Iowa PDL New Drug Review

Proprietary Name: Gomekli®
Common Name: mirdametinib
PDL Category: Antineoplastic Agents

Pharmacology/Usage: Mirdametinib, the active ingredient of Gomekli®, is a kinase inhibitor. It is an inhibitor of mitogen-activated protein kinase kinases 1 and 2 (MEK1/2). MEK 1/2 proteins are upstream regulators of the extracellular signal-related kinase (ERK) pathway. In vitro, mirdametinib inhibited kinase activity of MEK1 and MEK2 and downstream phosphorylation of ERK.

Indication: For the treatment of adult and pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic plexiform neurofibromas (PN) not amenable to complete resection.

There is no pregnancy category for this medication; however, based on findings from clinical trials, animal studies, and its mechanism of action, Gomekli® can cause fetal harm or loss of pregnancy when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Verify the pregnancy status of females of reproductive potential prior to starting treatment. Advise females of reproductive potential to use effective contraception during treatment with Gomekli® and for 6 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Gomekli® and for 3 months after the last dose. The safety and efficacy of use have not been established in the pediatric population younger than 2 years of age.

Dosage Form: Available as:

- Capsules: 1mg and 2mg.
  - Swallow whole; do not open, break, or chew capsules. Thus do not administer to patients unable to swallow a capsule whole.
  - If more than one capsule is required for a dose, swallow one capsule at a time.
- Tablets for Oral Suspension: 1mg.
  - Can be swallowed whole or can be dispersed in drinking water and administered orally as a liquid.
  - If more than one tablet is required for a dose, swallow one tablet at a time.
  - If unable to swallow whole tablets, prepare for oral suspension by adding prescribed number of tablets to a dosing cup containing about 5ml to 10ml of drinking water. Gently swirl until the tablets are fully dispersed. It takes about 2-4 minutes to fully disperse the tablets. Administer the oral suspension immediately after preparation from a dosing cup or oral syringe. After administration of prepared suspension, add about 5-10ml of water to the dosing cup and gently swirl. Administer the suspension to ensure the full dose is taken. Discard the oral suspension if not administered within 30 minutes after preparation.

Recommended Dosage: Prior to administration:

- Conduct comprehensive ophthalmic assessment.
- Assess ejection fraction (EF) by echocardiogram.

The recommended dosage is 2mg/m^2 PO BID (about every 12 hours) with or without food for the first 21 days of each 28-day cycle. The maximum dose is 4mg BID. Continue treatment until disease progression or unacceptable toxicity. Note that the recommended dose is based on body surface area (BSA). The recommended dosage for patients with a BSA less than 0.40m^2 has not been established. Refer to the prescribing information for additional information.

If the patient misses a dose, do not take an additional dose. Take the next scheduled dose at the prescribed time. If vomiting occurs after administration, do not take an additional dose. Take the next scheduled dose at the prescribed time.

Refer to the prescribing information for information regarding dosage modifications for adverse reactions, such as ocular toxicity, left ventricular dysfunction, dermatologic adverse reactions, or other adverse reactions.

Dosage adjustments are not required with mild or moderate renal impairment; however, Gomekli® has not been studied in patients with severe renal impairment. Dosage adjustments are not required in patients with mild hepatic impairment; however, the pharmacokinetics of mirdametinib in patients with moderate or severe hepatic impairment have not been assessed.

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

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 (Gomekli®) in adult and pediatric patients of all grades. There was no placebo data to compare with in the prescribing information.* The most frequently reported adverse events included rash (82%), diarrhea (57%), nausea (40%), vomiting (39%), abdominal pain (32%), stomatitis (12%), musculoskeletal pain (41%), fatigue (21%), pyrexia (13%), COVID-19 (24%), paronychia (17%), upper respiratory tract infection (11%), headache (24%), peripheral neuropathy (12%), left ventricular dysfunction (21%), and cough (15%).

Select laboratory abnormalities included increased creatine phosphokinase (57%), increased triglycerides (37%), decreased glucose (21%), decreased calcium (21%), increased creatinine (21%), increased cholesterol (20%), increased alkaline phosphatase (21%), decreased bicarbonate (16%), increased alanine aminotransferase (15%), increased aspartate aminotransferase (13%), decreased hemoglobin (25%), decreased leukocytes (23%), decreased neutrophils (19%), increased lymphocytes (17%), and decreased lymphocytes (9%).

Gomekli® can cause ocular toxicity, including retinal vein occlusion (RVO), retinal pigment epithelium detachment (RPED), and blurred vision. Conduct comprehensive ophthalmic assessments prior to starting treatment, at regular intervals during treatment, and to assess any new or worsening visual changes such as blurred vision. Continue, withhold, reduce the dose, or permanently discontinue Gomekli® as clinically indicated.

Gomekli® can cause left ventricular dysfunction. Treatment with Gomekli® has not been studied in patients with a history of clinically significant cardiac disease or left ventricular ejection fraction (LVEF) <55% prior to initiation of treatment. Assess EF by echocardiogram before starting treatment, and monitor EF every 3 months during the first year and then as clinically indicated. Withhold, reduce the dose, or permanently discontinue Gomekli® based on the severity of adverse reactions.

Gomekli® can cause dermatologic adverse reactions, including rash. Start supportive care at first signs of dermatologic adverse reactions. Withhold, reduce the dose, or permanently discontinue Gomekli® based on severity of adverse reactions.

Contraindications: There are no contraindications listed with this product.

Manufacturer: SpringWorks Therapeutics, Inc.

Analysis: The efficacy of Gomekli® was assessed in the ReNeu study, a multicenter, single-arm study that included patients (N=114) ≥2 years of age with symptomatic, inoperable neurofibromatosis type 1 (NF1) associated plexiform neurofibromas (PN) causing significant morbidity. An inoperable PN was defined as a PN that cannot be completely surgically removed without risk for substantial morbidity due to: encasement of or close proximity to vital structures, invasiveness, or high vascularity of the PN. Patients received Gomekli® until disease progression or unacceptable toxicity.

There were 58 adults who received Gomekli®, with a median age of 35 years (range 18 to 69 years). In addition, 64% were female, 85% were white, about 53% had a progressing PN at study entry, 7% had prior treatment with a MEK inhibitor, and 69% had prior surgery. Morbidities reported in >25% of patients were pain (90%), disfigurement or major deformity (52%), and motor dysfunction (40%).

There were 56 pediatric patients who received Gomekli®, with a median age of 10 years (range 2 to 17 years). In addition, 54% were female, 66% were white, 63% had a progressing PN at study entry, 11% had prior treatment with a MEK inhibitor, and 36% had prior surgery. Morbidities reported in >25% of patients were pain (70%), disfigurement or major deformity (50%), and motor dysfunction (27%).

The major efficacy outcome measure was confirmed overall response rate (ORR), defined as the percentage of patient with complete response (disappearance of the target PN) or partial response (≥20% reduction in PN volume). Responses were assessed by blinded independent central review (BICR) using volumetric magnetic resonance imaging (MRI) analysis per Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) criteria modified to be confirmed at a subsequent tumor assessment within 2 to 6 months during the 24-cycle treatment phase. A secondary efficacy outcome measure was duration of response for patients who achieved a confirmed response.

Efficacy results are presented in the table below, which was adapted from the prescribing information. Note that the median time to onset of response was 7.8 months (range 4 months to 19 months) for the adult cohort and 7.9 months (range 4.1 months to 18.8 months) for the pediatric cohort.

	Gomekli® Adult (N=58)	**Gomekli® Pediatric (N=56)**
Confirmed Overall Response Rate, n (%)	24 (41%)	29 (52%)
95% Confidence Interval (CI)	(29, 55)	(38, 65)
Duration of Response (DoR)		
DoR ≥12 months	21 (88%)	26 (90%)
DoR ≥24 months	12 (50%)	14 (48%)

Place in Therapy: Gomekli® is a kinase inhibitor indicated for the treatment of adult and pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic plexiform neurofibromas (PN) not amenable to complete resection. Continue treatment with Gomekli® until disease progression or unacceptable toxicity. Prior to administration, conduct a comprehensive ophthalmic assessment (as well as conduct at regular intervals during treatment and evaluate any new or worsening visual changes) and assess ejection fraction (EF) by echocardiogram (as well as monitor EF every 3 months during the first year and then as clinically indicated). Treatment with Gomekli® has not been studied in patients with a history of clinically significant cardiac disease or LVEF <55% prior to the start of treatment. The efficacy of Gomekli® was assessed in a multicenter, single-arm study that included adult and pediatric patients with symptomatic, inoperable NF1 associated plexiform neurofibromas causing significant morbidity. The major efficacy outcome measure was confirmed overall response rate; the ORR in adults was 41% while the ORR in pediatric patients was 52%.

Summary

It is recommended that Gomekli® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

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

References

[1] Gomekli® [package insert]. Stamford, CT: SpringWorks Therapeutics, Inc; 2025.

Prepared By: Iowa Medicaid Date: 06/23/2025