktu
tofacitinib	Xeljanz/XR
upadactinib	Rinvoq

Appendix 3 - List of Preferred Products

Diagnosis	Standard Option/Basic Option Preferred Products	Blue Focus Preferred Products
Crohn's disease (CD)	*must try **TWO** preferred products: Humira** Rinvoq Skyrizi Stelara (SC)	Humira
Ulcerative colitis (UC)	*must try **TWO** preferred products: Humira** Rinvoq Stelara (SC)	Humira

**Including all preferred biosimilars (see reference product criteria)