Iowa Medicaid
IOWA HHS

PDL DRUG REVIEW

Proprietary Name: Omvoh® Auto-Injector
Common Name: mirikizumab-mrkz injection
PDL Category: Anti-Inflammatories Non-NSAID

Comparable Products	Preferred Drug List Status
Humira	Preferred with Conditions
Stelara	Non-Preferred with Conditions

Pharmacology/Usage: Mirikizumab-mrkz, the active ingredient of Omvoh®, is a humanized immunoglobulin G4 (IgG4) variant monoclonal antibody that is directed against the p19 subunit of IL-23 and does not bind IL-12. It selectively binds to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor. Note that IL-23 is involved in mucosal inflammation and affects the differentiation, expansion, and survival of T cell subsets, and innate immune cell subsets, which represent sources of pro-inflammatory cytokines. Mirikizumab-mrkz inhibits the release of pro-inflammatory cytokines and chemokines.

Indication: For the treatment of moderately to severely active ulcerative colitis (UC) in adults.

There is no pregnancy category for this medication; however, the risk summary indicates that available data from case reports of use in pregnant women are not sufficient to assess for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. While there is no data with mirikizumab-mrkz, monoclonal antibodies can be actively transported across the placenta, and mirikizumab-mrkz may cause immunosuppression in the utero-exposed infant. There are risks of adverse pregnancy outcomes associated with increased disease activity in women with inflammatory bowel disease. There will be a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Omvoh® during pregnancy. Pregnant women and healthcare providers are encouraged to call Eli Lilly at 1-800-545-5979. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Solution for Injection, available as:

- IV infusion: 300mg/15ml (20mg/ml) solution in a single-dose vial.
- SC: 100mg/ml solution in a single-dose prefilled pen.

Omvoh® is preservative-free; thus, discard any unused product. Do not reuse.

Recommended Dosage: Prior to treatment initiation:

- Evaluate patients for tuberculosis (TB) infection.
- Obtain liver enzymes and bilirubin levels.
- Complete all age-appropriate vaccinations per current immunization guidelines.

The recommended *induction dosage* is 300mg administered by IV infusion over at least 30 minutes at week 0, week 4, and week 8. The recommended *maintenance dosage* is 200mg administered by SC injection (given as two consecutive injections of 100mg each) at week 12, and every 4 weeks thereafter.

Omvoh® for IV use is intended for administration by a healthcare provider using aseptic technique. Each vial is for single use only. Refer to the prescribing information for further details on preparation and administration for IV infusion.

Omvoh® for SC injection is intended for use under the guidance and supervision of a healthcare professional. Patients may self-inject Omvoh® after training in SC injection technique. Note that a full maintenance dose will require 2 prefilled pens. Before injection, remove Omvoh® prefilled pen from the refrigerator and leave at room temperature for 30 minutes. Sites for injection include the abdomen, thigh, and back of the upper arm, and inject in a different location every time. If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing every 4 weeks.

Drug Interactions: There are no drug interactions listed with this product.

Avoid use of live vaccines in patients treated with Omvoh®. Medications that interact with the immune system may increase the risk of infection following the administration of live vaccines. Prior to starting therapy with Omvoh®, complete all age-appropriate vaccinations per current immunization guidelines. No data are available on the response to live or non-live vaccines in patients treated with Omvoh®.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Omvoh® IV) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included upper respiratory tract infections (2%) and arthralgia (1%).

Listed % incidence for adverse drug reactions= reported % incidence for drug (Omvoh® SC) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo. The most frequently reported adverse events included upper respiratory tract infections (2%), injection site reactions (5%), arthralgia (3%), rash (3%), headache (3%), and herpes viral infection (1%).

Serious hypersensitivity reactions, including anaphylaxis during IV infusion, have been reported with Omvoh® administration. Infusion-related hypersensitivity reactions, including mucocutaneous erythema and pruritus, were reported during induction. If a severe hypersensitivity reaction occurs, discontinue Omvoh® immediately and start appropriate treatment.

Omvoh® may increase the risk of infection. Do not start Omvoh® treatment in patients with a clinically important active infection until the infection resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits before prescribing Omvoh®. If a serious infection develops or an infection is not responding to standard therapy, monitor the patient closely and do not administer Omvoh® until the infection resolves.

Assess patients for tuberculosis (TB) infection prior to starting treatment with Omvoh®. Do not administer Omvoh® to patients with active TB infection. Start treatment of latent TB prior to administering Omvoh®. Consider anti-TB therapy prior to initiation of Omvoh® in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor for signs and symptoms of active TB during and after Omvoh® treatment. (In clinical trials, subjects were excluded if they had evidence of active TB, a past history of active TB, or were diagnosed with latent TB at screening.)

A case of drug-induced liver injury in conjunction with pruritis was reported in a clinical trial subject following a longer than recommended induction regimen. Omvoh® was discontinued, and liver test abnormalities eventually returned to baseline. Assess liver enzymes and bilirubin at baseline and for at least 24 weeks of treatment. Monitor thereafter per routine patient management. In addition, consider other treatment options in patients with evidence of liver cirrhosis.

Contraindications: In patients with a history of serious hypersensitivity reaction to mirikizumab-mrkz or any of the excipients.

Manufacturer: Eli Lilly and Company.

Analysis: The safety and efficacy of Omvoh® were assessed in 2 randomized, double-blind, placebo-controlled studies, with one being an induction study (UC-1) and one being a maintenance study (UC-2), that included adults with moderately to severely active ulcerative colitis who had inadequate response, loss of response, or failed to tolerate any of the following, including corticosteroids, 6-mercaptopurine, azathioprine, biologic therapy (TNF blocker,

vedolizumab), or tofacitinib. The 12-week IV induction study (UC-1) was followed by the 40-week SC randomized withdrawal maintenance study (UC-2).

The UC-1 study included subjects (N=1062) who were randomized at week 0 to receive 300mg Omvoh® or placebo by IV infusion at week 0, week 4, and week 8. Included subjects had a mean age of 43 years (range 18 to 79 years), while 40% were female and 71% were white. Subjects were allowed to use stable doses of aminosalicylates, immunomodulators (6-mercaptopurine, azathioprine, methotrexate), and oral corticosteroids. At baseline, 41% of subjects were receiving oral corticosteroids, 24% were receiving immunomodulators, and 75% were receiving aminosalicylates. In addition, at baseline, 57% were biologic and Janus kinase (JAK) inhibitor naïve, 41% had failed at least one biologic, 3% had failed a JAK inhibitor, and 2% had previously received but had not failed a biologic or JAK inhibitor.

Disease activity was assessed based on the modified Mayo score (mMS), which ranges from 0 to 9 and has three sub scores that are each scored from 0 (normal) to 3 (most severe), including stool frequency, rectal bleeding, and findings on centrally read endoscopy sub score. At baseline, subjects had a mMS of 5 to 9, including a centrally read endoscopy sub score of 2 or 3. An endoscopy sub score of 2 was defined by marked erythema, absent vascular pattern, friability, and erosions; and a sub score 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. Results are presented in the table below, which was adapted from the prescribing information.

Endpoint	Placebo	Omvoh® 300mg IV	Treatment difference
Clinical Remission			
Total population	N=267 15%	N=795 24%	10%[1] (NNT = 10)
Biologic & JAK inhibitor naïve	N=155 18%	N=450 31%	
Prior biologic or JAK inhibitor failure	N=107 8%	N=331 15%	
Clinical Response			
Total population	N=267 43%	N=795 65%	22%[1] (NNT = 5)
Biologic & JAK inhibitor naïve	N=155 52%	N=450 71%	
Prior biologic or JAK inhibitor failure	N=107 31%	N=331 56%	
Endoscopic Improvement			
Total population	N=267 21%	N=795 34%	14%[1] (NNT = 8)
Biologic & JAK inhibitor naïve	N=155 28%	N=450 44%	
Prior biologic or JAK inhibitor failure	N=107 10%	N=331 22%	
Histologic-Endoscopic Mucosal Improvement			
Total population	N=267 14%	N=795 25%	11%[1] (NNT = 10)
Biologic & JAK inhibitor naïve	N=155 19%	N=450 34%	
Prior biologic or JAK inhibitor failure	N=107 7%	N=331 13%	

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

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

Decreases in rectal bleeding and stool frequency sub scores were observed as early as week 3 in subjects treated with Omvoh® compared to subjects treated with placebo.

The maintenance study (UC-2) included subjects (N=506) who achieved clinical response at week 12 in study UC-1. These subjects were randomized to receive 200mg Omvoh® or placebo subcutaneously every 4 weeks for 40 weeks in UC-2, for a total of 52 weeks of treatment. Subjects who were on concomitant UC therapies during UC-1 were required to continue on stable doses of oral aminosalicylates and immunomodulators. 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. Results are presented in the table below, which was adapted from the prescribing information.

Endpoint	Placebo	Omvoh® 200mg SC	Treatment difference
Clinical Remission			
Total population	N=169 27%	N=337 51%	22% * (NNT = 5)
Biologic & JAK inhibitor naïve	N=109 33%	N=208 53%	
Prior biologic or JAK inhibitor failure	N=59 15%	N=121 45%	
Endoscopic Improvement			
Total population	N=169 30%	N=337 58%	27% * (NNT = 4)
Biologic & JAK inhibitor naïve	N=109 35%	N=208 62%	
Prior biologic or JAK inhibitor failure	N=59 20%	N=121 50%	
Maintenance of clinical remission in patients who achieved clinical remission at week 12			
Total population	N=62 40%	N=128 66%	23% ** (NNT = 5)
Biologic & JAK inhibitor naïve	N=48 48%	N=91 66%	
Prior biologic or JAK inhibitor failure	N=14 14%	N=34 65%	
Corticosteroid-free clinical remission			
Total population	N=169 27%	N=337 50%	22% * (NNT = 5)
Biologic & JAK inhibitor naïve	N=109 33%	N=208 52%	
Prior biologic or JAK inhibitor failure	N=59 15%	N=121 45%	
Histologic-endoscopic mucosal improvement			
Total population	N=169 22%	N=337 43%	19% * (NNT = 6)
Biologic & JAK inhibitor naïve	N=109 27%	N=208 47%	

Endpoint	Placebo	Omvoh® 200mg SC	Treatment difference
Prior biologic or JAK inhibitor failure	N=59 14%	N=121 36%	

*p<0.001 **p<0.01

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 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% vs 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.

Regarding endoscopic assessment, normalization of the endoscopic appearance of the mucosa (endoscopic remission) was defined as a Mayo endoscopic sub score 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% vs 14%).

Place in Therapy: Omvoh®, an IL-23 antagonist, is indicated for the treatment of moderately to severely active ulcerative colitis in adults. Prior to starting treatment, assess for TB infection, obtain liver enzymes and bilirubin levels, and complete all age-appropriate vaccinations. Omvoh® administered by intravenous infusion is utilized for induction dosage, while the recommended maintenance dosage is administered by subcutaneous injection. Patients may self-inject Omvoh® after training in subcutaneous injection technique.

The safety and efficacy of Omvoh® were assessed in 2 randomized, double-blind, placebo-controlled, phase 3 studies, with one being an induction study and one being a maintenance study, that included adults with moderately to severely active ulcerative colitis who had inadequate response, loss of response, or failed to tolerate any of the following, including corticosteroids, 6-mercaptopurine, azathioprine, biologic therapy, or tofacitinib. The 12-week IV induction study was followed by the 40-week SC randomized withdrawal maintenance study. The primary endpoint of study 1 was clinical remission at week 12, and significantly more in the Omvoh® 300mg IV group achieved clinical remission compared with placebo (p<0.001). The primary endpoint in study 2 was clinical remission at week 40, and significantly more in the Omvoh® 200mg SC group achieved clinical remission as compared with placebo (p<0.001). Head-to-head comparator studies with other active ingredients were not currently found.

There is no evidence at this time to support that Omvoh® is safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Omvoh® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred with Conditions**

References

[1] Omvoh® [package insert]. Indianapolis, IN: Eli Lilly and Company; 2023.