NCCN CATEGORY 1 PREFERRED

NATIONAL COMPREHENSIVE CANCER NETWORK® (NCCN®) RECOMMENDATION

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma recommend nirogacestat (OGSIVEO) as a Category 1 Preferred systemic therapy option for patients with desmoid tumors (aggressive fibromatosis).[1]

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

Evidence Compendium

A Reference Compendium to support further documentation of medical necessity of OGSIVEO for your adult patients with progressing desmoid tumors who require systemic treatment[2]

- When making coverage decisions for OGSIVEO, some health plans may require documentation such as patient chart information, lab results, and scientific literature to be submitted alongside prior authorization requests, letters of medical necessity, and/or appeal letters to support the use of OGSIVEO for the particular patient
- Included within this resource are links to access peer-reviewed publications and other resources on topics such as desmoid tumors, challenges in disease management, guideline-recommended treatment options for patients with desmoid tumors, and information on OGSIVEO, which may be provided to health plans to support payor coverage determinations for individual patients
- Publications within this resource contain data and analyses that are not included in the OGSIVEO Prescribing Information
- This compendium is not comprehensive of all information related to desmoid tumors or OGSIVEO that may be necessary or informative for payor interactions for specific patient coverage requests. Including any of the reference sources in this Compendium within coverage communications to payors does not guarantee access or payment for OGSIVEO, but this information may help decision-makers appreciate the evidence base that supports the decision to prescribe OGSIVEO. It is your responsibility to determine which publications and materials may be appropriate to submit alongside any individual patient request for coverage for OGSIVEO

INDICATION

OGSIVEO is indicated for adult patients with progressing desmoid tumors who require systemic treatment.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Diarrhea:** Diarrhea, sometimes severe, can occur in patients treated with OGSIVEO. Diarrhea occurred in 84% of patients treated with OGSIVEO, and included Grade 3 events in 16% of patients. Median time to first diarrhea event was 9 days (range: 2 to 434 days). Monitor patients and manage using antidiarrheal medications. Modify dose as recommended.

Please see additional Important Safety Information on page 4 and page 5, and click here for full Prescribing Information.

OGSIVEO® (nirogacestat) Clinical Profile

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

- The clinical profile of OGSIVEO, including information demonstrating safe and effective use
- DeFi, the double-blind, placebo-controlled, Phase 3 study that evaluated the use of OGSIVEO in adult patients with progressing desmoid tumors
- Exploratory, post-hoc analysis of OGSIVEO from the open-label extension of DeFi

OGSIVEO. Prescribing Information. SpringWorks Therapeutics, Inc.

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Gounder M, Ratan R, Alcindor T, et al. Nirogacestat, a γ-secretase inhibitor for desmoid tumors. *N Engl J Med*. 2023;388(10):898-912. doi:10.1056/NEJMoa2210140

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Ratan R, Kasper B, Alcindor T, et al. Efficacy and safety of long-term continuous nirogacestat treatment in adults with desmoid tumors: results from the DeFi trial. *J Clin Oncol*. 2025;43(34):3646-3651. doi:10.1200/JCO-25-00582

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Clinical Guideline Recommendations for Desmoid Tumor Management

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

- Guideline recommendations for initiation of treatment, and systemic therapies that are recommended as a first-line treatment option for progressive, morbid, or symptomatic desmoid tumors, according to the NCCN Guidelines® and Desmoid Tumor Working Group (DTWG) Guideline
- The NCCN Guidelines recommendation for nirogacestat (OGSIVEO) as a NCCN Category 1 Preferred systemic therapy option for patients with desmoid tumors

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Kasper B, Baldini EH, Bonvalot S, et al; for the Desmoid Tumor Working Group. Current management of desmoid tumors: a review. *JAMA Oncol*. 2024;10(8):1121-1128. doi:10.1001/jamaoncol.2024.1805

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Desmoid Tumors: Diagnosis, Overview, and Burden of Disease

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

- Diagnosis and the unpredictable clinical course of desmoid tumors
- The debilitating, disfiguring, and locally aggressive nature of desmoid tumors
- The high and multifaceted burden of disease, which is characterized by pain, disfigurement, and decreased physical function

Bektas M, Bell T, Khan S, et al. Desmoid tumors: a comprehensive review. *Adv Ther*. 2023;40(9):3697-3722. doi: 10.1007/s12325-023-02592-0

CLICK HERE to View Information

Gounder M, Maddux L, Paty J, Atkinson TM. Prospective development of a patient-reported outcomes instrument for desmoid tumors or aggressive fibromatosis. *Cancer*. 2020;126(3):531-539. doi:10.1002/cncr.32555

CLICK HERE to View Information

Lucas A, Zhou S, Hernandez L, et al. The impact of desmoid tumors: insights from the Desmoid Tumor Research Foundation Natural History Study, 2017–2023. *Orphanet J Rare Dis*. 2025;20(1):515. doi:10.1186/s13023-025-04021-7

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Considerations Regarding Surgical Intervention

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

- Surgery no longer being recommended as a first-line treatment for most clinical situations, and being considered a "less preferred" treatment intervention for progressive, morbid, or symptomatic desmoid tumors by the NCCN Guidelines®
- The NCCN Guidelines notes that surgery often results in physical disability
- The high risk of morbidity and recurrence rates associated with surgical resection

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Kasper B, Baumgarten C, Garcia J, et al; Desmoid Working Group. An update on the management of sporadic desmoid-type fibromatosis: a European Consensus Initiative between Sarcoma PAtients EuroNet (SPAEN) and European Organization for Research and Treatment of Cancer (EORTC)/Soft Tissue and Bone Sarcoma Group (STBSG). *Ann Oncol*. 2017;28(10):2399-2408. doi:10.1093/annonc/mdx323

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Fernandez MM, Bell T, Tumminello B, Khan S, Zhou S, Oton AB. Disease and economic burden of surgery in desmoid tumors: a review. *Expert Rev Pharmacoecon Outcomes Res*. 2023;23(6):607-618. doi:10.1080/14737167.2023.2203915

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SpringWorks CareConnections®

- **SpringWorks CareConnections®** provides personalized support services and resources to help your patients get started and stay on track with **OGSIVEO® (nirogacestat)**
- **Coverage and Access Support**
  - Resources, education, and assistance to support timely access to OGSIVEO
- **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 OGSIVEO by providing you and your office staff regional payor education and timely responses to questions
  - If you have questions about patient access to OGSIVEO and wish to connect with a FAM, please visit **https://springworkstxcares.com/ogsiveo/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) | M-F 8 AM-10 PM ET

or visit our website at springworkstxcares.com/ogsiveo/hcp/about

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

- **Ovarian Toxicity:** Female reproductive function and fertility may be impaired in patients treated with OGSIVEO. Impact on fertility may depend on factors like duration of therapy and state of gonadal function at time of treatment. Long-term effects of OGSIVEO on fertility have not been established. Advise patients on the potential risks for ovarian toxicity before initiating treatment. Monitor patients for changes in menstrual cycle regularity or the development of symptoms of estrogen deficiency, including hot flashes, night sweats, and vaginal dryness.
- **Hepatotoxicity:** ALT or AST elevations occurred in 30% and 33% of patients, respectively. Grade 3 ALT or AST elevations (>5 × ULN) occurred in 6% and 2.9% of patients. Monitor liver function tests regularly and modify dose as recommended.
- **Non-Melanoma Skin Cancers:** New cutaneous squamous cell carcinoma and basal cell carcinoma occurred in 2.9% and 1.4% of patients, respectively. Perform dermatologic evaluations prior to initiation of OGSIVEO and routinely during treatment.
- **Electrolyte Abnormalities:** Decreased phosphate (65%) and potassium (22%) occurred in OGSIVEO-treated patients. Phosphate <2 mg/dL occurred in 20% of patients. Grade 3 decreased potassium occurred in 1.4% of patients. Monitor phosphate and potassium levels regularly and supplement as necessary. Modify dose as recommended.
- **Embryo-Fetal Toxicity:** OGSIVEO can cause fetal harm when administered to pregnant women. Oral administration of nirogacestat to pregnant rats during the period of organogenesis resulted in embryo-fetal toxicity and death at maternal exposures below human exposure at the recommended dose of 150 mg twice daily. Advise pregnant women of the potential risk to a fetus. Advise females and males of reproductive potential to use effective contraception during treatment with OGSIVEO and for 1 week after the last dose.

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IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

- The most common (≥15%) adverse reactions were diarrhea (84%), ovarian toxicity (75% in the 36 females of reproductive potential), rash (68%), nausea (54%), fatigue (54%), stomatitis (39%), headache (30%), abdominal pain (22%), cough (20%), alopecia (19%), upper respiratory tract infection (17%), and dyspnea (16%).
- Serious adverse reactions occurred in 20% of patients who received OGSIVEO. Serious adverse reactions occurring in ≥2% of patients were ovarian toxicity (4%).
- The most common laboratory abnormalities (≥15%) were decreased phosphate, increased urine glucose, increased urine protein, increased AST, increased ALT, and decreased potassium.

DRUG INTERACTIONS

- **CYP3A Inhibitors and Inducers:** Avoid concomitant use with strong or moderate CYP3A inhibitors (including grapefruit products, Seville oranges, and starfruit) and strong or moderate CYP3A inducers.
- **Gastric Acid Reducing Agents:** Avoid concomitant use with proton pump inhibitors and H2 blockers. If concomitant use cannot be avoided, OGSIVEO can be staggered with antacids (e.g., administer OGSIVEO 2 hours before or 2 hours after antacid use).
- Consult the full Prescribing Information prior to and during treatment for important drug interactions.

USE IN SPECIFIC POPULATIONS

- Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with OGSIVEO and for 1 week after the last dose.
- OGSIVEO may reduce the effectiveness of hormonal contraceptives. Addition of a barrier method is recommended for females using hormonal contraceptives.

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

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SpringWorks® THERAPEUTICS

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