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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Gastrointestinal Agents	**Original Policy Date:**	October 1, 2014
Subject:	Entyvio (IV)	**Page:**	1 of 7

Last Review Date: March 12, 2021

Entyvio (IV)

Description

Entyvio (vedolizumab) for injection, for intravenous use

Background
Entyvio (vedolizumab) is used to treat adult patients with moderate to severe ulcerative colitis and Crohn‘s disease. Entyvio is used to treat these conditions when one or more standard therapies (corticosteroids, immunomodulators, or tumor necrosis factor blocker medications) have not resulted in an adequate response or patients were intolerant to therapy. Entyvio works by blocking the migration of circulating inflammatory cells to areas of inflammation in the gastrointestinal tract (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)

Patients treated with Entyvio are at increased risk for developing infections. Patients who develop a severe infection while on treatment with Entyvio should have treatment withheld. Entyvio is not recommended in patients with active, severe infections until the infections are controlled (1).

Physicians will need to discontinue therapy in patients who show no evidence of therapeutic benefit by week 14. Safety and effectiveness of Entyvio in pediatric patients have not been established (1).

Although no cases of Progressive Multifocal Leukoencephalopathy (PML) were documented at the time of FDA approval, a risk of PML cannot be ruled out. Patients should be monitored for any new or worsening neurological signs or symptoms (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** in patients 18 years of age or older for the treatment of ulcerative colitis and Crohn's disease; and if the conditions indicated below are met.

Entyvio may be considered **investigational** in patients less than 18 years of age and 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:

a. Inadequate response, intolerance or contraindication to at least **ONE** conventional therapy option (see Appendix 1)
b. Inadequate 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 be dosing the patient within the FDA labeled maintenance dose of 300 mg every 8 weeks
e. **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:

a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of 300 mg every 8 weeks
b. **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 9 vials
(1 vial each at weeks 0, 2, and 6 and then maintenance dosing of 1 vial every 8 weeks)

Duration 12 months

Prior – Approval *Renewal* Limits

Quantity 10 vials

Duration 18 months

Rationale

Summary
Entyvio (vedolizumab) injection is used to treat adult patients with moderate to severely active ulcerative colitis and moderate to severely active Crohn‘s disease when one or more standard therapies have not resulted in an improvement or remission. 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.; March 2020.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.

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
tildrakizumab-asmn	Ilumya
tocilizumab	Actemra
ustekinumab	Stelara
vedolizumab	Entyvio

Targeted synthetic disease-modifying drugs (DMARDs)

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