INPHARMD™ **MONOGRAPHS**

Omvoh™

(Mirikizumab-mrkz)

The latest evidence on drug efficacy & recommendations.

InpharmD™

UPDATED AUGUST 2024

OVERVIEW

REGIMEN

Generic Name	Mirikizumab-mrkz
Trade Name	Omvoh™
Manufacturer	Eli Lilly and Company
FDA Approval	2023
Therapeutic Class	56:44 Immunomodulatory Agents

Dosage

Induction Dosage: 300 mg administered by IV infusion over at least 30 minutes at Weeks 0, 4, and 8

Maintenance Dosage: 200 mg administered by subcutaneous injection (given as two consecutive injections of 100 mg each) at Week 12, and every 4 weeks thereafter

Indications

Treatment of moderately to severely active ulcerative colitis in adults

PHARMACOLOGY

Mirikizumab is a humanized IgG4 monoclonal antibody that selectively binds to the p19 subunit of human interleukin-23 (IL-23) cytokine and inhibits its interaction with the IL-23 receptor. 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. Research in animal models has shown that pharmacologic inhibition of IL-23p19 can ameliorate intestinal inflammation. Mirikizumab inhibits the release of pro-inflammatory cytokines and chemokines.

PHARMACODYNAMICS

In studies of induction and maintenance, a positive relationship was observed between mirikizumab average concentration and rates of clinical remission and clinical response.

PHARMACOKINETICS

Absorption

Cmax, ss:

300 mg IV infusion: 99.7 µg/mL

200 mg SUBQ injection: 10.1 µg/mL

Tmax: median of 5 days (3.08 to 6.75 days) following SUBQ injection

Distribution

Volume of distribution: 4.83 L

Metabolism

Expected to be degraded into small peptides and amino acids via catabolic pathways

Half-Life

9.3 days

CLINICAL DATA OVERVIEW

N= 249 • Sandborn et al., 2020 • Phase 2, multi-center, randomized, placebo-control trial (I6T-MC-AMAC)

POPULATION

Objective: To investigate the effects of mirikizumab, a monoclonal antibody against the p19 subunit of interleukin 23, in a phase 2 study of patients with ulcerative colitis

N= 249

- Placebo (n= 63)
- Mirikizumab 50 mg (n= 63)
- Mirikizumab 200 mg (n= 62)
- Mirikizumab 600 mg (n= 61)

METHODS

Inclusion Criteria: Included adult patients age 18-75 with ulcerative colitis and moderately to severely active disease

Patients were randomized 1:1:1:1 to IV placebo, mirikizumab 50 mg or 200 mg with exposure-based (EB) dosing, or mirikizumab 600 mg with fixed dosing at weeks 0, 4, and 8. Clinical responders at week 12 who had received mirikizumab were randomly assigned to groups that received maintenance treatment with mirikizumab 200 mg subcutaneously every 4 weeks or every 12 weeks.

RESULTS

Primary outcome: Clinical remission (Mayo subscores of 0 for rectal bleeding, with 1-point decrease from baseline for stool frequency, and 0 or 1 for endoscopy) at week 1 (mirikizumab 50 mg vs. 200 mg vs. 600 mg vs. placebo):
-Week 12: 15.9% vs. 22.6% vs. 11.5% vs. 4.8% (p= 0.066; p= 0.004; p= 0.142, respectively vs. placebo)
-At week 52 (mirikizumab 200 mg Q4W vs. 200 mg Q12W vs. placebo Q4W): 46.8% vs. 37.0% vs. 7.7%

Secondary outcomes:
Clinical response:
-Week 12: 41.3% vs. 59.7% vs. 49.2% vs. 20.6% (p= 0.014; p< 0.001; p= 0.001, respectively vs. placebo)
-Week 52: 80.9% vs. 76.1% vs. 53.8%

Safety outcomes:
Treatment-emergent adverse event (TEAEs ≥5%) at week 52 (mirikizumab 200 mg Q4W vs. 200 mg Q12W vs. placebo):
-Worsening of UC (2.1% vs. 15.2% vs. 46.2%); nasopharyngitis (10.6% vs. 15.2% vs. 0); headache (10.6% vs. 6.5% vs. 7.7%); upper respiratory tract infection (10.6% vs. 4.3% vs. 15.4%)

CONCLUSIONS

Authors' Conclusions: Mirikizumab was effective in inducing a clinical response after 12 weeks. Additional studies are required to determine the optimal dose for induction of remission. Mirikizumab showed durable efficacy throughout the maintenance period.

Comment/Critique: Given the imbalance of patients' baseline characteristics across the dose groups, and the relatively small sample size, efficacy results of this phase 2, dose-ranging study should be confirmed by a phase 3 quality study.

Study sponsor: Eli Lilly and Company

N = 128 • Sandborn et al., 2022 • Open-label continuation of the I6T-MC-AMAC trial)

POPULATION

Objective: To present results of the open-label extended induction period in patients who did not initially respond to treatment with mirikizumab.

-Mirikizumab IV 600 mg (n= 32)

-Mirikizumab IV 1000 mg (after protocol amendment)(n= 96)

METHODS

The I6T-MC-AMAC trial Included adult patients age 18-75 with ulcerative colitis and moderately to severely active disease

Among the induction non-responders.

Patients without a clinical response at week 12 participated in an open-label, extended induction study for another 12 weeks, in which given either 600 mg IV mirikizumab (n= 20) or, following a protocol amendment, 1000 mg IV mirikizumab (n= 64) every 4 weeks. At week 24, patients with a clinical response continued the extension maintenance period and

RESULTS

No outcome specified as primary

Efficacy Outcomes:
Clinical response after 12-week extension (600 mg vs. 1000 mg mirikizumab): 50% vs. 43.8%

Clinical remission after 12-week extension: 15.0% vs. 9.4%

Endoscopic improvement at 24 weeks: 20% vs. 15.6%

Among initial non-responders who had clinical response at study week 24 and continued into maintenance therapy, 65.8% maintained the clinical response, 26.3% achieved clinical remission, and 34.2% had endoscopic improvement at week 52.

Safety outcomes:
No new safety concerns were identified.

CONCLUSIONS

Authors' Conclusions: Extended doses of mirikizumab (600 mg and 1000 mg) for an additional 12 weeks produce a clinical response in up to 50% of patients who did not have a clinical response to 12 weeks of induction doses (50 mg, 200 mg, or 600 mg). Most of the responders to the extended doses maintained clinical response for up to 52 weeks

Comment/Critique: No active comparator or placebo arm was used in the trial, thus conclusions regarding comparative literature are limited.

Study sponsor: Eli Lilly and Company

N = 2 RCTs • Dubinsky et al., 2022 • Post-hoc analysis of Post-hoc analysis of LUCENT-1 and LUCENT-2 trials

POPULATION

Objective: To use the Urgency Numeric Rating Scale to examine mirikizumab's efficacy for the treatment of bowel urgency in patients with ulcerative colitis

Induction (LUCENT-1): N= 1,281
Placebo (n= 294)
Mirikizumab (n= 868)

Maintenance (LUCENT-2): N= 544
Placebo (n= 179)
Mirikizumab (n= 365)

METHODS

The LUCENT-1 induction and LUCENT-2 maintenance trials included adult patients age 18-80 with moderately to severely active ulcerative colitis

In the LUCENT-1 and LUCENT-2 trials, patients were randomized 3:1 to mirikizumab 300 mg IV or placebo every 4 weeks for 12 weeks for the induction phase. Those that had a clinical response were randomized (2:1) to mirikizumab 200 mg SUBQ or placebo every 4 weeks for 40 weeks for the maintenance phase. Post-hoc analysis was done to examine bowel urgency and remission.

RESULTS

No outcome designated as primary

Reduction in Urgency Numeric Rating Scale at 24 weeks (mirikizumab vs. placebo): least square mean (LSM) −3.81 ± 0.13 vs. −3.39 ± 0.18 (p= 0.034)

Bowel urgency clinically meaningful improvement at week 52: 65.2% vs. 41.9% (p< 0.001)

Associations between bowel urgency and clinical outcomes at week 52: bowel urgency clinically meaningful improvement significantly associated with higher rates of achieving clinical remission (p< 0.0001)

CONCLUSIONS

Authors' Conclusions: In patients with ulcerative colitis, bowel urgency improvement was associated with better clinical outcomes than in patients without improvement during induction and maintenance. A greater proportion of mirikizumab patients achieved sustainable bowel urgency improvement and remission compared to placebo patients.

Comment/Critique: Bowel urgency was reported merely as subjective patient-reported evaluation, potentially introducing biases. Further objective assessments are warranted to evaluate bowel urgency as an independent factor for the assessment of ulcerative colitis therapy response.

Study sponsor: Eli Lilly and Company

N = 191 • Sands et al., 2022 • Phase 2, randomized, double-blind, placebo-controlled trial

POPULATION

Objective: To investigate the safety and efficacy of mirikizumab in patients with moderate-to-severe Crohn's disease

N= 191
Placebo (n= 64)
Mirikizumab 200 mg (n= 31)
Mirikizumab 600 mg (n= 32)
Mirikizumab 1,000 mg (n= 64)

METHODS

Included patients with active Crohn's Disease and inadequate response or failure to tolerate at least one of the following: aminosalicylates; budesonide; systemic corticosteroids; immunosuppressants (e.g., azathioprine, 6-mercaptopurine, or methotrexate); or prior exposure to biologics for the treatment of Crohn's Disease

Patients were randomized 2:1:1:2 to receive placebo, mirikizumab 200 mg, mirikizumab 600 mg, or mirikizumab 1,000 mg given IV Q4W through week 12. After week 12, all who received mirikizumab during induction and achieved improvement in Simple Endoscopic Score (SES)-CD score from baseline were randomized (1:1) to continue their induction IV treatment or receive 300 mg mirikizumab SUBQ every 4 weeks through week 52.

RESULTS

Primary outcome: endoscopic response (50% reduction from baseline in Simple Endoscopic Score-CD) at Week 12

Placebo vs. 200 mg vs. 600 mg vs. 1,000 mg): 10.9% vs. 25.8% vs. 37.5% vs. 43.8% (p-values vs. placebo: p= 0.79, p= 0.003, p< 0.001, respectively).

Secondary outcomes:
Endoscopic remission at week 12: 1.6% vs. 6.5% vs. 15.6% vs. 20.3% (p-values vs. placebo: p= not significant, p= 0.032, p= 0.009, respectively)

Endoscopic response at week 52 (IV-continued cohort vs. IV/SUBQ cohort): 58.5% vs. 58.7%

Endoscopic remission at week 52: 19.5% vs. 32.6%

Safety outcomes:
Through Week 52, frequencies of treatment-emergent adverse events were similar across all groups.

CONCLUSIONS

Authors' Conclusions: Mirikizumab effectively induced endoscopic response after 12 weeks in patients with moderate-to-severe Crohn's disease and demonstrated durable efficacy to Week 52.

Comment/Critique: A relatively small sample size for individual dosing groups. A lack of a placebo group in the maintenance phase limits conclusions regarding its safety and efficacy.

Study sponsor: Eli Lilly and Company

N = 249 • Dubinsky et al., 2023 • Post-hoc analysis of Phase 2, I6T-MC-AMAC trial

POPULATION

Objective: To evaluate mirikizumab's impact on health-related quality of life (HRQoL) compared with placebo in the induction and maintenance periods of the study (baseline to week 12 and weeks 12–52, respectively)

N= 249

Placebo (n= 63)

Mirikizumab 50 mg EB dosing (n= 63)

Mirikizumab 200 mg EB dosing (n= 62)

Mirikizumab 600 mg fixed dose (n= 61)

METHODS

Included adult patients age 18-75 with ulcerative colitis and moderately to severely active disease

Patients were randomized 1:1:1:1 to IV placebo, mirikizumab 50 mg or 200 mg with exposure-based (EB) dosing, or mirikizumab 600 mg with fixed dosing at weeks 0, 4, and 8. Clinical responders at week 12 who had received mirikizumab were randomly assigned to groups that received maintenance treatment with mirikizumab 200 mg subcutaneously every 4 weeks or every 12 weeks.

RESULTS

Primary outcome: HRQoL during induction and maintenance using the disease-specific Inflammatory Bowel Disease Questionnaire (IBDQ) and the Medical Outcomes Study 36-Item Short Form Health Survey Version 2 Standard (SF-36) including the Physical Component Score (PCS) and Mental Component Score (MCS)

Induction (baseline to week 12):
- IBDQ total score: Significantly improved for mirikizumab 200 mg and 600 mg vs. placebo (50 mg, p= 0.073; 200 mg, p< 0.001; 600 mg, p< 0.001)
- SF-36 PCS: Significantly higher in all mirikizumab groups vs. placebo (50 mg, p= 0.011; 200 mg, p= 0.022; 600 mg, p= 0.002)
- SF-MCS: Significantly higher with mirikizumab 200 and 600 mg vs. placebo (50 mg, p= 0.429; 200 mg, p= 0.028; 600 mg, p< 0.001

Secondary outcomes: association between changes in HRQoL and clinical efficacy endpoints
- Significant improvements found in HRQoL measures for patients achieving clinical endpoints vs. patients who did not by week 52, except for SF-36
- SF-36 PCS and IBDQ emotional, social, and systemic domain scores not meaningfully different between groups

CONCLUSIONS

Authors' Conclusions: Treatment with mirikizumab improved disease-specific and general health HRQoL in patients with moderately-to-severely active UC. These improvements were present after 12 weeks of induction mirikizumab treatment and were sustained among mirikizumab responders during an additional 40 weeks of maintenance therapy (SUBQ mirikizumab 200mg Q4W or Q12W).

Comment/Critique: A relatively small patient population potentially limits the generalizability of the results. Data for SF-36 survey were compared with US population norms, which may not be extrapolated to other geographic regions.

Study sponsor: Eli Lilly and Company

N = 1,281 • D'Haens et al., 2023 • Phase 3, randomized, double-blind, placebo-controlled trial

POPULATION

Objective: To report the efficacy and safety results of the phase 3 LUCENT-1 induction and LUCENT-2 maintenance trials of mirikizumab in patients with moderately to severely active ulcerative colitis

N= 1,281 (1,162 ITT)

Induction trial: mirikizumab (n= 868) vs. placebo (n= 294)

Maintenance trial: mirikizumab (n= 365) vs. placebo (n= 179)

METHODS

The LUCENT-1 induction and LUCENT-2 maintenance trials included adult patients age 18-80 with moderately to severely active ulcerative colitis

Patients during induction were randomized (3:1) to receive either mirikizumab 300mg or placebo IV every 4 weeks (at weeks 0, 4, and 8) for 12 weeks. At week 12, if patients reached clinical response, they were blindly randomized (2:1) to receive mirikizumab 200mg or placebo (mirikizumab withdrawal) SUBQ every 4 weeks for 40 weeks of maintenance therapy; the remainder patients without a response discontinued maintenance therapy and received rescue therapy with 3 doses of open-label mirikizumab 300mg IV every 4 weeks.

RESULTS

INDUCTION TRIAL

Primary outcome:
12 week clinical remission (mirikizumab 300mg Q4W 24.2% vs placebo 13.3%, p< 0.001)

Secondary outcomes:
12 week clinical response (63.5% vs 42.2%, p< 0.001), endoscopic remission (36.3% vs 21.1%, p< 0.001) and histologic-endoscopic mucosal improvement (27.1% vs 13.9%, p< 0.001)

MAINTENANCE TRIAL

Primary outcome:
40 week clinical remission (mirikizumab 200mg Q4W 49.9% vs placebo 25.1%, p< 0.001)

Secondary outcomes:
40 week glucocorticoid-free clinical remission (44.9% vs 21.8%, p< 0.001), maintenance of clinical remission (63.6% vs 36.9%, p< 0.001), endoscopic remission (58.6% vs 29.1%, p< 0.001), histologic-endoscopic mucosal improvement (43.3% vs 21.8%, p< 0.001), and bower-urgency remission (42.9% vs 25%, p< 0.001)

Safety outcomes:
Adverse events at week 52 (induction placebo vs induction mirikizumab 300 mg Q4W vs maintenance placebo vs maintenance 200 mg Q4W):
-Any adverse event (46.1% vs 44.5% vs 68.8% vs 64.5%)
-Common events: nasopharyngitis (3.1% vs 4.1% vs 5.7% vs 7.2%), arthralgia (1.2% vs 2.1% vs 4.2% vs 6.7%), UC (7.5% vs 1.8% vs 20.8% vs 6.7%)
-Adverse events of interest: serious infections (0.6% vs 0.7% vs 1.6% vs 0.8%), opportunistic infections (0.3% vs

CONCLUSIONS

Authors' Conclusions:
Mirikizumab was more effective than placebo in inducing and maintaining clinical remission in patients with moderately to severely active ulcerative colitis. Opportunistic infection or cancer occurred in a small number of patients treated with mirikizumab.

Comment/Critique: Lack of comparator, short duration of follow-up (52wks)

Study sponsor: Eli Lilly

0.5% vs 0 vs 1.3%), cancer (0 vs 0.2% vs 0.5%. vs 0.3%), depression (0.6% vs 0.4% vs 0 vs 1%), suicide/self-injury (0 vs 0 vs 0 vs 0.3%), hepatic-related event (1.6% vs 1.6% vs 2.1% vs 3.1%), infusion- or injection-site reaction (0.3% vs 0.4% vs 4.2% vs 8.7%)

N = 1,825 • Magro et al., 2023 • Post-hoc analysis of LUCENT-1 and LUCENT-2 trials

POPULATION

Objective: To evaluate the effect of mirikizumab, a p19-targeted anti-interleukin-23, on histological and/or endoscopic outcomes in moderately-to-severely active ulcerative colitis

Induction (LUCENT-1): N= 1,281

-Placebo (n= 294)

-Mirikizumab (n= 868)

Maintenance (LUCENT-2): N= 544

-Placebo (n= 179)

-Mirikizumab (n= 365)

METHODS

The LUCENT-1 and LUCENT-2 trials included adult patients age 18-80 with moderately to severely active ulcerative colitis

In the Lucent-1 and LUCENT 2 trials, patients were randomized 3:1 to mirikizumab 300 mg IV or placebo every 4 weeks for 12 weeks for the induction phase. Those that had a clinical response were randomized (2:1) to mirikizumab 200 mg SUBQ or placebo every 4 weeks for 40 weeks for the maintenance phase. Data from this trial was analyzed post-hoc to assess histological and endoscopic outcomes.

RESULTS

No outcome specified as primary aside from the outcomes listed in the LUCENT-1 and LUCENT-2 trials (see summary)

Significantly more patients treated with mirikizumab achieved histological improvement, histological remission, ER, histological-endoscopic mucosal improvement, and histological-endoscopic mucosal remission vs placebo [p <0.001], irrespective of prior biologic/tofacitinib failure [p <0.05].

Lower clinical baseline disease activity, female sex, no baseline immunomodulator use, and no prior biologic/tofacitinib failure were predictors of histological-endoscopic mucosal improvement at week 12 [p < 0.05].

Corticosteroid use and longer disease duration were negative predictors of achieving histological-endoscopic mucosal remission at week 40 [p <0.05].

Week 12 histological improvement, histological remission, or Endoscopic remission was associated with week 40 histological-endoscopic mucosal improvement or histological-endoscopic mucosal remission [p <0.05]

Endoscopic remission at week 12 was associated with clinical remission [p <0.05] and corticosteroid-free remission at week 40 [p = 0.052].

Histological remission and histological-endoscopic mucosal remission at week 12 were associated with corticosteroid-free remission, clinical remission, and symptomatic remission at week 40.

CONCLUSIONS

Authors' Conclusions: Early resolution of endoscopic and histological inflammation with mirikizumab is associated with better ulcerative colitis outcomes.

Comment/Critique: Despite the large patient population included in LUCENT-1 and LUCENT-2 trials, the results are limited to 52 weeks period which may not be sufficient to show histological remission.

Study sponsor: Eli Lilly and Company

N = 1,465 • Papp et al., 2023 • Phase 3, multicenter, randomized, double-blind study

POPULATION

Objective: To investigate the efficacy and safety of the IL-23 p19 inhibitor mirikizumab versus placebo and secukinumab for patients with moderate-to-severe plaque psoriasis

N= 1465

Mirikizumab 250 mg for induction and maintenance (n= 454)

Mirikizumab 250 mg for induction and 125 mg for maintenance (n=451)

Secukinumab 300 mg (n=448)

Placebo followed by mirikizumab (n=112)

METHODS

Included patients aged at least 18 years who had a confirmed diagnosis of chronic plaque psoriasis for at least 6 months before baseline that involved at least 10% of body surface area, an absolute Psoriasis Area and Severity Index score of at least 12, and a Static Physician's Global Assessment score of at least 3 at both the screening and baseline visits

Participants were randomly assigned to receive mirikizumab 250 mg for induction and maintenance (n=454 [31·0%]), mirikizumab 250 mg for induction and 125 mg for maintenance (n=451 [30·8%]), secukinumab 300 mg (n=448 [30·6%]), or placebo followed by mirikizumab (n=112 [7·6%]).t

RESULTS

Primary outcome: proportion of patients with an Static Physician's Global Assessment score of 0 or 1 with an improvement from baseline of at least 2 points, and the proportion of patients with at least 90% improvement from baseline in PASI score (PASI 90)

At week 16, 721 (79.7% [95% CI 77.0-82.3]) of 905 participants in the mirikizumab 250 mg induction groups had an sPGA score of 0 or 1 versus seven (6.3% [1.8-10.7]) of 112 participants in the placebo group (p< 0.0001 for superiority).

At week 16, 673 (74.4% [71.5-77.2]) of 905 participants in the mirikizumab groups had PASI 90 compared with seven (6.3% [1.8-10.7]) in the placebo group (p< 0.0001 for superiority).

Safety outcomes: Treatment-emergent adverse events were reported with similar frequency across treatment groups during weeks 0-52.

Four major adverse cardiovascular events were reported in the mirikizumab groups versus none in the placebo and secukinumab groups up to week 16, with one fatal acute myocardial infarction in a patient treated with mirikizumab, which the investigator considered to be related to the study drug.

CONCLUSIONS

Authors' Conclusions: This trial showed superiority of mirikizumab at a dose of 250 mg over placebo in patients with moderate-to-severe plaque psoriasis, with a safety profile consistent with that of the IL-23 class. The study sponsor is not pursuing licensing of mirikizumab in this patient population because of a reprioritized development strategy with a focus on gastrointestinal-related indications.

Comment/Critique: More than 80% of the included population were described as White, which may limit generalizability. Study was funded by the manufacturer.

Study sponsor: Eli Lilly and Company

ADVERSE EFFECTS

Infectious Disease	Upper respiratory tract infections (induction: 8%; maintenance: 14%), herpes viral infection (maintenance: 2%)
Musculoskeletal	Arthralgia (induction: 2%, maintenance 7%)
Dermatologic	Rash (maintenance: 4%)
Miscellaneous	Injection site reactions (induction: 9%; maintenance: 9%)

CONTRA-INDICATIONS

History of serious hypersensitivity reaction to mirikizumab or any of the excipients

DRUG INTERACTIONS

Not expected to have clinically significant interactions based on cytochrome P450 enzymes

STORAGE

How Supplied:

Single-dose Vial for IV infusion (300 mg/15 mL, carton of 1): NDC 002-7575-01

Single-dose Prefilled Pen for Subcutaneous use (100 mg/mL, carton of 2): NDC 002-8011-27

Single-dose prefilled Syringe for Subcutaneous use (100 mg/mL, carton of 2): NDC 002-8870-27

Each single-dose prefilled pen or prefilled syringe consists of a 1 mL glass syringe with a fixed 27-gauge ½ inch needle.

Storage and Stability:

- Store refrigerated at 2°C to 8°C (36°F to 46°F).
- Do not freeze. Do not use mirikizumab if it has been frozen.
- Do not shake.
- Keep mirikizumab in the original carton to protect from light until the time of use.
- Mirikizumab is sterile and preservative-free. Discard any unused portion.
- If needed, the prefilled pen or prefilled syringe may be stored at room temperature up to 30°C (86°F) for up to 2 weeks in the original carton to protect from light. Once mirikizumab has been stored at room temperature, do not return to the refrigerator. If these conditions are exceeded, mirikizumab must be discarded.
- The vial, prefilled pen, and prefilled syringe are not made with dry natural rubber latex.

SAFETY CONSIDERATIONS

BOXED WARNINGS

None

WARNINGS & PRECAUTIONS

- **Hypersensitivity reactions:** Serious hypersensitivity reactions, including anaphylaxis and infusion-related reactions, have been reported. If a severe hypersensitivity reaction occurs, discontinue and initiate appropriate treatment.

- **Infections**: Mirikizumab may increase the risk of infection. Do not initiate treatment with mirikizumab in patients with a clinically important active infection until the infection resolves or is adequately treated. If a serious infection develops, do not administer mirikizumab until the infection resolves.

- **Tuberculosis (TB):** Do not administer mirikizumab to patients with active TB infection. Monitor patients receiving mirikizumab for signs and symptoms of active TB during and after treatment.

- **Hepatotoxicity:** Drug-induced liver injury has been reported. Monitor liver enzymes and bilirubin levels at baseline and for at least 24 weeks of treatment and thereafter according to routine patient management. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded.

- **Immunizations**: Avoid use of live vaccines.

USE IN SPECIFIC POPULATIONS

Renal impairment	There were no clinically significant differences in the pharmacokinetics of mirikizumab based on mild and moderate renal impairment (i.e., estimated creatinine clearance by Cockcroft-Gault equation: 30 to 89 mL/min)
Hepatic impairment	Consider other treatment options in patients with evidence of liver cirrhosis.
Geriatrics	Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger adult subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger subjects. No clinically meaningful differences in the pharmacokinetics of mirikizumab were observed in subjects 65 years of age and older compared to younger adult subjects
Pediatrics	Safety and effectiveness not established in pediatric patients
Reproductive potential	No human studies; animal studies did not identify any organ weight or histopathology effects in the male or female reproductive tract
Pregnancy	Available data from case reports of mirikizumab use in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes Monoclonal antibodies can be actively transported across the placenta, and mirikizumab may cause immunosuppression in the in utero-exposed infant Animal studies at a dose 69 times the maximum recommended human dose revealed no adverse developmental effects to the developing fetus, or harm to infant animal from birth through 6 months of age Pregnancy Exposure Registry: Pregnant women exposed to mirikizumab and healthcare providers are encouraged to call Eli Lilly and Company at 1-800-Lilly-Rx (1-800-545-5979)..

Lactation	No data on the presence of mirikizumab in human milk, the effects on the breastfed infant, or the effects on milk production Endogenous maternal IgG and monoclonal antibodies are transferred in human milk The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed infant to mirikizumab are unknown Consider risk/benefit.

DOSAGE & ADMINISTRATION

Induction Dosage: 300 mg administered by IV infusion over at least 30 minutes at Week 0, Week 4, and Week 8

Maintenance Dosage: 200 mg administered by SUBQ injection (given as two consecutive injections of 100 mg each) at Week 12, and every 4 weeks thereafter

Preparation and Administration for Intravenous Infusion

1. Mirikizumab for IV use is intended for administration by a healthcare provider using aseptic technique. Each vial is for single use only.
2. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The solution should be a clear to opalescent, colorless to slightly yellow to slightly brown solution, and free of visible particles. Do not use mirikizumab if it is cloudy or there are visible particles.
3. Using an 18 to 21 gauge needle withdraw 15 mL of mirikizumab solution from the vial and transfer to an infusion bag ranging in size from 50 mL to 250 mL of 0.9% Sodium Chloride Injection or 5% Dextrose Injection. Do not mix with other drugs. Do not dilute or infuse through the same intravenous line with solutions other than 0.9% Sodium Chloride or 5% Dextrose Injection.
4. Gently invert the infusion bag to mix the contents. Do not shake the prepared infusion bag.
5. Connect the intravenous administration set (infusion line) to the prepared infusion bag and prime the line.
6. Administer the infusion over at least 30 minutes.
7. At the end of the infusion, flush the line with 0.9% Sodium Chloride Injection or 5% Dextrose Injection.
    - Administer the flush at the same infusion rate as used for mirikizumab administration.
    - The time required to flush mirikizumab solution from the infusion line is in addition to the minimum 30-minute infusion time.

Preparation and Administration for Subcutaneous Injection

- A full maintenance dose will require 2 prefilled pens or 2 prefilled syringes.
- Mirikizumab is intended for use under the guidance and supervision of a healthcare professional. Patients may self-inject mirikizumab after training in subcutaneous injection technique. Provide proper training to patients and/or caregivers on the subcutaneous injection technique of mirikizumab according to the “Instructions for Use”, included with the packaged product.

- Before injection, remove mirikizumab prefilled pen or mirikizumab prefilled syringe from the refrigerator and leave at room temperature for 30 minutes. Do not shake the prefilled pens or syringes.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The solution should be a clear to opalescent, colorless to slightly yellow to slightly brown solution, and free of visible particles. Do not use mirikizumab if it is cloudy, discolored, or there are visible particles.
- Sites for injection include the abdomen, thigh, and back of the upper arm. Instruct patients to inject in a different location every time. For example, if the first injection was in the abdomen, administer the second injection (to complete a full dose) in another area of the abdomen, or upper arm, or thigh. Administration of mirikizumab in the back of upper arm may only be performed by another person.
- Do not inject into areas where the skin is tender, bruised, erythematous, or indurated.
- Mirikizumab does not contain preservatives; therefore, discard any unused product. Do not reuse.
- If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing every 4 weeks.

REFERENCES

1. Omvoh (mirikizumab-mrkz injection). Package insert. Eli Lilly and Company; 2024.
2. Lynch WD, Hsu R. Ulcerative Colitis. [Updated 2023 Jun 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459282/
3. IBD Medications List: Ulcerative Colitis: Biologics/Biosimilars + Targeted Synthetic Small Molecules. Crohn's & Colitis Foundation. Updated 2024. Accessed June 20, 2024. https://www.crohnscolitisfoundation.org/patientsandcaregivers/ibd-medication?field_disease_target_id[4566]=4566&field_drug_class_target_id[4571]=4571&field_drug_class_target_id[4836]=4836
4. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020;158(5):1450-1461. doi:10.1053/j.gastro.2020.01.006
5. Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021;160(7):2496-2508. doi:10.1053/j.gastro.2021.04.022
6. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019;114(3):384-413. doi:10.14309/ajg.0000000000000152
7. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults [published correction appears in Am J Gastroenterol. 2018 Jul;113(7):1101]. Am J Gastroenterol. 2018;113(4):481-517. doi:10.1038/ajg.2018.27
8. RED BOOK Online. IBM Micromedex [database online]. Truven Health Analytics/IBM Watson Health; 2024. Accessed June 2024. https://www.micromedexsolutions.com

Clinical Guidance

9. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020;158(5):1450-1461. doi:10.1053/j.gastro.2020.01.006
10. Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021;160(7):2496-2508. doi:10.1053/j.gastro.2021.04.022
11. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019;114(3):384-413. doi:10.14309/ajg.0000000000000152

12. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults [published correction appears in Am J Gastroenterol. 2018 Jul;113(7):1101]. Am J Gastroenterol. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Clinical Efficacy

13. Sandborn WJ, Ferrante M, Bhandari BR, et al. Efficacy and safety of mirikizumab in a randomized phase 2 study of patients with ulcerative colitis. Gastroenterology. 2020;158(3):537-549.e10. doi:10.1053/j.gastro.2019.08.043

14. Sandborn WJ, Ferrante M, Bhandari BR, et al. Efficacy and safety of continued treatment with mirikizumab in a phase 2 trial of patients with ulcerative colitis. *Clin Gastroenterol Hepatol.* 2022;20(1):105-115.e14. doi:10.1016/j.cgh.2020.09.028

15. Dubinsky MC, Clemow DB, Hunter Gibble T, et al. Clinical effect of mirikizumab treatment on bowel urgency in patients with moderately to severely active ulcerative colitis and the clinical relevance of bowel urgency improvement for disease remission. *Crohns Colitis 360.* 2022;5(1):otac044. doi:10.1093/crocol/otac044

16. Sands BE, Peyrin-Biroulet L, Kierkus J, et al. Efficacy and safety of mirikizumab in a randomized phase 2 study of patients with crohn's disease. *Gastroenterology.* 2022;162(2):495-508. doi:10.1053/j.gastro.2021.10.050

17. Dubinsky MC, Jairath V, Feagan BG, et al. Changes in health-related quality of life and associations with improvements in clinical efficacy: a Phase 2 study of mirikizumab in patients with ulcerative colitis. *BMJ Open Gastroenterol.* 2023;10(1):e001115. doi:10.1136/bmjgast-2023-001115

18. D'Haens G, Dubinsky M, Kobayashi T, et al. Mirikizumab as induction and maintenance therapy for ulcerative colitis [published correction appears in N Engl J Med. 2023 Aug 24;389(8):772]. *N Engl J Med.* 2023;388(26):2444-2455. doi:10.1056/NEJMoa2207940

19. Magro F, Pai RK, Kobayashi T, et al. Resolving histological inflammation in ulcerative colitis with mirikizumab in the LUCENT induction and maintenance Trial Programmes. *J Crohns Colitis.* 2023;17(9):1457-1470. doi:10.1093/ecco-jcc/jjad050

20. Papp K, Warren RB, Green L, et al. Safety and efficacy of mirikizumab versus secukinumab and placebo in the treatment of moderate-to-severe plaque psoriasis (OASIS-2): a phase 3, multicentre, randomised, double-blind study. *Lancet Rheumatol*. 2023;5(9):e542-e552. doi:10.1016/S2665-9913(23)00120-0