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

GOMEKLI Evidence Compendium

A **Reference Compendium** to support further documentation for your patients with NF1-PN and payor coverage for GOMEKLI.

When prescribing GOMEKLI for your adult and pediatric patients ≥2 years of age with neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN), some health plans may require documentation including patient chart information, lab results, and scientific literature that supports the use of GOMEKLI to be submitted alongside prior authorization requests, letters of medical necessity, and/or appeal letters.

Included within this resource are some peer-reviewed publications on NF1-PN, key challenges in disease management, general approaches to treatment, and information on GOMEKLI to support payor coverage determinations with respect to individual patient requests.

This compendium is not comprehensive of all information related to NF1-PN or GOMEKLI that may be necessary for payor interactions for a specific patient request. Capturing the provided publications within coverage communications to payors does not guarantee access or payment for GOMEKLI but may help decision-makers appreciate the evidence base that supports the decision to prescribe GOMEKLI. It is your responsibility to determine which publications and materials may be appropriate to submit with respect to any individual patient request.

INDICATION

GOMEKLI (mirdametinib) is 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.

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.

Please see Important Safety Information on page 5 and click here for full Prescribing Information.

GOMEKLI Clinical Studies and Prescribing Information

The following references may be used to support coverage communications related to:

- The clinical profile of GOMEKLI, including information needed to ensure safe and effective use
- ReNeu, the pivotal Phase 2b clinical trial for GOMEKLI, evaluated the use of GOMEKLI in adult and pediatric patients with symptomatic NF1-PN

GOMEKLI. Prescribing Information. SpringWorks Therapeutics, Inc.

CLICK HERE to View Information

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.* Epub ahead of print. doi:10.1200/JCO.24.01034

CLICK HERE to View Information

Challenges With Swallowing in NF1-PN

The following references may be used to support coverage communications related to:

- Challenges with swallowing (or dysphagia) in NF1-PN, which is observed in about one-fourth of adults with NF1-PN
- The importance of treatment options that are appropriate for patients with difficulty swallowing capsules

Rapado F, Simo R, Small M. Neurofibromatosis type 1 of the head and neck: dilemmas in management. *J Laryngol Otol*. 2001;115(2):151-154. doi:10.1258/0022215011907587

CLICK HERE to View Information

Yoo HK, Porteous A, Ng A, et al. Impact of neurofibromatosis type 1 with plexiform neurofibromas on the health-related quality of life and work productivity of adult patients and caregivers in the UK: a cross-sectional survey. *BMC Neurol*. 2023;23(1):419. doi: 10.1186/s12883-023-03429-7

CLICK HERE to View Information

Please see Important Safety Information on page 5 and click here for full Prescribing Information.

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

Surgery Feasibility and Potential Limitations

The following references may be used to support coverage communications related to:

- Up to 85% of plexiform neurofibromas are not amenable to complete resection
- Risk of postoperative complications in patients with NF1-PN
- Potential for plexiform neurofibroma tumor regrowth after surgery

Prada CE, Rangwala FA, Martin LJ, et al. Pediatric plexiform neurofibromas: impact on morbidity and mortality in neurofibromatosis type 1. *J Pediatr*. 2012;160(3):461-467. doi:10.1016/j.jpeds.2011.08.051

CLICK HERE to View Information

Nguyen R, Ibrahim C, Friedrich RE, Westphal M, Schuhmann M, Mautner V-F. Growth behavior of plexiform neurofibromas after surgery. *Genet Med*. 2013;15(9):691-697. doi:10.1038/gim.2013.30

CLICK HERE to View Information

Ejerskov C, Farholt S, Nielsen FSK, et al. Clinical characteristics and management of children and adults with neurofibromatosis type 1 and plexiform neurofibromas in Denmark: a nationwide study. *Oncol Ther*. 2023;11(1):97-110. doi:10.1007/s40487-022-00213-4

CLICK HERE to View Information

Management of NF1-PN

The following references may be used to support coverage communications related to:

- Achieving the goals of care for patients with NF1-PN involves reducing the plexiform neurofibroma tumor volume or stabilizing tumor growth
- Lack of a defined standard of care and treatment sequence in NF1-PN

Stewart DR, Korf BR, Nathanson KL, Stevenson DA, Yohay K. Care of adults with neurofibromatosis type 1: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2018;20(7):671-682. doi:10.1038/gim.2018.28

CLICK HERE to View Information

Miller DT, Freedenberg D, Schorry E, Ullrich NJ, Viskochil D, Korf BR; for the Council on Genetics and American College of Medical Genetics and Genomics. Health supervision for children with neurofibromatosis type 1. *Pediatrics*. 2019;143(5):e20190660. doi:10.1542/peds.2019-0660

CLICK HERE to View Information

Armstrong AE, Belzberg AJ, Crawford JR, Hirbe AC, Wang ZJ. Treatment decisions and the use of MEK inhibitors for children with neurofibromatosis type 1-related plexiform neurofibromas. *BMC Cancer*. 2023;23(1):553. doi:10.1186/s12885-023-10996-y

CLICK HERE to View Information

Fisher MJ, Blakeley JO, Weiss BD, et al. Management of neurofibromatosis type 1-associated plexiform neurofibromas. *Neuro Oncol*. 2022;24(11):1827-1844. doi:10.1093/neuonc/noac146

CLICK HERE to View Information

Please see Important Safety Information on page 5 and click here for full Prescribing Information.

NF1-PN: Diagnosis, Overview, and Burden of Disease

The following references may be used to support coverage communications related to:

- Appropriate differential and clinical diagnosis of NF1-PN
- The clinical burden, symptomatology, and pathophysiology of NF1-PN
- The need for active intervention that helps to target the mechanism of disease

Gutmann DH, Ferner RE, Listernick RH, Korf BR, Wolters PL, Johnson KJ. Neurofibromatosis type 1. *Nat Rev Dis Primers*. 2017;3:17004. doi:10.1038/nrdp.2017.4

CLICK HERE to View Information

Jett K, Friedman JM. Clinical and genetic aspects of neurofibromatosis 1. *Genet Med*. 2010;12(1):1-11. doi:10.1097/GIM.0b013e3181bf15e3

CLICK HERE to View Information

Kresak JL, Walsh M. Neurofibromatosis: a review of NF1, NF2, and schwannomatosis. *J Pediatr Genet*. 2016;5(2):98-104. doi: 10.1055/s-0036-1579766

CLICK HERE to View Information

Legius E, Messiaen L, Wolkenstein P, et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. *Genet Med*. 2021;23(8):1506-1513. doi: 10.1038/s41436-021-01170-5

CLICK HERE to View Information

SpringWorks CareConnections™ provides personalized support services and resources to help your patients get started and stay on track with **GOMEKLI**™ **(mirdametinib)**

Coverage and Access Support

- Resources, education, and assistance to support timely access to GOMEKLI

Financial Assistance

- Financial support options for eligible patients

Field Access Manager (FAM) Support

- FAMs can provide in-person or virtual support to help facilitate access to GOMEKLI by providing you and your office staff regional payor education and timely responses to questions
- If you have questions about patient access to GOMEKLI and wish to connect with a FAM, please visit springworkstxcares.com/gomekli/hcp/connect-with-field-access-manager/

To connect and learn more about additional supporting access materials, please contact SpringWorks CareConnections at **844-CARES-55 (844-227-3755), Monday – Friday, 8 AM – 10 PM ET**, or visit our website at **springworkstxcares.com/gomekli/hcp**

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

To report SUSPECTED ADVERSE REACTIONS, contact SpringWorks Therapeutics Inc. at 1-888-400-7989 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please click here for full Prescribing Information including Patient Information and Instructions for Use.

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