BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

OGSIVEO™ (nirogacestat) oral
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 OGSIVEO (nirogacestat)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an Oncologist

Indication
- Progressive desmoid tumor requiring systemic treatment
- Other oncologic direct treatment use listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

ORIGINAL EFFECTIVE DATE: 02/15/2024 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 08/15/2024

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Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Evidence for **ANY** of the following:
  - Newly diagnosed, progressive desmoid tumor/aggressive fibromatosis not suitable for surgery or radiation
  - Recurrent or progressing tumor after initial complete response
  - Preexisting tumor with prior therapy and ongoing progression
- Eastern Cooperative Oncology Group (ECOG) status 0 to 2
- Negative pregnancy test in a woman of childbearing potential

Alternative Therapies
- Failure (trial for at least three months duration), contraindication per FDA label, intolerance, or not a candidate for sorafenib

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 concomitant use of moderate or strong CYP3A inhibitors (e.g., erythromycin, fluconazole, diltiazem, ketoconazole, itraconazole, posaconazole, voriconazole, grapefruit products, Seville oranges, starfruit)
- No concomitant use of moderate or strong CYP3A inducers (e.g., armodafinil, bexarotene, bosentan, rifampin, rifabutin, phenobarbital, carbamazepine)
- No concomitant use of proton pump inhibitors and H2 blockers (e.g., lansoprazole, omeprazole, cimetidine, ranitidine)
- No concomitant use of other tyrosine kinase inhibitors

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (ECOG status, pregnancy test)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 12 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 the diagnosis or in consultation with an Oncologist

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Clinical Response
- No documentation of disease progression
- No documentation of unacceptable drug toxicity

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 development of significant adverse drug effects such as:
  - Severe or life threatening hepatotoxicity (ALT or AST elevations greater than 5 times upper limit of normal)
  - Severe or life threatening adverse reaction that recurs upon rechallenge at reduced dose
- No concomitant use of moderate or strong CYP3A inhibitors, CYP3A inducers, proton pump inhibitors, H2 blockers, or other tyrosine kinase inhibitors

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use (e.g., liver function tests)

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:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Ogsiveo (nirogacestat) is a selective, reversible, noncompetitive inhibitor of gamma secretase (GS) indicated for adult patients with progressing desmoid tumors who require systemic treatment. GS inhibitors block proteolytic activation of the Notch receptor. When dysregulated, Notch can activate pathways that contribute to tumor growth.

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Desmoid tumors, also known as aggressive fibromatosis, are rare, locally invasive, and slow growing soft tissue tumors. Although believed to be benign because of their inability to metastasize, desmoid tumors can cause significant morbidity and occasionally mortality in patients. The cause of death is through invasion and destruction of adjacent vital structures and organs. Disease recurrence after surgery and/or radiation and diagnosis of multifocal desmoid tumors highlight the need for effective systemic treatments.

The most common primary tumor sites include abdominal walls, limbs, girdles, and mesenteric areas. Desmoid tumors infiltrate surrounding structures and spread along plains and muscle, which can lead to severe pain and functional impairment.

There are no evidence-based or consensus-based guidelines for management of unresectable desmoids. Systemic therapy is increasingly being integrated into a multidisciplinary approach for selected patients with unresectable desmoids or for management of intraabdominal desmoids for which local therapy options may cause unacceptable outcomes.

Initial observation is an acceptable strategy for most patients with no or minimal symptoms at initial presentation. Systemic therapy may be needed when unresectable tumors that are symptomatic or are asymptomatic but are progressing; there have been multiple recurrences despite adequate therapy; and symptomatic tumors where surgery would have unacceptable outcomes. Tumors that are asymptomatic or minimally or moderately symptomatic, slow growing, and in locations at which local growth, if rapid, would not cause irreparable harm are more often treated with noncytotoxic forms of therapy (e.g., nirogacestat or oral tyrosine kinase inhibitors [TKI]). Rapidly growing or severely symptomatic tumors, especially those located in critical locations, are appropriate for more aggressive treatments such as cytotoxic chemotherapy. Nirogacestat is a reasonable alternative for selected patients if cytotoxic chemotherapy is not feasible.

If cytotoxic therapy is chosen, pegylated liposomal doxorubicin (PLD), doxorubicin, combinations of doxorubicin plus dacarbazine, or methotrexate plus vinblastine or methotrexate alone are all reasonable options. If a TKI is chosen for initial treatment, sorafenib, pazopanib, or imatinib, may be given. There are no data addressing the optimal duration of treatment. Response to systemic therapy can be slow to become evident and may take six to eight months or more.

Definitions:

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

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma Version 1.2025 – Updated May 02, 2025

Desmoid Tumors (Aggressive Fibromatosis)

Preferred regimens:

- Nirogacestat (category 1)
- Sorafenib (category 1)
- Methotrexate and vinorelbine
- Methotrexate and vinblastine
- Imatinib
- Liposomal doxorubicin

- Doxorubicin ± dacarbazine
- Pazopanib

Useful in certain circumstances:

- Sulindac or other nonsteroidal anti-inflammatory drugs (NSAIDs), including celecoxib (for pain)

Resources:

Ogsiveo (nirogacestat) product information, revised by SpringWorks Therapeutics, Inc. 04-2024. Available at DailyMed http://dailymed.nlm.nih.gov. October 24, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma Version 1.2025 – Updated May 02, 2025. Available at https://www.nccn.org. Accessed November 14, 2025.

Ravi V, Patel SR, Raut CP, Baldini EH. Desmoid tumors: Treatment. In: UpToDate, Maki R, Yushak M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through October 2025. Topic last updated on September 20, 2024. Accessed November 14, 2025.

Gounder M, Ratan R, Alcindor T, et al.: Nirogacestat, a gamma-secretase inhibitor for desmoid tumors. NEJM 2023 Mar 9;388(10):898-912. DOI: 10.1056/NEJMoa2210140. Accessed July 08, 2024. Re-evaluated December 02, 2025.

Gounder MM, Mahoney MR, Van Tine BA, et al.: Sorafenib for advanced and refractory desmoid tumors. NEJM 2018 Dec 20; 379(25): 2417-2428. doi:10.1056/NEJMoa1805052. Accessed December 02, 2025.

Kummar S, O'Sullivan-Coyne G, Do KT, et al.: Clinical activity of the gamma--secretase inhibitor PF-03084014 in adults with desmoid tumors (aggressive fibromatosis). J Clin Oncol. 2017 May 10;35(14):1561-1569. DOI: 10.1200/JCO.2016.71.1994. Accessed July 08, 2024. Re-evaluated December 02, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03785964: A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial of Nirogacestat Versus Placebo in Adult Patients With Progressing Desmoid Tumors/Aggressive Fibromatosis (DT/AF). Available from: http://clinicaltrials.gov. Last update posted May 16, 2024. Last verified May 2024. Accessed July 08, 2024. Re-evaluated December 02, 2025.

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.