GOMEKLI™
(mirdametinib)
1 mg tablets for oral suspension
1 mg and 2 mg capsules

Dosing and Adverse Reaction Management Guide

GOMEKLI is FDA-approved for the treatment of adults and children 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic plexiform neurofibromas (PN) not amenable to complete resection.[1]

Important Safety Information

Warnings and Precautions associated with GOMEKLI include Ocular Toxicity, Left Ventricular Dysfunction, Dermatologic Adverse Reactions, and Embryo-Fetal Toxicity.

Adverse Reactions (>25%) in both adult and pediatric patients include rash, diarrhea, musculoskeletal pain, vomiting, and nausea, as well as fatigue in adult patients and abdominal pain, headache, paronychia, and left ventricular dysfunction in pediatric patients.

Please see Important Safety Information on pages 18-19, and click here for full Prescribing Information, including Patient Information and Instructions for Use.

Helping your patients start and stay on GOMEKLI

You play a vital role in a patient's experience with GOMEKLI

One of the important ways you care for patients is knowing how to confidently manage dosing and address adverse reactions that may occur during treatment. This guide provides information on GOMEKLI dosing and safety and presents guidance on how specific adverse reactions can be managed to support you and your patients throughout treatment.

ReNeu: A pivotal NF1-PN study that included both adult and pediatric patients[1,2]

GOMEKLI was evaluated in ReNeu, a phase 2b single-arm study, and one of the largest (N=114) NF1-PN studies conducted to date. 58 adult patients (aged 18 to 69) and 56 pediatric patients (aged 2 to 17) received GOMEKLI orally at a dose of 2 mg/m^2 twice daily (max 4 mg twice daily). Dosing was on a 28-day cycle (4-week course), using a 3-weeks-on/1-week-off schedule for up to 24 cycles. The primary endpoint was confirmed overall response rate, defined as the proportion of patients with complete response (disappearance of the target PN) or partial response (≥20% reduction) on magnetic resonance imaging of the target PN volume from baseline to Cycle 24 (treatment phase) as assessed by blinded independent central review on ≥2 consecutive scans within 2 to 6 months.

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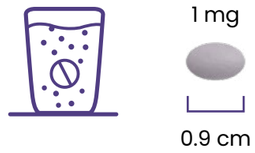
GOMEKLI dosing was designed with patient needs in mind

GOMEKLI is taken on a 3-weeks-on/ 1-week-off dosing schedule[1]

- The recommended dose is 2 mg/m^2 twice daily, with a maximum dose of 4 mg twice daily
- **GOMEKLI can be taken with or without food**

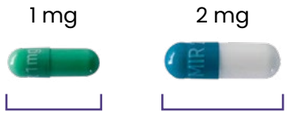
GOMEKLI is available in 2 formulations[1]

Tablet for oral suspension (can be dispersed in water or swallowed whole)



Liquid can be administered orally by cup or syringe

A capsule that comes in 2 sizes



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Personalized dosing based on body surface area (BSA)

Recommended dose of GOMEKLI[1]

BSA (m^2)*	Recommended dosage for capsules or tablets for oral suspension
0.40 to 0.69	1 mg twice daily
0.70 to 1.04	2 mg twice daily
1.05 to 1.49	3 mg twice daily
≥1.50	4 mg twice daily

It is important to monitor your patients and reassess dosage based on any BSA changes.

Continue treatment with GOMEKLI until disease progression or unacceptable toxicity.

Recommended dose reductions for adverse reactions[1]

BSA (m^2)	Reduced dose†	
	Morning	Evening
0.40 to 0.69	1 mg once daily	
0.70 to 1.04	2 mg	1 mg
1.05 to 1.49	2 mg	2 mg
≥1.50	3 mg	3 mg

Even with a dose reduction, patients should continue to take GOMEKLI on a 3-weeks-on/1-week-off dosing schedule.

*The recommended dosage for patients with a BSA less than 0.40 m^2 has not been established.
†Permanently discontinue GOMEKLI in patients unable to tolerate GOMEKLI after one dose reduction.

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GOMEKLI safety profile in adults

Adverse reactions (≥20%) in adult patients who received GOMEKLI in ReNeu (n=58)[1]

	All grades	Grade 3 or 4*
Skin and subcutaneous tissue disorders		
Rash†	90%	10%
Gastrointestinal disorders		
Diarrhea‡	59%	0%
Nausea	52%	0%
Vomiting	38%	0%
Abdominal pain§	24%	3%
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain‖	41%	5%
General disorders and administration site conditions		
Fatigue	29%	2%
Infections and infestations		
COVID-19¶	22%	5%
Nervous system disorders		
Peripheral neuropathy#	21%	0%

The majority of adverse reactions were mild to moderate, with low rates of severe (Grade 3) reactions observed.[1]

*All reactions were Grade 3 except one fatal case of COVID-19 in an adult.
†Rash includes dermatitis acneiform, eczema, maculo-papular rash, pustular rash, dermatitis, erythematous rash, palmar-plantar erythrodysesthesia syndrome, exfoliative rash, skin exfoliation, pruritic rash, papule, papular rash, and macular rash.
‡Diarrhea includes frequent bowel movements.
§Abdominal pain includes upper abdominal pain, gastrointestinal pain, and abdominal discomfort.
‖Musculoskeletal pain includes noncardiac chest pain, back pain, pain in extremity, neck pain, musculoskeletal chest pain, myalgia, arthralgia, and bone pain.
¶Includes one fatal case in an adult.
#Peripheral neuropathy includes paresthesia, hypoesthesia, neuralgia, and peripheral sensory neuropathy.

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Laboratory abnormalities[1,**,††,‡‡]

The select all-grade laboratory abnormalities (≥15%) that worsened from baseline in adult patients were increased creatine phosphokinase (55%), increased triglycerides (29%), decreased calcium (23%),[§§] increased cholesterol (23%), decreased hemoglobin (21%), increased aspartate aminotransferase (AST) (18%), and decreased lymphocytes (16%). The most common Grade 3 or 4 laboratory abnormality (>2%) was increased creatine phosphokinase.

Dose interruption, reduction, and discontinuation due to adverse reactions[1]

31% (18/58) of patients had a dose interruption

17% (10/58) of patients had a dose reduction

Adverse reactions that required dose interruption in ≥5% of adult patients included left ventricular dysfunction and COVID-19. Adverse reactions that required dose reductions in ≥5% of patients included rash.

22% (13/58) permanently discontinued treatment

Adverse reactions that resulted in permanent discontinuation of GOMEKLI in ≥1% of adult patients were rash, diarrhea, nausea, abdominal pain, alopecia, dry skin, left ventricular dysfunction, cough, wheezing, COVID-19, peripheral swelling, retinal vein occlusion, dizziness, and vomiting.

GOMEKLI has no contraindications.[1]

**The denominator used to calculate the rate was 56 based on the number of patients with a baseline value and at least 1 posttreatment value.
††Graded per NCI-CTCAE version 5.0.
‡‡No Grade 5 laboratory abnormalities were reported in the ReNeu study.
§§Calcium corrected for albumin (mmol/L).
CTCAE=Common Terminology Criteria for Adverse Events; NCI=National Cancer Institute.

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Pediatric cohort

GOMEKLI safety profile in children and adolescents

Adverse reactions (≥20%) in pediatric patients who received GOMEKLI in ReNeu (n=56)[1]

	All grades	Grade 3 or 4*
Skin and subcutaneous tissue disorders		
Rash†	73%	4%
Gastrointestinal disorders		
Diarrhea‡	55%	5%
Nausea	27%	0%
Vomiting	39%	0%
Abdominal pain§	39%	4%
Stomatitis‖	20%	0%
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain¶	41%	2%
General disorders and administration site conditions		
Pyrexia	20%	0%
Infections and infestations		
COVID-19#	25%	0%
Paronychia	32%	0%
Upper respiratory tract infection	23%	0%
Nervous system disorders		
Headache**	34%	2%
Cardiac disorders		
Left ventricular dysfunction	27%	2%
Respiratory, thoracic, and mediastinal disorders		
Cough††	21%	0%

The majority of adverse reactions were mild to moderate, with low rates of severe (Grade 3) reactions observed.[1]

*All reactions were Grade 3 except one fatal case of COVID-19 in an adult.

†Rash includes dermatitis acneiform, eczema, maculo-papular rash, pustular rash, dermatitis, erythematous rash, palmar-plantar erythrodysesthesia syndrome, exfoliative rash, skin exfoliation, pruritic rash, papule, papular rash, and macular rash.

‡Diarrhea includes frequent bowel movements.

§Abdominal pain includes upper abdominal pain, gastrointestinal pain, and abdominal discomfort.

‖Stomatitis includes mouth ulceration and aphthous ulcer.

¶Musculoskeletal pain includes noncardiac chest pain, back pain, pain in extremity, neck pain, musculoskeletal chest pain, myalgia, arthralgia, and bone pain.

#Includes one fatal case in an adult.

**Headache includes migraine.

††Cough includes upper-airway cough syndrome.

Laboratory abnormalities[1,‡‡,§§,‖‖‖]

The select all-grade laboratory abnormalities (≥15%) that worsened from baseline in pediatric patients were increased creatine phosphokinase (59%), increased triglycerides (45%), decreased leukocytes (40%), decreased glucose (36%), decreased neutrophils (31%), increased creatinine (30%), increased alkaline phosphatase (29%), decreased hemoglobin (29%), increased lymphocytes (27%), decreased bicarbonate (21%), increased alanine aminotransferase (ALT) (21%), decreased calcium (20%),¶¶ and increased cholesterol (16%). The most common Grade 3 or 4 laboratory abnormalities (>2%) were decreased neutrophil count and increased creatine phosphokinase.

Dose interruption, reduction, and discontinuation due to adverse reactions[1]

30% (17/56) of patients had a dose interruption

13% (7/56) of patients had a dose reduction

Adverse reactions that required dose interruption in ≥5% of patients included COVID-19. Adverse reactions that required dose reduction in ≥3% of pediatric patients were rash and decreased neutrophil count.

9% (5/56) permanently discontinued treatment

Adverse reactions that required permanent discontinuation of GOMEKLI in ≥1% of patients were urticaria, rash, abdominal pain, constipation, and diarrhea.

‡‡The denominator used to calculate the rate varied from 55 to 56 based on the number of patients with a baseline value and at least 1 posttreatment value.

§§Graded per NCI-CTCAE version 5.0.

‖‖‖No Grade 5 laboratory abnormalities were reported in the ReNeu study.

¶¶Calcium corrected for albumin (mmol/L).

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Dermatologic

Incidence[1]

- Rash (all grades) was reported in 90% of adult patients and 73% of pediatric patients
- Low rates of Grade ≥3 dermatologic adverse reactions were reported with GOMEKLI
  - Grade ≥3 rash was reported in 10% of adult patients and 4% of pediatric patients
- Rash includes dermatitis acneiform, eczema, maculo-papular rash, pustular rash, dermatitis, erythematous rash, palmar-plantar erythrodysesthesia syndrome, exfoliative rash, skin exfoliation, pruritic rash, papule, papular rash, and macular rash
- Dermatitis acneiform occurred with a higher frequency in patients aged 12 to 17 years than in those aged 2 to 11 years. Nonacneiform rash occurred with a higher frequency in patients aged 2 to 11 years than in those aged 12 to 17 years[1]

Of the patients who had dermatologic adverse reactions, the majority (80%) experienced first onset during Cycle 1 of treatment.[3]

Supportive care and dose modifications

- Per the prescribing information, supportive care should be initiated at first signs of dermatologic adverse reactions. GOMEKLI should be withheld, dose reduced, or permanently discontinued based on severity of adverse reaction. For intolerable Grade 2 or Grade 3 dermatologic adverse reactions, or Grade 3 or Grade 4 dermatitis acneiform or nonacneiform rash, GOMEKLI should be withheld until ≤Grade 1, then resumed at a reduced dose[1]

The ReNeu Scientific Steering Committee, in collaboration with expert dermatologists, provided the following guidance for managing dermatologic adverse reactions that may occur during GOMEKLI treatment. These recommendations were not included in the ReNeu study protocol, and should be used at the discretion of the healthcare provider, while maintaining consistency with the local standard of care.[4]

- You may suggest hygienic skincare practices, including daily baths and the use of mild cleansers and hypoallergenic skin moisturizers (creams or ointments) at least twice a day to prevent dry skin. Recommend limiting soap to essential areas (eg, face, armpits, groin, and between toes)[4]
- Patients may be advised to avoid topical retinoids and agents with the potential to dry out or irritate skin, such as benzoyl peroxide, salicylic acid, acne skin washes, scrubs, exfoliants, antiaging creams, and alcohol (in some cleansers and wipes)[4]
- Referral to a dermatologist may be considered[4]:
  - For prepubescent patients with uncontrolled dermatitis, moderate/severe acneiform rash concurrent with initiation of cephalexin/amoxicillin, or suspected infection
  - For postpubescent patients with worsening acneiform rash or suspected infection

Dermatologic adverse reaction management recommendations[4]

	Prepubescent patients		Postpubescent patients
Upon initiation of GOMEKLI treatment	Direction for bleach baths should be provided to patients and can begin with GOMEKLI treatment or in reaction to development of rash • 1/4 to 1/2 cup of regular-strength bleach may be added to a full bathtub (approximately 1 teaspoon per gallon) for a 5- to 10-minute soak 3 to 4 times a week, followed by the application of a high-quality hypoallergenic skin moisturizer • Patients are advised to strictly follow guidance for bleach baths and avoid contact of nondiluted bleach with eyes, which can cause irreversible eye damage and skin burns		Prophylactic treatment with topical clindamycin and an oral tetracycline at an anti-inflammatory dose is suggested • Topical clindamycin lotion, 1.0%, should be applied to the face twice daily • Begin treatment with a tetracycline (eg, doxycycline or minocycline) 50 mg/day for 3 months
Reactive treatment for mild rash	**Dermatitis** • Hydrocortisone cream, 2.5%, BID for face and skinfold areas • Triamcinolone ointment, 0.1%, BID for trunk and extremities • If the condition does not resolve within 2 weeks, consider consulting a dermatologist	**Acneiform rash** • Topical clindamycin lotion, 1.0%, BID until rash is clear and as needed thereafter • Hydrocortisone cream, 2.5%, can be added twice daily	**Acneiform rash** If acneiform rash still develops and is bothersome, patient may use • Hydrocortisone cream, 2.5%, BID **OR** • Triamcinolone ointment, 0.1%, BID
Reactive treatment for moderate to severe rash		**Acneiform rash** • Cephalexin (20 mg/kg/day divided BID; 500 mg max daily dosage) for up to 6 weeks **OR** • Amoxicillin (25 mg/kg/day divided BID; 875 mg max daily dosage) for up to 6 weeks **OR** • Fluconazole (20 mg/kg/day; 100 mg max daily dosage) for 5 days, and then 1× per week for 3 months • Referral to a dermatologist should be made at initiation of cephalexin or amoxicillin treatment	

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Gastrointestinal

Incidence[1]

- In the adult cohort, the gastrointestinal (GI) adverse reactions reported in ≥20% of patients were diarrhea (59%), nausea (52%), vomiting (38%), and abdominal pain (24%)
  - There were no Grade ≥3 cases of diarrhea, nausea, or vomiting reported; 3% of patients had Grade 3 abdominal pain
- In the pediatric cohort, the GI adverse reactions reported in ≥20% of patients were diarrhea (55%), vomiting (39%), abdominal pain (39%), nausea (27%), and stomatitis (20%)
  - There were no cases of Grade 3 vomiting, nausea, or stomatitis; 5% of patients had Grade 3 diarrhea and 4% had Grade 3 abdominal pain

Of the patients who had GI adverse reactions, the majority experienced first onset early (Cycles 1-3).[3]

Proportion of patients experiencing first onset of GI reactions in the first 2 cycles of treatment[3]

	Adult cohort	Pediatric cohort
Diarrhea	71% (24/34)	55% (17/31)
Nausea	80% (24/30)	47% (7/15)
Vomiting	55% (12/22)	55% (12/22)
Abdominal pain	43% (6/14)	55% (12/22)

Supportive care[2]

The following guidance for managing GI adverse reactions that may occur during GOMEKLI treatment is based on the ReNeu study protocol. These recommendations should be used at the discretion of the healthcare provider, while maintaining consistency with the local standard of care.

- Patients may consider adopting the BRAT diet (bananas, rice, applesauce, and toast or plain pasta), avoiding fried, fatty, or spicy foods, and increasing fluid intake
- Noninfectious diarrhea can be treated with loperamide; additional agents may be used concurrently if loperamide is not adequate

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Ocular

Incidence

- 3 patients in the adult cohort and 1 patient in the pediatric cohort of ReNeu reported blurred vision[2]
- Retinal pigment epithelium detachment (RPED) occurred in 1 adult patient[1]
- Retinal vein occlusion (RVO) occurred in 2.7% of adult patients, including one Grade 3 case that was diagnosed on Day 130 and resulted in permanent treatment discontinuation[1,3]
  - Confounding factors: Grade 3 RVO occurred 4 months after patient initiated hormonal contraception and 9 days after receiving a COVID-19 vaccination[2]
- No cases of RPED or RVO observed in the pediatric cohort[1]
- No cases of uveitis, optic neuropathy, or retinopathy were reported[3]

Dose modifications[1]

- Permanently discontinue GOMEKLI in patients with RVO
- Withhold GOMEKLI in patients with symptomatic RPED until ≤Grade 1 or baseline, then resume GOMEKLI at the same dose
- For ocular toxicity ≤Grade 2, continue GOMEKLI at current dose level and consider ophthalmologic examinations every 2 to 4 weeks until resolution to ≤Grade 1 or baseline
- For ocular toxicity ≥Grade 3, withhold GOMEKLI until ≤Grade 1 or baseline
  - If recovery occurs ≤14 days, resume GOMEKLI at the next lower dose
  - If recovery occurs in >14 days, consider permanent discontinuation of GOMEKLI

Baseline and ongoing monitoring[1]

- Conduct comprehensive ophthalmic assessments prior to initiating GOMEKLI, at regular intervals during treatment, and to evaluate any new or worsening visual changes such as blurred vision. Continue, withhold, reduce the dose, or permanently discontinue GOMEKLI based on severity of adverse reaction

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Cardiac

Incidence

- 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[1]
- Decreased LVEF of 10% to <20% occurred in 16% of patients in the adult cohort and 25% of patients in the pediatric cohort. Decreased LVEF of ≥20% occurred in 1.8% of patients in the pediatric cohort[1]
  - Of the adult patients with decreased LVEF, 5 (9%) required dose interruption, 1 (1.7%) required a dose reduction, and 1 patient required permanent discontinuation of GOMEKLI; the median time to first onset was 70 days
  - Of the pediatric patients with decreased LVEF, 1 (1.8%) required dose interruption of GOMEKLI; the median time to first onset was 132 days
- No cases of cardiac failure were reported in either cohort[3]

Routine echocardiograms are important during GOMEKLI treatment. All patients with decreased LVEF were identified during a routine echocardiogram, and the issue resolved in 75% of patients.[1]

Dose modifications[1]

- For an asymptomatic, absolute decrease in LVEF of 10% or greater from baseline and below the lower limit of normal, withhold GOMEKLI until ≤Grade 1, then resume GOMEKLI at reduced dose
- Permanently discontinue GOMEKLI for any absolute decrease in LVEF 20% or greater from baseline

Baseline and ongoing monitoring

- Ejection fraction should be assessed by echocardiogram prior to initiating treatment, every 3 months during the first year, then as clinically indicated thereafter[1]

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Paronychia and other adverse reactions

Incidence[1]

- 32% of pediatric patients experienced paronychia; none of these reactions were Grade ≥3

First onset of paronychia occurred sporadically throughout the ReNeu study.[3]

Supportive care[2]

The following guidance for managing paronychia is based on the ReNeu study protocol. These recommendations should be used at the discretion of the healthcare provider, while maintaining consistency with the local standard of care.

- If acute and nonsurgical (ie, without any fluctuance that would suggest the presence of an abscess), paronychia may resolve with the use of warm soaks 3 to 4 times daily
- If there is extensive redness suggesting cellulitis, consider an oral antibiotic that covers *staphylococcus aureus*
- If an abscess develops, consider surgical treatment with incision and drainage

Other adverse reactions[1]

For intolerable Grade 2 or Grade 3 adverse reactions, withhold GOMEKLI until improvement and then resume at a reduced dose. For Grade 4 reactions, withhold GOMEKLI until improvement, then resume at a reduced dose. Consider discontinuation.

Please note: A pregnancy test should be conducted prior to initiating treatment, as GOMEKLI can cause fetal harm when administered to a patient who is pregnant. Blood tests and urinalysis should be initiated prior to treatment and at regular intervals during treatment to assess for abnormalities (ie, changes in serum creatine phosphokinase).[1,2]

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Getting patients started with personalized support

SpringWorks CareConnections provides personalized support services and resources to help your patients get started and stay on track with GOMEKLI

SpringWorks CareConnections™

Coverage and access support

- We offer support to help navigate insurance coverage, including:
  - Benefits investigation
  - Prior authorization requirements and appeal processes for GOMEKLI
- Field Access Managers (FAMs) can provide in-person or virtual support to help facilitate access to GOMEKLI by providing you and your office staff with regional payer education and timely responses to questions

Click here to download sample letters of medical necessity, exception, and appeals, as well as other useful resources.

Temporary free medication programs

- We offer temporary free medication programs for your eligible patients experiencing coverage delays or interruptions
- **Quick start:** SpringWorks CareConnections can help eligible commercially insured patients who experience a qualified delay in their insurance coverage get started on GOMEKLI at no cost for a limited period of time*
- **Bridge:** Eligible commercially or government-insured patients currently on GOMEKLI who experience a qualified lapse in their insurance coverage may qualify to receive GOMEKLI at no cost for a limited period of time*

Financial assistance

- **Commercial Copay Program:** Eligible patients with commercial insurance may pay as little as a $0 copay per 21-day supply of GOMEKLI†
- **Reimbursement for eligible GOMEKLI treatment-related costs:** SpringWorks CareConnections may also help with eligible out-of-pocket costs incurred by your patients for certain treatment-related tests, examinations, and/or specialty visits during treatment with GOMEKLI†
- **Patient Assistance Program (PAP):** Patients who are uninsured, underinsured, or lack coverage for GOMEKLI may be eligible to receive medication at no cost‡

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Personalized educational and emotional support

- SpringWorks CareConnections Nurse Advocates serve as a single point of contact for your patients throughout the treatment journey with GOMEKLI and can provide personalized educational and emotional support upon request§
  - Information on disease state, treatment expectations, access support, product-related questions, nonclinical questions, and SpringWorks CareConnections services
  - Education and guidance to help your patients stay on track with GOMEKLI
  - Emotional support and encouragement for your patients and their caregivers

Acquisition and ordering information

- GOMEKLI is available through a limited Specialty Pharmacy network
- GOMEKLI is also available for eligible medically integrated dispensing (MID) pharmacies by ordering directly through one of our Specialty Distributor partners

SpringWorks CareConnections representatives are available Monday - Friday, 8AM to 10PM ET. Click here to learn more.

*Terms and conditions apply. Full terms and conditions provided during enrollment process and are available upon request by contacting SpringWorks CareConnections at 844-CARES-55 (844-227-3755).

†Terms and conditions apply. The copay program for GOMEKLI and reimbursement for eligible treatment-related costs are subject to annual benefit maximums. To receive the reimbursement of eligible treatment-related expenses, an Explanation of Benefits (EOB) form must be submitted, along with copies of receipts for any payments made. Full terms and conditions are provided during the enrollment process and are available upon request by contacting SpringWorks CareConnections at 844-CARES-55 (844-227-3755).

‡Terms and conditions apply. PAP eligibility criteria and annal household income limits apply. Full terms and conditions are provided during the enrollment process and are available upon request by contacting SpringWorks CareConnections at 844-CARES-55 (844-227-3755).

§The SpringWorks CareConnections Patient Support Program is not intended to take the place of a healthcare provider, and our team of Nurse Advocates cannot provide medical or clinical advice.

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Important Safety Information

Warnings and Precautions

Ocular Toxicity: GOMEKLI can cause ocular toxicity including retinal vein occlusion (RVO), retinal pigment epithelium detachment (RPED), and blurred vision. In the adult pooled safety population, ocular toxicity occurred in 28% of patients treated with GOMEKLI: 21% were Grade 1, 5% were Grade 2 and 1.3% were Grade 3. RVO occurred in 2.7%, RPED occurred in 1.3%, and blurred vision occurred in 9% of adult patients. In the pediatric pooled safety population, ocular toxicity occurred in 19% of patients: 17% were Grade 1 and 1.7% were Grade 2. Conduct comprehensive ophthalmic assessments prior to initiating GOMEKLI, at regular intervals during treatment, and to evaluate any new or worsening visual changes such as blurred vision. Continue, withhold, reduce the dose, or permanently discontinue GOMEKLI as clinically indicated.

Left Ventricular Dysfunction: GOMEKLI can cause left ventricular dysfunction. GOMEKLI has not been studied in patients with a history of clinically significant cardiac disease or LVEF <55% prior to initiation of treatment. In the ReNeu study, decreased LVEF of 10 to <20% occurred in 16% of adult patients treated with GOMEKLI. Five patients (9%) required dose interruption, one patient (1.7%) required a dose reduction, and one patient required permanent discontinuation of GOMEKLI. The median time to first onset of decreased LVEF in adult patients was 70 days. Decreased LVEF of 10 to <20% occurred in 25%, and decreased LVEF of ≥20% occurred in 1.8% of pediatric patients treated with GOMEKLI. One patient (1.8%) required dose interruption of GOMEKLI. The median time to first onset of decreased LVEF in pediatric patients was 132 days. All patients with decreased LVEF were identified during routine echocardiography, and decreased LVEF resolved in 75% of patients. Before initiating GOMEKLI, assess ejection fraction (EF) by echocardiogram. Monitor EF every 3 months during the first year and then as clinically indicated. Withhold, reduce the dose, or permanently discontinue GOMEKLI based on severity of adverse reaction.

Dermatologic Adverse Reactions: GOMEKLI can cause dermatologic adverse reactions including rash. The most frequent rashes included dermatitis acneiform, rash, eczema, maculo-papular rash and pustular rash. In the pooled adult safety population, rash occurred in 92% of patients treated with GOMEKLI (37% were Grade 2 and 8% were Grade 3) and resulted in permanent discontinuation in 11% of patients. In the pooled pediatric safety population, rash occurred in 72% of patients treated with GOMEKLI (22% were Grade 2 and 3.4% were Grade 3) and resulted in permanent discontinuation in 3.4% of patients. Initiate supportive care at first signs of dermatologic adverse reactions. Withhold, reduce the dose, or permanently discontinue GOMEKLI based on severity of adverse reaction.

Embryo-Fetal Toxicity: GOMEKLI can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to the initiation of GOMEKLI. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Also advise patients to use effective contraception during treatment with GOMEKLI and for 6 weeks after the last dose (females) or 3 months after the last dose (males).

Adverse Reactions

The most common adverse reactions (>25%) in adult patients were rash (90%), diarrhea (59%), nausea (52%), musculoskeletal pain (41%), vomiting (38%), and fatigue (29%). Serious adverse reactions occurred in 17% of adult patients who received GOMEKLI. The most common Grade 3 or 4 laboratory abnormality (>2%) was increased creatine phosphokinase.

The most common adverse reactions (>25%) in pediatric patients were rash (73%), diarrhea (55%), musculoskeletal pain (41%), abdominal pain (39%), vomiting (39%), headache (34%), paronychia (32%), left ventricular dysfunction (27%), and nausea (27%). Serious adverse reactions occurred in 14% of pediatric patients who received GOMEKLI. The most common Grade 3 or 4 laboratory abnormalities (>2%) were decreased neutrophil count and increased creatine phosphokinase.

Use in Specific Populations

Verify the pregnancy status of patients of reproductive potential prior to initiating GOMEKLI. Due to the potential for adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with GOMEKLI and for 1 week after the last dose.

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With GOMEKLI dosing and adverse reaction management strategies, you can confidently care for your patients

- **Available in 2 dosing formulations designed with patient needs in mind[1]**
- **Dosing modifications and supportive care may help address adverse reactions that occur during treatment[1,2,4]**
- **Personalized support can help your patients start and stay on track with GOMEKLI**

Visit **GOMEKLI.com/hcp** to find additional tools for your practice and your patients.

References: 1. GOMEKLI. Prescribing Information. SpringWorks Therapeutics, Inc. **2.** Moertel CL, Hirbe AC, Shuhaiber HH, et al. ReNeu: a pivotal, phase IIb trial of mirdametinib in adults and children with symptomatic neurofibromatosis type 1-associated plexiform neurofibroma. *J Clin Oncol.* Published online November 8, 2024. doi.org/10.1200/JCO.24.01034 **3.** Data on file: SpringWorks Therapeutics, Inc. **4.** Hirbe A, Anadkat MJ, Boull C, et al. Addressing skin adverse events during mirdametinib treatment in patients with neurofibromatosis type 1-associated plexiform neurofibromas: guidance from a multidisciplinary group of experts involved in the ReNeu trial. Poster presented at: 29th Annual Meeting of the Society for Neuro-Oncology; November 21-24, 2024; Houston, TX.

Please see Important Safety Information on pages 18-19, and click here for full Prescribing Information, including Patient Information and Instructions for Use.

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