BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

GOMEKLI™ (mirdametinib)
KOSELUGO™ (selumetinib)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for GOMEKLI (mirdametinib)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by an Oncologist, Pediatrician, or Geneticist or in consultation with one

Indication
- Neurofibromatosis type 1 (NF1) with symptomatic plexiform neurofibromas not amenable to complete resection

ORIGINAL EFFECTIVE DATE: 05/2/2020 | ARCHIVE DATE: | LAST REVIEW DATE: 05/21/2026 | LAST CRITERIA REVISION DATE: 05/21/2026

- Other oncologic direct treatment listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 2 years of age or older with BSA of at least 0.40m^2

Baseline Clinical Evaluation
- Ejection fraction above institutional lower limit of normal
- Comprehensive ophthalmic assessment
- Negative pregnancy test (if applicable)

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No moderate (bilirubin greater than 1.5 to 3 times upper limit of normal and any AST) or severe (bilirubin greater than 3 times upper limit of normal and any AST) hepatic impairment
- No severe renal impairment (creatinine clearance less than 30 mL/min) or end stage renal disease

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (liver function, CMP)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualification
- Continues to be seen by a physician specializing in or is in consultation with an Oncologist, Pediatrician, or Geneticist

Clinical Response
- **TWO** of the following:
  - Disappearance of the target plexiform neurofibroma

- At least a 20 percent reduction in plexiform neurofibroma volume confirmed at a subsequent tumor assessment
- No evidence of disease progression

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No symptomatic or life threatening decrease in left ventricular ejection fraction
- No new or worsening visual changes
- No retinal vein occlusion
- No severe skin toxicity such as palmar plantar erythrodysesthesia syndrome
- No other life threatening adverse reaction that does not improve with dose modification
- Permanently discontinue use if unable to tolerate after one dose reduction due to adverse reaction
- No moderate (bilirubin greater than 1.5 to 3 times upper limit of normal and any AST) or severe (bilirubin greater than 3 times upper limit of normal and any AST) hepatic impairment
- No severe renal impairment (creatinine clearance less than 30 mL/min) or end stage renal disease

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

Medical Necessity Requirements for KOSELUGO (selumetinib)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by an Oncologist, Pediatrician, or Geneticist or in consultation with one

PHARMACY COVERAGE GUIDELINE

GOMEKLI™ (mirdametinib)
KOSELUGO™ (selumetinib)
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Indication
- Neurofibromatosis type 1 (NF1) with symptomatic, inoperable plexiform neurofibromas
- Other oncologic direct treatment uses listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 1 year of age or older with BSA greater than or equal to 0.55m² for capsule formulation or BSA greater than or equal to 0.44m² for granule formulation

Baseline Clinical Evaluation
- Ejection fraction above institutional lower limit of normal
- Comprehensive ophthalmic assessment
- Serum creatine phosphokinase (CPK)
- Negative pregnancy test (if applicable)

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No severe hepatic impairment (Child Pugh Class C)
- No concomitant use with moderate or strong cytochrome CYP3A4 inducers (e.g., armodafinil, bexarotene, bosentan, dabrafenib, rifampin, rifabutin, phenobarbital, carbamazepine, etc.)

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (LFTs, CMP, CPK
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualification
- Continues to be seen by a physician specializing in or is in consultation with an Oncologist, Pediatrician, or Geneticist

PHARMACY COVERAGE GUIDELINE

GOMEKLI™ (mirdametinib)
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Clinical Response

- **TWO** of the following:
  - Disappearance of the target plexiform neurofibroma
  - At least a 20 percent reduction in plexiform neurofibroma volume confirmed at a subsequent tumor assessment
  - No evidence of disease progression

Adherence

- Adherence to the prescribed therapy regimen has been documented

Safety

- No symptomatic or life threatening decrease in left ventricular ejection fraction
- No new or worsening visual changes
- No retinal vein occlusion
- No severe skin toxicity such as palmar plantar erythrodysesthesia syndrome
- No other life threatening adverse reaction that does not improve with dose modification
- Permanently discontinue use if unable to tolerate after two dose reductions due to adverse reaction
- No life threatening diarrhea or severe diarrhea that does not improve in 3 days of dose modification
- No severe or life threatening colitis
- No life threatening increase in CPK or any increase CPK with myalgia that does not improve in 3 weeks of dose modification
- No rhabdomyolysis
- No bleeding due to vitamin E in capsule or supplements
- No severe hepatic impairment
- No concomitant use with moderate or strong cytochrome CYP3A4 inducers (e.g., armodafinil, bexarotene, bosentan, dabrafenib, rifampin, rifabutin, phenobarbital, carbamazepine, etc.)

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

PHARMACY COVERAGE GUIDELINE

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1. Off-Label Use of Non-Cancer Medications
2. Off-Label Use of Cancer Medications

Description:

Gomekli (mirdametinib) and Koselugo (selumetinib) are a selective mitogen-activated extracellular kinase (MEK) inhibitor indicated for the treatment of individuals 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN).

Mirdametinib and selumetinib are inhibitors of mitogen-activated protein kinase kinases 1 and 2 (MEK1/2). MEK1/2 proteins are upstream regulators of the extracellular signal-related kinase (ERK) pathway. Both MEK and ERK are critical components of the RAS-regulated RAF-MEK-ERK pathway, which is often activated in different types of cancers. Mirdametinib and selumetinib inhibit ERK phosphorylation, and reduces neurofibroma numbers, volume, and proliferation.

Neurofibromatosis type 1 (NF1) is a condition characterized by changes in skin pigmentation and the growth of tumors along nerves in the skin, brain, and other areas of the body. The most common form is neurofibromatosis type 1 (NF1, 96%), followed by neurofibromatosis type 2 (NF2, 3%), and schwannomata's (SWN or sometimes referred to as NF type 3).

NF1, is also known as von Recklinghausen disease or peripheral neurofibromatosis, is an autosomal dominant tumor syndrome characterized by the development of multiple neurofibromas of the peripheral nerves. Malignancies associated with NF1 include malignant peripheral nerve sheath tumors, gliomas, leukemia, pheochromocytomas, gastrointestinal (GI) stromal tumors, and others. NF1 is caused by a mutation in the neurofibromin tumor suppressor gene located on chromosome 17.

NF1, NF2, and SWN are tumor suppressor syndromes caused by germline mutations in a tumor suppressor gene (TSG). TSG encode proteins that are responsible for regulating cell division. Tumor suppressor syndromes are due to mutations in a TSG, which results in dysregulation of pathways responsible for cell division and proliferation.

The hallmarks of NF1 are multiple café-au-lait macules and associate cutaneous neurofibromas. Cutaneous and subcutaneous neurofibromas can cause significant deformity and discomfort. The major peripheral nerve tumor impacting patients with NF1 is the plexiform neurofibroma (pNF). The tumors composed of a variety of cell types including neuronal axons, Schwann cells, fibroblasts, mast cells, macrophages, perineural cells, and extracellular matrix; they can be confined to diffuse. They occur in the trunk, head and neck and the extremities. The pNFs can be a source of neuropathic pain and neurologic dysfunction.

Key differences between NF1 and NF2 include: a) Café-au-lait macules can be seen but are much less frequent in NF2, and Lisch nodes are not seen; b) The schwannomas associated with NF2 do not undergo malignant transformation into a malignant peripheral nerve sheath tumor (MPNST); c) The spinal root tumors that are seen with both NF2 and NF1 are schwannomas in NF2 and neurofibromas in NF1; d) NF2 is not associated with the cognitive impairment that is often seen with NF1; and e) NF2 is associated with a very high prevalence of bilateral acoustic schwannomas and meningiomas.

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Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Target plexiform neurofibromas (PN) defined as the PN that caused relevant clinical symptoms or complications (PN-related morbidities)

Symptomatic PN defined as disfigurement, motor dysfunction, pain, airway dysfunction, visual impairment, and bladder/bowel dysfunction

Inoperable PN defined as a PN that could not 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

Significant morbidity related to PN include disfigurement, motor dysfunction, pain, airway dysfunction, visual impairment, and bladder/bowel dysfunction

Responses:
Complete defined as disappearance of the target PN
Partial defined as ≥ 20% reduction in PN volume

Diagnostic Criteria of NF1:

A: The diagnostic criteria for NF1 are met in an individual who does not have a parent diagnosed with NF1 if 2 or more of the following are present:
• At least 6 café-au-lait macules (> 5 mm in greatest diameter in prepubertal individuals and > 15 mm in greatest diameter in postpubertal individuals*
• Freckling in axillary or inguinal regions*
• At least 2 neurofibromas of any type or 1 plexiform neurofibroma
• Optic pathway glioma
• At least 2 iris Lisch nodules (iris hamartomas) identified by slit lamp examination or 2 or more choroidal abnormalities (CAs) – defined as bright, patchy nodules imaged by optical coherence tomography (OCT)/near-infrared reflectance (NIR) imaging
• A distinctive osseous lesion such as sphenoid dysplasia¶, anterolateral bowing of the tibia, or pseudarthrosis of a long bone
• A heterozygous pathogenic neurofibromin 1 (NF1) variant with a variant allele fraction of 50% in apparently normal tissue such as white blood cells
B: A child of a parent who meets the diagnostic criteria specified in A merits a diagnosis of NF1 if 1 or more of the criteria in A are present
* If only café-au-lait macules and freckling are present, the diagnosis is most likely NF1, but exceptionally the person might have another diagnosis such as Legius syndrome. At least 1 of the 2 pigmentary findings (café-au-lait macules or freckling) should be bilateral ¶ Sphenoid wing dysplasia is not a separate criterion in case of an ipsilateral orbital plexiform neurofibroma

Activities of daily living (ADL):

Instrumental ADL:
Prepare meals, shop for groceries or clothes, use the telephone, manage money, etc.
Self-care ADL:
Bathe, dress and undress, feed self, use the toilet, take medications, not bedridden

NCCN recommendation definitions:
Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

The Child-Pugh classification system:
The Child-Pugh classification is a scoring system used to determine the prognosis of individuals with cirrhosis. Scoring is based upon several factors: albumin, ascites, total bilirubin, prothrombin time, and encephalopathy, as follows:

	Score: 1 point	Score: 2 points	Score: 3 points
Serum Albumin (g/dL)	> 3.5	3.0 - 3.5	< 3.0
Serum Bilirubin (mg/dL)	< 2.0	2.0 - 3.0	> 3.0
Prothrombin time (seconds)	1 - 4	4 - 6	> 6
Ascites	none	moderate	severe
Encephalopathy	none	mild	severe

The three classes and their scores are:
- **Class A** is score 5 – 6: Well compensated
- **Class B** is score 7 – 9: Significant functional compromise
- **Class C** is score > 9: Decompensated disease

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Resources:

Gomekli (mirdametinib) caps and tabs for oral suspension product information, revised by SpringWorks Therapeutics, Inc. 02-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed January 29, 2026.

Koselugo (selumetinib) product information, revised by AstraZenica Pharmaceuticals, LP 11-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed January 29, 2026.

Korf BR, Lobbous M, Metrock LK. Neurofibromatosis type 1 (NF1): Pathogenesis, clinical features, and diagnosis. In: UpToDate, Gajjar A, Firth HV, Tung GA, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2026. Topic last updated January 26, 2026. Accessed March 11, 2026.

Korf BR, Lobbous M, Metrock LK. Neurofibromatosis type 1 (NF1): Management and prognosis. In: UpToDate, Gajjar A, Firth HV, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2026. Topic last update February 23, 2026. Accessed March 11, 2026.

Jordan JT, Evans DG. *NF2*-related schwannomatosis (formerly neurofibromatosis type 2). In: UpToDate, de Groot J, Shih HA, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2026. Topic last updated September 02, 2025. Accessed March 11, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Central Nervous System Cancers Version 3.2025 –Updated December 05, 2025. Available at https://www.nccn.org. Accessed March 11, 2026.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.