Entyvio® (Vedolizumab)

Policy Number: 2026D0053Q
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➲ Instructions for Use

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Related Commercial Policy
- Provider Administered Drugs – Site of Care

Community Plan Policy
- Entyvio® (Vedolizumab)

Application

UnitedHealthcare Commercial
This Medical Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange
This Medical Policy applies to Individual Exchange benefit plans.

Coverage Rationale

➲ See Benefit Considerations

This policy refers to Entyvio (vedolizumab) injection for intravenous infusion. Entyvio (vedolizumab) for self-administered subcutaneous injection is obtained under the pharmacy benefit, unless otherwise specified in the member's benefit plan documents. Exception: For members enrolled in UnitedHealthcare of California plans with a delegated provider group conducting the prior authorization review, the self-administered Entyvio may be obtained under the medical benefit.

Crohn's Disease (CD)
Entyvio is proven for the treatment of Crohn's disease (CD) when all of the following criteria are met:
- For **initial therapy**, **all** of the following:
  - Diagnosis of moderately to severely active Crohn's disease; **and**
  - Entyvio is initiated and titrated according to U.S. Food and Drug Administration (FDA) labeled dosing for Crohn's disease; **and**
  - Patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Cimzia (certolizumab), Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Skyrizi (risankizumab), Tremfya (guselkumab), ustekinumab] for treatment of the same indication; **and**
  - Initial authorization will be for no more than 12 months
- For continuation of therapy, all of the following:
  - Documentation of positive clinical response to Entyvio; **and**
  - Entyvio dosing for Crohn's disease is in accordance with the FDA labeled dosing; **and**
  - Patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Cimzia (certolizumab), Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Skyrizi (risankizumab), Tremfya (guselkumab), ustekinumab] for treatment of the same indication; **and**

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- Reauthorization will be for no more than 12 months

Entyvio is medically necessary for the treatment of Crohn's disease (CD) when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of moderately to severely active Crohn's disease; **and**
  - One of the following:
    - History of failure to **one** of the following conventional therapies at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced:
      - Corticosteroids (e.g., prednisone, methylprednisolone, budesonide)
      - 6-mercaptopurine (Purinethol)
      - Azathioprine (Imuran)
      - Methotrexate (Rheumatrex, Trexall)

      or
    - Patient has been previously treated with a systemic targeted immunomodulator FDA-approved for the treatment of Crohn's disease [e.g., adalimumab, Cimzia (certolizumab), Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Skyrizi (risankizumab), Tremfya (guselkumab), ustekinumab]; **or**
    - Patient is currently on Entyvio therapy

    and
  - Entyvio is initiated and titrated according to U.S. Food and Drug Administration (FDA) labeled dosing for Crohn's disease; **and**
  - Patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Cimzia (certolizumab), Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Skyrizi (risankizumab), Tremfya (guselkumab), ustekinumab] for treatment of the same indication; **and**
  - Prescribed by or in consultation with a gastroenterologist; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Documentation of positive clinical response to Entyvio; **and**
  - Entyvio dosing for Crohn's disease is in accordance with the FDA labeled dosing; **and**
  - Patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Cimzia (certolizumab), Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Skyrizi (risankizumab), Tremfya (guselkumab), ustekinumab] for treatment of the same indication; **and**
  - Reauthorization will be for no more than 12 months

Ulcerative Colitis (UC)

Entyvio is proven for the treatment of ulcerative colitis (UC) when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of moderately to severely active ulcerative colitis; **and**
  - Entyvio is initiated and titrated according to U.S. Food and Drug Administration (FDA) labeled dosing for ulcerative colitis; **and**
  - Patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Simponi (golimumab), Skyrizi (risankizumab), Tremfya (guselkumab), Xeljanz/Xeljanz XR (tofacitinib), ustekinumab, Zeposia (ozanimod)] for treatment of the same indication; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Documentation of positive clinical response to Entyvio; **and**
  - Entyvio dosing for ulcerative colitis is in accordance with the FDA labeled dosing; **and**
  - Patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Simponi (golimumab), Skyrizi (risankizumab), Tremfya (guselkumab), Xeljanz/Xeljanz XR (tofacitinib), ustekinumab, Zeposia (ozanimod)] for treatment of the same indication; **and**
  - Reauthorization will be for no more than 12 months

Entyvio is medically necessary for the treatment of ulcerative colitis (UC) when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of moderately to severely active ulcerative colitis; **and**
  - **One** of the following:

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        - Patient has had prior or concurrent inadequate response to a therapeutic course of oral corticosteroids and/or immunosuppressants (e.g., azathioprine, 6-mercaptopurine); **or**
        - Patient has been previously treated with a systemic targeted immunomodulator FDA-approved for the treatment of ulcerative colitis [e.g., adalimumab, Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Simponi (golimumab), Skyrizi (risankizumab), Tremfya (guselkumab), Xeljanz/Xeljanz XR (tofacitinib), ustekinumab, Zeposia (ozanimod)]; **or**
        - Patient is currently on Entyvio therapy

      and
    - Entyvio is initiated and titrated according to U.S. Food and Drug Administration (FDA) labeled dosing for ulcerative colitis; **and**
    - Patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Simponi (golimumab), Skyrizi (risankizumab), Tremfya (guselkumab), Xeljanz/Xeljanz XR (tofacitinib), ustekinumab, Zeposia (ozanimod)] for treatment of the same indication; **and**
    - Prescribed by or in consultation with a gastroenterologist; **and**
    - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
    - Documentation of positive clinical response to Entyvio; **and**
    - Entyvio dosing for ulcerative colitis is in accordance with the FDA labeled dosing; **and**
    - Patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Simponi (golimumab), Skyrizi (risankizumab), Tremfya (guselkumab), Xeljanz/Xeljanz XR (tofacitinib), ustekinumab, Zeposia (ozanimod)] for treatment of the same indication; **and**
    - Reauthorization will be for no more than 12 months

Immune Checkpoint Inhibitor-Related Toxicities

Entyvio is proven and medically necessary for the treatment of Immune checkpoint inhibitor-related toxicities when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
    - **One** of the following immunotherapy-related diagnosis:
        - Moderate to severe esophagitis, gastritis, or duodenitis if no improvement on corticosteroids or budesonide
        - Mild (G1) diarrhea or colitis if persistent or progressive symptoms and positive lactoferrin/calprotectin
        - Moderate (G2) or severe (G3-4) immunotherapy-related diarrhea or colitis

      and
    - Patient is receiving a checkpoint inhibitor [e.g., Keytruda (Pembrolizumab), Opdivo (Nivolumab)]; **and**
    - One of the following:
        - History of failure, contraindication, or intolerance to infliximab
        - Patient has immune-related hepatitis

      and
    - Initial authorization will be for no more than 3 doses of Entyvio
- For **continuation of therapy**, **all** of the following:
    - Documentation of positive clinical response; **and**
    - Patient continues to experience checkpoint inhibitor-related toxicities; **and**
    - Reauthorization will be for no more than 3 doses of Entyvio

Gastrointestinal (GI) Acute Graft-Versus-Host Disease

Entyvio is proven and medically necessary for the treatment of GI acute graft-versus-host disease (aGVHD) when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
    - Diagnosis of steroid-refractory acute GI aGVHD; **and**
    - **One** of the following:
        - Patient is receiving Entyvio in combination with systemic corticosteroids
        - Patient is intolerant to systemic corticosteroid therapy

      and
    - Initial authorization will be for no more than 4 doses
- For **continuation of therapy**, **all** of the following:
    - Documentation of positive clinical response; **and**
    - Patient continues to experience acute GI aGVHD; **and**
    - Reauthorization will be for no more than 4 doses

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other policies and guidelines may apply.

HCPCS Code	Description
J3380	Injection, vedolizumab, IV,1 mg

Diagnosis Code	Description
D89.810	Acute graft-versus-host disease
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K51.00	Ulcerative (chronic) pancolitis without complications
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013	Ulcerative (chronic) pancolitis with fistula
K51.014	Ulcerative (chronic) pancolitis with abscess
K51.018	Ulcerative (chronic) pancolitis with other complication
K51.019	Ulcerative (chronic) pancolitis with unspecified complications

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Diagnosis Code	Description
K51.20	Ulcerative (chronic) proctitis without complications
K51.211	Ulcerative (chronic) proctitis with rectal bleeding
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction
K51.213	Ulcerative (chronic) proctitis with fistula
K51.214	Ulcerative (chronic) proctitis with abscess
K51.218	Ulcerative (chronic) proctitis with other complication
K51.219	Ulcerative (chronic) proctitis with unspecified complications
K51.30	Ulcerative (chronic) rectosigmoiditis without complications
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications
K51.40	Inflammatory polyps of colon without complications
K51.411	Inflammatory polyps of colon with rectal bleeding
K51.412	Inflammatory polyps of colon with intestinal obstruction
K51.413	Inflammatory polyps of colon with fistula
K51.414	Inflammatory polyps of colon with abscess
K51.418	Inflammatory polyps of colon with other complication
K51.419	Inflammatory polyps of colon with unspecified complications
K51.50	Left sided colitis without complications
K51.511	Left sided colitis with rectal bleeding
K51.512	Left sided colitis with intestinal obstruction
K51.513	Left sided colitis with fistula
K51.514	Left sided colitis with abscess
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complications
K51.80	Other ulcerative colitis without complications
K51.811	Other ulcerative colitis with rectal bleeding
K51.812	Other ulcerative colitis with intestinal obstruction
K51.813	Other ulcerative colitis with fistula
K51.814	Other ulcerative colitis with abscess
K51.818	Other ulcerative colitis with other complication
K51.819	Other ulcerative colitis with unspecified complications
K51.90	Ulcerative colitis, unspecified, without complications
K51.911	Ulcerative colitis, unspecified with rectal bleeding
K51.912	Ulcerative colitis, unspecified with intestinal obstruction
K51.913	Ulcerative colitis, unspecified with fistula
K51.914	Ulcerative colitis, unspecified with abscess
K51.918	Ulcerative colitis, unspecified with other complication
K51.919	Ulcerative colitis, unspecified with unspecified complications
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs, sequela

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Background

Entyvio is a humanized monoclonal antibody that reduces chronically inflamed gastrointestinal parenchymal tissue associated with ulcerative colitis and Crohn's disease by binding specifically to the alpha-4-beta-7-integrin receptor and blocking its interaction with mucosal addressing cell adhesion molecule-1 which then inhibits the movement of memory T-lymphocytes across the endothelium into inflamed gastrointestinal tissue.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Clinical Evidence

Professional Societies

Crohn's Disease

American College of Gastroenterology

The American College of Gastroenterology published their clinical practice guidelines for the management of adults with Crohn's disease in 2018. In regards to vedolizumab, the guidelines recommend:

- Moderate-to-severe disease/moderate-to-high-risk disease:
  - For patients with moderately to severely active Crohn's disease and objective evidence of active disease, anti-integrin therapy (with vedolizumab) with or without an immunomodulator is more effective than placebo and should be considered to be used for induction of symptomatic remission in patients with Crohn's disease (strong recommendation, high level of evidence).
- Maintenance therapy of luminal Crohn's disease:
  - Vedolizumab should be used for maintenance of remission of vedolizumab-induced remission of Crohn's disease (conditional recommendation, moderate level of evidence).

Ulcerative Colitis

American College of Gastroenterology

The American College of Gastroenterology Practice Guidelines for Ulcerative Colitis in Adults, published in February 2019, provide the following recommendations for the induction and maintenance of remission in UC.
Recommendations for the induction of remission in moderately to severely active ulcerative colitis:

- In patients with moderately active UC, we recommend oral budesonide for induction of remission (strong recommendation, moderate quality of evidence).
- In patients with moderately to severely active UC of any extent, we recommend oral systemic corticosteroids to induce remission (strong recommendation, moderate quality of evidence).
- In patients with moderately to severely active UC, we recommend against monotherapy with thiopurines or methotrexate for induction of remission (strong recommendation, low quality of evidence).
- In patients with moderately to severely active UC, we recommend anti-TNF therapy using adalimumab, golimumab, or infliximab for induction of remission (strong recommendation, high quality of evidence).
- In patients with moderately to severely active UC who have failed 5-ASA therapy and in whom anti-TNF therapy is used for induction of remission, we suggest against using 5-ASA for added clinical efficacy (conditional recommendation, low quality of evidence).
- When infliximab is used as induction therapy for patients with moderately to severely active UC, we recommend combination therapy with a thiopurine (strong recommendation, moderate quality of evidence for azathioprine).
- In patients with moderately to severely active UC, we recommend vedolizumab for induction of remission (strong recommendation, moderate quality of evidence).
- In patients with moderately to severely active UC who have previously failed anti-TNF therapy, we recommend vedolizumab for induction of remission (strong recommendation, moderate quality of evidence).
- In patients with moderately to severely active UC, we recommend tofacitinib 10 mg orally twice daily for 8 weeks to induce remission (strong recommendation, moderate quality of evidence).

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- In patients with moderately to severely active UC who have previously failed anti-TNF therapy, we recommend tofacitinib for induction of remission (strong recommendation, moderate quality of evidence).
- In patients with moderately to severely active UC who are responders to anti-TNF therapy and now losing response, we suggest measuring serum drug levels and antibodies (if there is not a therapeutic level) to assess the reason for loss of response (conditional recommendation, very low quality of evidence).

Recommendations for the maintenance of remission in patients with previously moderately to severely active ulcerative colitis:

- In patients with previously moderately to severely active UC who have achieved remission but previously failed 5-ASA therapy and are now on anti-TNF therapy, we recommend against using concomitant 5-ASA for efficacy of maintenance of remission (conditional recommendation, low quality of evidence).
- We recommend against systemic corticosteroids for maintenance of remission in patients with UC (strong recommendation, moderate quality of evidence).
- For patients with previously moderately to severely active UC now in remission due to corticosteroid induction, we suggest thiopurines for maintenance of remission compared with no treatment or corticosteroids (conditional recommendation, low quality of evidence).
- In patients with previously moderately to severely active UC now in remission, we recommend against using methotrexate for maintenance of remission (conditional recommendation, low quality of evidence).
- We recommend continuing anti-TNF therapy using adalimumab, golimumab, or infliximab to maintain remission after anti-TNF induction in patients with previously moderately to severely active UC (strong recommendation, moderate quality of evidence).
- We recommend continuing vedolizumab to maintain remission in patients with previously moderately to severely active UC now in remission after vedolizumab induction (strong recommendation, moderate quality of evidence).
- We recommend continuing tofacitinib for maintenance of remission in patients with previously moderately to severely active UC now in remission after induction with tofacitinib (strong recommendation, moderate quality of evidence).

American Gastroenterological Association

In 2020, the American Gastroenterological Association (AGA) published a clinical practice guideline on the management of moderate to severe ulcerative colitis. In regards to vedolizumab, the guidelines recommend:

- In adult outpatients with moderate-severe ulcerative colitis, the AGA recommends using infliximab, adalimumab, golimumab, vedolizumab, tofacitinib or ustekinumab over no treatment (Strong recommendation, moderate quality evidence).
- In adult outpatients with moderate-severe ulcerative colitis who have previously been exposed to infliximab, particularly those with primary non-response, the AGA suggests using ustekinumab or tofacitinib, rather than vedolizumab or adalimumab for induction of remission (Conditional recommendation, low quality evidence).
- In adult outpatients with active moderate-severe ulcerative colitis, the AGA suggests using biologic monotherapy (TNFα antagonists, vedolizumab, ustekinumab) rather than thiopurine monotherapy for induction of remission (Conditional recommendation, low quality evidence).
- In adult outpatients with moderate-severe ulcerative colitis in remission, the AGA makes no recommendation in favor of, or against, using biologic monotherapy (TNFα antagonists, vedolizumab or ustekinumab), rather than thiopurine monotherapy for maintenance of remission (No recommendation, knowledge gap).
- In adult outpatients with moderate-severe ulcerative colitis, the AGA suggests combining TNFα antagonists, vedolizumab or ustekinumab with thiopurines or methotrexate, rather than biologic monotherapy (Conditional recommendation, low quality evidence).
- In adult outpatients with moderate-severe ulcerative colitis, the AGA suggests combining TNFα antagonists, vedolizumab or ustekinumab with thiopurines or methotrexate, rather than thiopurine monotherapy (Conditional recommendation, low quality evidence).
- In adult outpatients with moderate-severe ulcerative colitis, the AGA suggests early use of biologic agents with or without immunomodulator therapy, rather than gradual step up after failure of 5-aminosalicylates (Conditional recommendation, very low quality evidence).
- In adult outpatients with moderate-severe ulcerative colitis who have achieved remission with biologic agents and/or immunomodulators, or tofacitinib, the AGA suggests against continuing 5-aminosalicylates for induction and maintenance of remission (Conditional recommendation, very low quality evidence).

The National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®) include vedolizumab for the treatment immunotherapy-related diarrhea or colitis. The following NCCN Guidelines® state:

- Management of Immunotherapy-Related Toxicities (V 1.2020): Consider adding vendolizumab for management of moderate (G2) and strongly consider for severe (G3-4) immunotherapy-related diarrhea or colitis.

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- Duration of therapy with tumor necrosis factor alpha (TNF-alpha) blockers or integrin blocker is not clearly defined. Evidence supports up to three doses (at weeks 0, 2, and 6) and is associated with reduced recurrence rates.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Entyvio is indicated for treatment of adult patients with moderately to severely active ulcerative colitis (UC).

It is also indicated for treatment of adult patients with moderately to severely active Crohn's Disease (CD).

References

1. Entyvio [prescribing information]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; February 2026.
2. Vedolizumab. Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/. Accessed February 26, 2024.
3. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018 Apr;113(4):481-517.
4. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. American College of Gastroenterology Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019 Mar;114(3):384-413.
5. NCCN Clinical Practice Guidelines in Oncology® (NCCN Guidelines®). Management of Immunotherapy-Related Toxicities. Version 1.2025. Available at www.nccn.org. Accessed on April 9, 2025.
6. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020 Jan 13.

Policy History/Revision Information

Date	Summary of Changes

08/01/2026	**Template Update**
	• Transferred content to shared policy template that applies to both UnitedHealthcare Commercial and Individual Exchange benefit plans
	• Added *Application* section to indicate this policy applies to:
	  ○ UnitedHealthcare Commercial benefit plans
	  ○ Individual Exchange benefit plans
	Coverage Rationale
	• Added language to indicate Entyvio (vedolizumab) for self-administered subcutaneous injection is obtained under the pharmacy benefit, unless otherwise specified in the member's benefit plan documents; exception: for members enrolled in UnitedHealthcare of California plans with a delegated provider group conducting the prior authorization review, the self-administered Entyvio may be obtained under the medical benefit
	• Replaced references to "targeted immunomodulator" with "*systemic* targeted immunomodulator"
	• Revised coverage criteria for:
	Crohn's Disease (CD)
	Initial Therapy
	  ○ Added **medical necessity** criterion requiring:
	  ▪ One of the following:
	  – History of failure to one of the following conventional therapies at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced:
	  • Corticosteroids (e.g., prednisone, methylprednisolone, budesonide)
	  • 6-mercaptopurine (Purinethol)
	  • Azathioprine (Imuran)
	  • Methotrexate (Rheumatrex, Trexall)
	  – The patient has been previously treated with a systemic targeted immunomodulator U.S. FDA-approved for the treatment of Crohn's disease [e.g., adalimumab, Cimzia

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Date	Summary of Changes
	(certolizumab), Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Skyrizi (risankizumab), Tremfya (guselkumab), ustekinumab] – The patient is currently on Entyvio therapy ▪ Entyvio is prescribed by or in consultation with a gastroenterologist ○ Removed **proven/medically necessary** criterion requiring: ▪ History of failure, contraindication, or intolerance to at least one of the following conventional therapies: – Tumor necrosis factor (TNF) blocker – Immunomodulator – Corticosteroid ▪ The patient is corticosteroid dependent (e.g., unable to successfully taper corticosteroids without a return of the symptoms of CD) ▪ Updated list of examples of systemic targeted immunomodulator the patient must not be receiving in combination with Entyvio for treatment of the same indication; removed: – Simponi (golimumab) – Tysabri (natalizumab) – Xeljanz (tofacitinib) Continuation of Therapy ○ Added **proven/medically necessary** criterion requiring the patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Cimzia (certolizumab), Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Skyrizi (risankizumab), Tremfya (guselkumab), ustekinumab] for treatment of the same indication ***Ulcerative Colitis (UC)*** Initial Therapy ○ Added **medical necessity** criterion requiring: ▪ One of the following: – The patient has had prior or concurrent inadequate response to a therapeutic course of oral corticosteroids and/or immunosuppressants (e.g., azathioprine, 6-mercaptopurine) – The patient has been previously treated with a systemic targeted immunomodulator U.S. FDA-approved for the treatment of ulcerative colitis [e.g., adalimumab, Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Simponi (golimumab), Skyrizi (risankizumab), Tremfya (guselkumab), Xeljanz/Xeljanz XR (tofacitinib), ustekinumab, Zeposia (ozanimod)] – Patient is currently on Entyvio therapy ▪ Entyvio is prescribed by or in consultation with a gastroenterologist ○ Removed **proven/medically necessary** criterion requiring: ▪ History of failure, contraindication, or intolerance to at least one of the following conventional therapies: – Tumor necrosis factor (TNF) blocker – Immunomodulator – Corticosteroid ▪ The patient is corticosteroid dependent (e.g., unable to successfully taper corticosteroids without a return of the symptoms of CD) ▪ Updated list of examples of systemic targeted immunomodulator the patient must not be receiving in combination with Entyvio for treatment of the same indication: – Added Zeposia (ozanimod) – Removed: • Simponi (golimumab) • Tysabri (natalizumab) • Xeljanz (tofacitinib) – Replaced “Xeljanz (tofacitinib)” with “Xeljanz/*Xeljanz XR* (tofacitinib)” Continuation of Therapy ○ Added **proven/medically necessary** criterion requiring the patient is not receiving Entyvio in combination with another systemic targeted immunomodulator [e.g., adalimumab, Omvoh (mirikizumab-mrkz), Rinvoq (upadacitinib), Simponi (golimumab), Skyrizi (risankizumab), Tremfya (guselkumab), Xeljanz/Xeljanz XR (tofacitinib), ustekinumab, Zeposia (ozanimod)] for treatment of the same indication

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Date	Summary of Changes
	Immune Checkpoint Inhibitor-Related Toxicities Continuation of Therapy ○ Added criterion requiring: ▪ Documentation of positive clinical response ▪ Patient continues to experience checkpoint inhibitor-related toxicities ○ Removed criterion requiring: ▪ One of the following immunotherapy-related diagnosis: – Moderate to severe esophagitis, gastritis, or duodenitis if no improvement on corticosteroids or budesonide – Mild (G1) diarrhea or colitis if persistent or progressive symptoms and positive lactoferrin/calprotectin – Moderate (G2) or severe (G3-4) immunotherapy-related diarrhea or colitis ▪ Patient is receiving a checkpoint inhibitor [e.g., Keytruda (Pembrolizumab), Opdivo (Nivolumab)] ▪ One of the following: – History of failure, contraindication, or intolerance to infliximab – Patient has immune-related hepatitis ***Gastrointestinal (GI) Acute Graft-Versus-Host Disease*** ○ Removed criterion requiring one of the following: ▪ The patient is receiving Entyvio in combination with systemic corticosteroids ▪ The patient is intolerant to systemic corticosteroid therapy **Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy versions 2025D0053P and IEXD0053.08

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its policies and guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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