Potential GOMEKLI Utilization Management Document

Product Overview

GOMEKLI™ (mirdametinib) is the FIRST and ONLY treatment approved for both 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.[1]

GOMEKLI was approved by the FDA on February 11, 2025.[2]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers recommend mirdametinib (GOMEKLI) as a NCCN Category 2A systemic therapy option for the treatment of adult and pediatric patients ≥2 years of age with NF1 who have symptomatic plexiform neurofibromas not amenable to complete resection.[3]

The *Journal of Clinical Oncology* published the pivotal Phase 2b trial results for ReNeu, which evaluated GOMEKLI in adults and children with symptomatic NF1-PN. Access to the journal can be found **HERE**.

Disease Overview

Neurofibromatosis type 1 (NF1) is a rare, genetic, incurable, neuro-oncology disease that impacts both adult and pediatric patients.[4-8] NF1 affects multiple organ systems and has a birth incidence of ~1 in 2500.[4,9-11] Plexiform neurofibromas, a common clinical manifestation of NF1, are highly invasive peripheral nerve sheath tumors that may cause significant morbidities that are debilitating, and are found in approximately 30%-50% of patients with NF1.[4,5,9] Patients with NF1-PN may experience debilitating morbidity including severe pain, disfigurement, impaired physical function, and internal organ compression.[6,12] Malignant peripheral nerve sheath tumors (MPNSTs) arise from PN, can occur in up to 16% of adult patients with NF1, and are associated with a 5-year overall survival rate of up to 50%.[13,14]

Approval Criteria

Initial Authorization

- Prescribed by or in consultation with an oncologist, neurologist, or other specialists
- The patient is 2 years of age or older; AND
- The patient has BOTH OF the following:
    - Diagnosis of neurofibromatosis type 1 (NF1)
    - Symptomatic plexiform neurofibromas (PN) not amenable to complete resection

Duration of initial authorization approval: 12 months.

Reauthorization Criteria

- Prescriber attests that the patient does not show evidence of progressive disease while on therapy and does not experience unacceptable toxicity

Reauthorization will be provided for 12 months.

Drug Class

Antineoplastic: Mitogen-Activated Protein Kinase (MEK) Inhibitor

Dosage Forms

- Capsules: 1 mg and 2 mg
- Dispersible tablets for oral suspension: 1 mg

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.

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.

References: 1. GOMEKLI. Prescribing Information. SpringWorks Therapeutics, Inc. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers V.5.2024. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed April 29, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** SpringWorks Therapeutics. Accessed February 11, 2025. https://ir.springworkstx.com/news-releases/news-release-details/springworks-therapeutics-announces-fda-approval-gomeklitm **4.** Gutmann DH et al. *Nat Rev Dis Primers*. 2017;3:170004. **5.** Prada CE et al. *J Pediatr*. 2012;160(3):461-467. **6.** Miller DT et al. *Pediatrics*. 2019;143(5):e20190660. **7.** Centers for Medicare & Medicaid Services. Accessed December 16, 2024. https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=59125&ver=26 **8.** Centers for Medicare and Medicaid Services. Accessed May 8, 2025. https://www.cms.gov/files/zip/2024-code-tables-tabular-andindex-updated-02/01/2024.zip **9.** Ejerskov C et al. *Oncol Ther*. 2023;11(1):97-110. **10.** Lee T-SJ et al. *Orphanet J Rare Dis*. 2023;18(1):292. **11.** Children's Tumor Foundation. Accessed May 8, 2025. https://www.ctf.org/news/new-and-improved-the-way-to-talk-about-nf/ **12.** Darrigo LG Jr et al. *Brain Behav*. 2022;12(6):e2599. **13.** Higham CS et al. *Neuro Oncol*. 2018;20(6):818-825. **14.** Zehou O et al. *Orphanet J Rare Dis*. 2013;8:127.

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