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Mirikizumab-mrkz

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

NOTE 1: Mirikizumab-mrkz (Omvoh™) may be self-administered. For self-administered medications, please refer to applicable pharmacy benefit plan.

Intravenous administration of mirikizumab-mrkz (Omvoh™) **may be considered medically necessary** for the following U.S. Food and Drug Administration (FDA) labeled indications:

- Adults (18 years of age or older) with moderately to severely active ulcerative colitis (UC) when:
  - Individual has had inadequate response, loss of response, or failed to tolerate any of the following: corticosteroids, 6-mercaptopurine, azathioprine, biologic therapy (TNF blocker, vedolizumab), or tofacitinib AND
  - Absence of active infection.

- Adults (18 years of age or older) with moderately to severely active Crohn's disease when:
  - Individual has had an inadequate response, loss of response, or intolerance to corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine, and methotrexate), and/or biologics (TNF blockers, integrin receptor antagonists) AND
  - Absence of active infection.

Intravenous administration of mirikizumab-mrkz (Omvoh™) **is considered experimental, investigational and/or unproven** for all other non-FDA approved indications.

NOTE 2: Prior to treatment initiation, individuals should be evaluated for tuberculosis infection, baseline liver enzymes and bilirubin levels established, and all age-appropriate vaccinations completed according to current immunization guidelines.

Policy Guidelines

None.

Description

Mirikizumab-mrkz (Omvoh™) (1)
Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by inflammation and ulcers on the inner lining of the large intestine. The inflammation in UC is thought to be caused in part by overactivation of the interleukin-23 (IL-23) pathway.

Mirikizumab-mrkz (Omvoh™) works to reduce inflammation in ulcerative colitis by selectively targeting the p19 subunit of IL-23 to inhibit the IL-23 pathway.

During chronic inflammation associated with Crohn's disease, increased concentrations of cytokines (e.g., IL-1, IL-6, IL-10, TNFα, IFN) may suppress the formation of CYP450 enzymes. Therapeutic proteins, including mirikizumab-mrkz, that decrease the concentrations of these pro-inflammatory cytokines may increase the formation of CYP450 enzymes resulting in decreased CYP450 substrate exposure.

Regulatory Status
The U.S. Food and Drug Administration (FDA) approved mirikizumab-mrkz (Omvoh™) for the treatment of adults (18 years of age or older) with:

- Moderately to severely active ulcerative colitis (October 26, 2023); and
- Moderately to severely active Crohn's disease (January 15, 2025).

Refer to the applicable pharmacy benefit plan when medication is self-administered.

Rationale

Mirikizumab-mrka (1)
Ulcerative Colitis
The safety and efficacy of Omvoh™ was evaluated in two randomized, double-blind, placebo-controlled clinical studies, one induction study [UC-1 (NCT03518086)] and one maintenance study [UC-2 (NCT03524092)], in adult subjects with moderately to severely active ulcerative colitis who had inadequate response, loss of response, or failed to tolerate any of the following: corticosteroids, 6-mercaptopurine, azathioprine, biologic therapy (TNF blocker, vedolizumab), or tofacitinib. The 12-week intravenous induction study (UC-1) was followed by the 40-week subcutaneous randomized withdrawal maintenance study (UC-2).

Study UC-1
In UC-1, efficacy was evaluated in 1062 subjects who were randomized 3:1 at Week 0 to receive 300 mg Omvoh or placebo by intravenous infusion at Week 0, Week 4, and Week 8. Subjects had a mean age of 43 years (range 18 to 79 years); 40% were female; and 71% identified as White, 25% as Asian, 1% as American Indian or Alaska Native, 1% as Black or African American, and <2% as another racial group or did not report their racial group. Subjects were permitted to use stable doses of aminosalicylates, immunomodulators (6-mercaptopurine, azathioprine, methotrexate), and oral corticosteroids (prednisone ≤20 mg/day or equivalent, extended-release budesonide 9 mg/day, beclomethasone dipropionate 5 mg/day). At baseline, 41% of subjects were receiving oral corticosteroids, 24% were receiving immunomodulators, and 75% were receiving aminosalicylates.

At baseline, 57% were biologic and Janus Kinase inhibitor (JAKi) naive, 41% had failed at least one biologic, 3% had failed a JAKi, and 2% had previously received but had not failed a biologic or JAKi.

Disease activity was assessed based on the modified Mayo score (mMS), which ranges from 0 to 9 and has three subscores that are each scored from 0 (normal) to 3 (most severe): stool frequency, rectal bleeding, and findings on centrally read endoscopy subscore. At baseline, subjects had a mMS of 5 to 9, including a centrally read endoscopy subscore of 2 or 3. An endoscopy subscore of 2 was defined by marked erythema, absent vascular pattern, friability, and erosions; and a subscore of 3 was defined by spontaneous bleeding and ulceration. Subjects had a median mMS of 7, and 58% had severely active disease (mMS of 7 to 9).

The primary endpoint was clinical remission at Week 12. The secondary endpoints were clinical response, endoscopic improvement, and histologic-endoscopic mucosal improvement (see Table 1).

Table 1. Proportion of Subjects with Ulcerative Colitis Meeting Efficacy Endpoints in UC-1 at Week 12

Endpoint	**Placebo**	**Omvoh 300 mg Intravenous Infusion[a]**	**Treatment Difference[b] (95% CI)**
Clinical remission[c]			
Total Population	N=267 15%	N=795 24%	10%[d] (5, 15)
Biologic and JAKi naïve	N=155 18%	N=450 31%	
Prior biologic or JAKi failure[e]	N=107 8%	N=331 15%	
Clinical response[f]			
Total Population	N=267 43%	N=795 65%	22%[d] (15, 28)
Biologic and JAKi naïve	N=155 52%	N=450 71%	
Prior biologic or JAKi failure[d,e]	N=107 31%	N=331 56%	
Endoscopic improvement[g]			
Total Population	N=267 21%	N=795 34%	14%[d] (8, 20)
Biologic and JAKi naïve	N=155 28%	N=450 44%	
Prior biologic or JAKi failure[e]	N=107 10%	N=331 22%	
Histologic-endoscopic mucosal improvement[h]			
Total Population	N=267	N=795	11%[d]

	14%	25%	(6, 16)
Biologic and JAKi naïve	N=155 19%	N=450 34%	
Prior biologic or JAKi failure[e]	N=107 7%	N=331 13%	

JAKi = Janus Kinase inhibitor

[a] Omvoh 300 mg as an intravenous infusion at Week 0, Week 4, and Week 8.

[b] Adjusted treatment difference based on Cochran-Mantel-Haenszel method adjusted for randomization stratification factors.

[c] Clinical remission based on mMS is defined as: stool frequency subscore = 0 or 1, rectal bleeding subscore = 0, and centrally read endoscopy subscore = 0 or 1 (excluding friability).

[d] Tested at an alpha level of 0.00125, with a p-value <0.001.

[e] Prior biologic or JAKi failure includes loss of response, inadequate response, or intolerance to one or more biologic therapy (TNF blocker or vedolizumab), or tofacitinib.

[f] Clinical response is defined as a decrease in the mMS of ≥2 points with ≥30% decrease from baseline, and either a decrease of ≥1 point in the rectal bleeding subscore from baseline or a rectal bleeding subscore of 0 or 1.

[g] Endoscopic improvement is defined as a centrally read endoscopy subscore of 0 or 1 (excluding friability).

[h] Histologic-endoscopic mucosal improvement is defined as achieving both endoscopic improvement (centrally read endoscopy subscore of 0 or 1, excluding friability) and histologic improvement (neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue based on the Geboes scoring system).

Study UC-1 was not designed to evaluate the relationship of histologic-endoscopic mucosal improvement at Week 12 to disease progression and long-term outcomes.

Rectal Bleeding and Stool Frequency Subscores

Decreases in rectal bleeding and stool frequency subscores were observed as early as Week 3 in subjects treated with Omvoh compared to subjects on placebo.

Study UC-2

The maintenance study (UC-2) evaluated 506 subjects who achieved clinical response at Week 12 in Study UC-1. These subjects were randomized 2:1 to receive 200 mg Omvoh or placebo subcutaneously every 4 weeks for 40 weeks in UC2, for a total of 52 weeks of treatment. Subjects who were on concomitant ulcerative colitis therapies during UC-1 were required to continue on stable doses of oral aminosalicylates and immunomodulators (6-mercaptopurine, azathioprine, methotrexate). Corticosteroid tapering was required for subjects who were receiving corticosteroids at baseline and achieved clinical response in UC-1.

The primary endpoint was clinical remission at Week 40. The secondary endpoints were endoscopic improvement, maintenance of clinical remission in subjects who achieved clinical remission at Week 12, corticosteroid-free clinical remission, and histologic-endoscopic mucosal improvement (see Table 2).

Table 2. Proportion of Subjects with Ulcerative Colitis Meeting Efficacy Endpoints in UC-2 at Week 40 (a total of 52 weeks of treatment)

Endpoint	Placebo[a]	Omvoh 200 mg Subcutaneous Injection[b]	Treatment Difference[c] (95% CI)
Clinical remission[d,e]			
Total Population	N=169 27%	N=337 51%	22%[f] (14, 31)
Biologic and JAKi naive	N=109 33%	N=208 53%	
Prior biologic or JAKi failure[g]	N=59 15%	N=121 45%	
Endoscopic improvement[d,h]			
Total Population	N=169 30%	N=337 58%	27%[f] (19, 36)
Biologic and JAKi naive	N=109 35%	N=208 62%	
Prior biologic or JAKi failure[g]	N=59 20%	N=121 50%	
Maintenance of clinical remission in patients who achieved clinical remission at Week 12[i]			
Total Population	N=62 40%	N=128 66%	23%[J] (8, 38)
Biologic and JAKi naive	N=48 48%	N=91 66%	
Prior biologic or JAKi failure[g]	N=14 14%	N=34 65%	
Corticosteroid-free clinical remission[d,k]			
Total Population	N=169 27%	N=337 50%	22%[f] (13, 30)
Biologic and JAKi naive	N=109 33%	N=208 52%	
Prior biologic or JAKi failure[g]	N=59 15%	N=121 45%	
Histologic-endoscopic mucosal improvement[d,l]			
Total Population	N=169 22%	N=337 43%	19%[f] (11, 27)
Biologic and JAKi naive	N=109 27%	N=208 47%	
Prior biologic or JAKi failure[g]	N=59 14%	N=121 36%	

JAKi = Janus Kinase inhibitor

[a] The placebo arm includes subjects treated with Omvoh during the induction study (UC-1) and were randomized to receive placebo through Week 40.

[b] Omvoh 200 mg as a subcutaneous injection at Week 12 and every 4 weeks thereafter for up to an additional 40 weeks.
[c] Adjusted treatment difference (95% CI) based on Cochran-Mantel-Haenszel method adjusted for randomization stratification factors.
[d] Among subjects who achieved clinical response at Week 12 in UC-1 with Omvoh induction treatment.
[e] Clinical remission based on mMS is defined as: stool frequency subscore = 0 or 1, rectal bleeding subscore = 0, and centrally read endoscopy subscore = 0 or 1 (excluding friability).
[f] p<0.001.
[g] Prior biologic or JAKi failure includes loss of response, inadequate response, or intolerance to one or more biologic therapy (TNF blocker or vedolizumab), or tofacitinib.
[h] Endoscopic improvement is defined as a centrally read endoscopy subscore of 0 or 1 (excluding friability).
[I] Among subjects who achieved clinical remission at Week 12 in UC-1 with Omvoh induction treatment.
[J] p<0.01.
[K] Corticosteroid-free clinical remission is defined as clinical remission at Week 40 and no corticosteroid use for ≥12 weeks prior to Week 40 assessment.
[l] Histologic-endoscopic mucosal improvement is defined as achieving both endoscopic improvement (centrally read endoscopy subscore of 0 or 1, excluding friability) and histologic improvement (no neutrophils in crypts or lamina propria, no crypt destruction, and no erosions, ulcerations, or granulation tissue based on the Geboes scoring system).

Study UC-2 was not designed to evaluate the relationship of histologic-endoscopic mucosal improvement at Week 40 to disease progression and long-term outcomes.

Bowel Urgency
Bowel urgency was assessed during UC-1 and UC-2 with an Urgency Numeric Rating Scale (NRS) of 0 to 10. A greater proportion of subjects with a baseline Urgency NRS weekly average score ≥3 treated with Omvoh compared to placebo reported an Urgency NRS weekly average score of 0 or 1 (39% versus 23%) at Week 40. Urgency NRS weekly average scores of 0 to 1 were also observed in a greater proportion of subjects treated with Omvoh compared to placebo at Week 12.

Endoscopic Assessment
Normalization of the endoscopic appearance of the mucosa (endoscopic remission) was defined as a Mayo endoscopic subscore of 0. At Week 40 in UC-2, endoscopic remission was observed in a greater proportion of subjects treated with Omvoh compared to placebo (22% versus 14%).

Crohn's Disease
The safety and efficacy of Omvoh was evaluated in a randomized, double-blind, placebo-controlled study [CD-1 (NCT03926130)] in adult subjects with moderately to severely active Crohn's disease who had an inadequate response, loss of response, or intolerance to corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine, and methotrexate), and/or biologics (TNF blockers, integrin receptor antagonists).

In CD-1, the efficacy population consisted of 679 subjects who were randomized 3:1 at Week 0 to receive Omvoh 900 mg by intravenous infusion at Week 0, Week 4, and Week 8 followed by a dosage of 300 mg by subcutaneous injection at Week 12 and then every 4 weeks for 40 weeks, or placebo. Subjects had a mean age of 36 years (range 18 to 74 years); 42% were female; and 71% identified as White, 25% as Asian, <1% as American Indian or Alaska Native, 1% as Black or African American, and 2% as another racial group or did not report their racial group. Subjects were permitted to use stable doses of oral corticosteroids (prednisone ≤30 mg/day or equivalent, extended-release budesonide 9 mg/day), immunomodulators (6-mercatopurine, azathioprine, or methotrexate) and/or amino salicylates. At baseline, 31% of subjects were receiving oral corticosteroids, 26% were receiving immunomodulators, and 44% were receiving amino salicylates.

At baseline, 47% had a loss of response, inadequate response, or intolerance to one or more biologic therapy.

Disease activity at baseline was assessed by the Crohn's Disease Activity Index (CDAI) and the Simple Endoscopic Score for Crohn's disease (SES-CD). Moderately to severely active CD was defined by a CDAI of ≥220 and an SES-CD ≥7 (centrally read) for subjects with ileal-colonic disease or ≥4 for subjects with isolated ileal disease. At baseline, subjects had a median CDAI of 329 and SES-CD of 12.

The coprimary endpoints of clinical remission by CDAI and endoscopic response by SES-CD were assessed at Week 52. Secondary efficacy endpoints included endoscopic response at Week 12 and endoscopic remission and corticosteroid free clinical remission at Week 52 (see Table 3).

Table 3. Proportion of Subjects with Crohn's Disease Meeting Efficacy Endpoints in CD-1

	Placebo[a]	**Omvoh[b]**	**Treatment Difference[c] (95% CI)**
Coprimary Endpoints			
Clinical remission[d] at Week 52			
Total population	N=168 36%	N=511 53%	17%[e] (9%, 25%)
Without prior biologic failure	N=89 45%	N=268 56%	
Prior biologic failure[f]	N=79 25%	N=243 49%	
Endoscopic response[g] at Week 52			
Total population	N=168 23%	N=511 46%	23%[e] (15%, 30%)
Without prior biologic failure	N=89 27%	N=268 49%	
Prior biologic failure[f]	N=79 18%	N=243 43%	

Additional Endpoints			
Endoscopic response[g] at Week 12			
Total population	N=168 11%	N=511 32%	22%[e] (16%, 28%)
Without prior biologic failure	N=89 12%	N=268 37%	
Prior biologic failure[f]	N=79 9%	N=243 28%	
Corticosteroid-free clinical remission[i] at Week 52			
Total population	N=168 35%	N=511 50%	16%[e] (7%, 24%)
Without prior biologic failure	N=89 43%	N=268 54%	
Prior biologic failure[f]	N=79 25%	N=243 46%	
Endoscopic remission[h] at Week 52			
Total population	N=168 8%	N=511 19%	11%[e] (6%, 16%)
Without prior biologic failure	N=89 10%	N=268 22%	
Prior biologic failure[f]	N=79 5%	N=243 16%	

CI: confidence interval

[a] The placebo group includes all 168 subjects randomized to placebo at baseline. Of those, 67 (40%) subjects who did not achieve clinical response by patient-reported outcome at Week 12 were switched to treatment with Omvoh and their efficacy data are included here with the remaining subjects randomized to placebo who did not receive Omvoh.

[b] Following Omvoh 900 mg as an intravenous infusion at Week 0, Week 4, and Week 8, subjects received Omvoh 300 mg as a subcutaneous injection at Week 12 and every 4 weeks thereafter for up to an additional 40 weeks.

[c] Adjusted treatment difference was based on Cochran-Mantel-Haenszel method adjusted for randomization stratification factors.

[d] Clinical remission is defined as CDAI <150.

[e] p-value <0.001.

[f] Prior biologic failure includes loss of response, inadequate response, or intolerance to one or more biologic therapy (TNF blockers, and integrin receptor antagonists).

[g] Endoscopic response is defined as >50% reduction from baseline in SES-CD total score, based on central reading.

[h] Endoscopic remission is defined as SES-CD total score ≤4 and at least a 2-point reduction from baseline, with no segment subscore >1, based on central reading.

[i] Corticosteroid-free clinical remission is defined as subjects who were corticosteroid-free from Week 40 to Week 52 and had a CDAI <150 at Week 52.

Stool Frequency and Abdominal Pain

In CD-1, reductions in abdominal pain were observed as early as Week 6 and in stool frequency as early as Week 12 in subjects treated with Omvoh compared to placebo.

Fatigue
In CD-1, subjects treated with Omvoh experienced a clinically meaningful improvement in fatigue, assessed by the change from baseline in the Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-Fatigue), at Week 12, compared to placebo-treated subjects. The effect of Omvoh to improve fatigue after 12 weeks has not been established.

Other Assessments at Week 12
In CD-1, a greater proportion of subjects treated with Omvoh compared to placebo achieved clinical remission (34% versus 23%) and endoscopic remission (10% versus 4%) at Week 12.

Summary of Evidence
Based on the clinical studies provided to the U.S. Food and Drug Administration, mirikizumab-mrkz (Omvoh™) may be considered medically necessary for the treatment of moderate to severe ulcerative colitis (UC) and Crohn's disease in adults when meeting the specified coverage criteria.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J2267

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label

1. U.S. Food and Drug Administration, Drugs @ FDA. Highlights of Prescribing Information: Omvoh. (Jan 2025). Available at: <https://www.accessdata.fda.gov> (accessed April 17, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
09/01/2025	Document updated with literature review. The following changes were made to Coverage: 1) Modified conditional criteria for ulcerative colitis; 2) Added conditional criteria for Crohn's disease; and 3) Added "non-FDA [Food and Drug Administration] approved" to the experimental, investigational and/or unproven statement. No new references added, one updated.
08/01/2024	New medical document. Intravenous administration of mirikizumab-mrkz (Omvoh™) **may be considered medically necessary** for the following U.S. Food and Drug Administration (FDA) labeled indication: Adults (18 years of age or older) with moderately to severely active ulcerative colitis (UC) when: Individual has had an inadequate response to OR is intolerant to OR has a contraindication to conventional therapy (such as 5-Aminosalicylic acid products, systemic corticosteroids, or immunosuppressants [such as thiopurines]); AND Individual has had an inadequate response to OR is intolerant to OR has a contraindication to three (3) biologic therapies (e.g., integrin receptor antagonists, interleukin receptor antagonists, tumor necrosis factor (TNF) antagonists). Intravenous administration of mirikizumab-mrkz (Omvoh™) is considered experimental, investigational and/or unproven for all other indications. NOTE 1: Mirikizumab-mrkz (Omvoh™) may be self-administered. For self-administered medications, please refer to applicable pharmacy benefit plan. NOTE 2: Prior to treatment initiation, individuals should be evaluated for tuberculosis infection, baseline liver enzymes and bilirubin levels established, and all age-appropriate vaccinations completed according to current immunization guidelines.