nirogacestat (Ogsiveo™)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO296

Description

Nirogacestat (Ogsiveo) is a gamma secretase inhibitor.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
nirogacestat (Ogsiveo)	Desmoid Tumors	50 mg tablets	168 tablets /28 days

Initial Evaluation

I. **Nirogacestat (Osgiveo)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist **AND**
   C. Medication is not used in combination with any other oncology therapy; **AND**
   D. A diagnosis of **desmoid tumors** confirmed by:
      1. An image-guided (CT or ultrasound) core needle or surgical biopsy of the tumor site; **AND**
      2. Confirmation of diagnosis by a soft tissue pathologist; **AND**
      3. Provider attestation that other germline mutation syndromes (i.e., familial adenomatous polyposis [FAP], Gardner syndrome) and/or myofibroblastic diseases (e.g., sarcoma, gastrointestinal stromal tumor, nodular fasciitis, leiomyoma) have been ruled out; **AND**
   E. Documentation of tumor progression within the last 12 months; **AND**
      1. Documentation of significant symptoms (e.g., severe pain); **OR**
      2. Documentation of potential for morbidity (e.g., impairing, or threatening function, physical deformity).

II. Nirogacestat (Ogsiveo) is considered investigational when used for all other conditions, including but not limited to:
   A. Treatment of multiple myeloma
   B. Treatment of ovarian cancer
   C. Treatment in pediatrics and adolescents under the age of 18 years of age
   D. Use of nirogacestat (Ogsiveo) in combination with other oncology therapy

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms (e.g., tumor shrinkage, decreased morbidity, evidence of quality of life, symptoms, and/or functionality improvements)

Supporting Evidence

I. Desmoid tumors (DT), are rare, noncancerous growths, that are unable to metastasize and occur as a result of mutations in fibroblasts of connective tissue. DT can arise anywhere in the body, but most commonly appear in the abdominal/intra-abdominal area. The clinical course is variable, often with an initial growth phase followed by long periods of arrest and regression. Symptoms commonly include pain, fatigue, deformity, and functional impairment. Although non-malignant, DT can progress in size if left untreated and increase the risk of invasion into local organs.
II. The safety profile of nirogacestat (Ogsiveo) was reviewed in one Phase 3, international, double-blind, randomized, placebo controlled (DeFi) trial. Nirogacestat (Ogsiveo) was found to have a less favorable safety profile and resulted in significantly more side effects that led to dose reductions and permanent discontinuations compared to placebo. The nirogacestat (Ogsiveo) arm had a 42% dose reduction and 20% permanent discontinuation rate (versus 0% and 1% in the placebo arm, respectively) due to intolerable adverse events (AE). Split fill management is therefore recommended to reduce waste of unused medication due to a high risk of AE incidence, dose reduction, or permanent discontinuation with nirogacestat (Ogsiveo).
III. Safety and efficacy for an increased dosing frequency above the FDA-approved dose of 150mg twice daily has not been studied nor well-established.
IV. Safety and efficacy of nirogacestat (Ogsiveo) use in patients under the age of 18 has not been well-established. A Phase 2, interventional study to evaluate the efficacy and safety of nirogacestat (Ogsiveo) in pediatric patients 12 months to 18 years of age is expected to be completed by December of 2024. However, there is currently a lack of sufficient evidence or additional scientific literature to support the use of nirogacestat (Ogsiveo) in members <18 years of age.
V. Due to rarity of disease and association with other germline mutation syndromes (i.e., familial adenomatous polyposis [FAP], Gardner syndrome), it is essential to rule out potential for differential diagnosis without association to desmoid tumors (e.g., Gardner syndrome). DT also shares similarities with other myofibroblastic diseases (e.g., sarcoma, gastrointestinal stromal tumor, nodular fasciitis, leiomyoma) with 30% to 40% of DT cases reported to be misdiagnosed following histologic analysis.

VI. The use of nirogacestat (Ogsiveo) has not been studied in combination with other chemotherapy agents (e.g., methotrexate and vinorelbine) or tyrosine kinase inhibitors (TKI's) such as sorafenib. Due to the lack of safety and efficacy data with a combination regimen, use of nirogacestat (Ogsiveo) is not recommend with any other oncology therapy.

VII. A definitive diagnosis of DT requires histopathologic analysis of a biopsy sample of the tumor which is examined for presence of desmoid cells. Both DTWG (2020) and NCCN soft tissue sarcoma (2023) guidelines recommend a histological diagnosis of DT via an image-guided (CT or ultrasound) core needle or surgical biopsy of the tumor site. Due to rarity of disease and association with other germline mutation syndromes (i.e., familial adenomatous polyposis [FAP], Gardner syndrome), it is essential to rule out potential for differential diagnosis without association to desmoid tumors (e.g., Gardner syndrome). Desmoid Tumors also shares similarities with other myofibroblastic diseases (e.g., sarcoma, gastrointestinal stromal tumor, nodular fasciitis, leiomyoma) with 30% to 40% of DT cases reported to be misdiagnosed following histologic analysis. NCCN guidelines recommend evaluation and treatment by a multidisciplinary team with expertise and experience in desmoid tumors; however, DTWG guidelines require confirmation of diagnosis by a soft tissue pathologist.

VIII. Both DTWG (2020) and NCCN (V 2.2023) guidelines recommend active surveillance/observation alone until the tumor has shown progression and is accompanied by significant symptom burden, at which point, active treatment is pursued. NCCN guidelines also recommend active treatment if progression of DT is accompanied by potential for morbidity. The FDA-approved indication of nirogacestat (Ogsiveo) is specific to adult patients with progressing desmoid tumors. This indication is supported by the DeFi clinical trial which included patients with histologically confirmed diagnosis of progressing desmoid tumors within 12 months before screening. There is insufficient evidence to support the use of nirogacestat (Ogsiveo) in patients with nonprogressive DT at this time. Although guidelines also recommend earlier active treatment in the case of nonprogressive DT in anatomical locations where progression of the tumor would be morbid, there's insufficient evidence to support nirogacestat (Ogsiveo) as the treatment of choice in this scenario.

IX. In the Phase 3, international, double-blind randomized, placebo controlled (DeFi) trial, eligible patients were required to have progressing DT and either had not received previous treatment for progressing DT that were not amenable to surgery or had refractory or recurrent DT after at least one line of therapy. Median subject age was 34 years, majority female (64%), with *CTNNB1* genetic mutation (61%), and extra-abdominal tumor-location (76%). The majority had received previous treatment (74%) with a median of two lines of previous therapy. Treatments included surgery (44%), radiation therapy (23%), chemotherapy (34%), and TKIs (33%) with sorafenib being the most common TKI received (24%). The primary outcome was progression-free survival (PFS). Secondary endpoints included objective response rate (ORR) and patient-reported outcomes. Results showed a statistically significant 71% reduction of disease risk progression in subjects who received nirogacestat (Ogsiveo) in 28-day cycles versus subjects who received

placebo (hazard ratio [HR] = 0.29; p< 0.001). However, data is of low/uncertain value for clinical decision-making, as the primary and objective secondary outcomes are surrogate endpoints and are not validated to correlate with morbidity, mortality, quality of life, symptom, or functionality improvements. Although the study found statistically and clinically significant differences in favor of nirogacestat (Ogsiveo) compared to placebo in patient-reported outcomes at cycle 10, there remains uncertainty in whether clinically meaningful results were attained throughout the course of treatment as only cycle 10 data is reported.

Investigational or Not Medically Necessary Uses

I. Nirogacestat (Ogsiveo) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Multiple myeloma
      i. A phase 1b interventional study of belantamab mafodotin in combination with nirogacestat (Ogsiveo) and pomalidomide in patients with multiple myeloma is currently in the recruitment phase and is estimated to be completed by October of 2026. There is currently a lack of sufficient evidence or additional scientific literature to support the use of nirogacestat (Ogsiveo) in multiple myeloma.
   B. Ovarian Cancer
      i. A phase 2 interventional study of nirogacestat (Ogsiveo) in ovarian granulosa cell tumors is currently in the active phase and is expected to be completed by July of 2026. There is currently a lack of sufficient evidence or additional scientific literature to support the use of nirogacestat (Ogsiveo) in ovarian cancer.
   C. Pediatrics and adolescents under the age of 18 years old
      i. A phase 2 interventional study to evaluate the efficacy and safety of nirogacestat (Ogsiveo) in pediatric patients >12 months to 18 years of age is currently in the active phase and is expected to be completed by December of 2024. There is currently a lack of sufficient evidence or additional scientific literature to support the use of nirogacestat (Ogsiveo) in members <18 years of age.
   D. Use of nirogacestat (Ogsiveo) in combination with other oncology therapy
      i. There are currently no ongoing or active trials to study the use of nirogacestat (Ogsiveo) in combination with other oncology therapy. There is currently a lack of additional scientific literature to support the use of nirogacestat (Ogsiveo) in combination with other chemotherapy agents.

References

1. OGSIVEO. Prescribing Information. SpringWorks Therapeutics, Inc; 2023
2. Unapproved nirogacestat (Ogsiveo) Dossier. SpringWorks Therapeutics. May, 2023
3. Approved nirogacestat (Ogsiveo) Dossier. SpringWorks Therapeutics. December, 2023.

4. National Comprehensive Cancer Network. Soft Tissue Sarcoma (Version 3.2023). NCCN. Updated December 12, 2023. Accessed December 18, 2023. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf
5. 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
6. Nieuwenhuis MH, Lefevre JH, Bülow S, et al. Family history, surgery, and APC mutation are risk factors for desmoid tumors in familial adenomatous polyposis: an international cohort study. Dis Colon Rectum. 2011;54(10):1229-1234. doi:10.1097/DCR.0b013e318227e4e8
7. Nooka AK, Weisel K, van de Donk NW, et al. Belantamab mafodotin in combination with novel agents in relapsed/refractory multiple myeloma: DREAMM-5 study design. Future Oncol. 2021;17(16):1987-2003. doi:10.2217/fon-2020-1269
8. Children's Oncology Group. A Study of a New Drug, Nirogacestat, for Treating Desmoid Tumors That Cannot be Removed by Surgery. Clinicaltrial.gov. December 11, 2019. Updated November 11, 2023. Accessed December 19, 2023. https://clinicaltrials.gov/study/NCT04195399

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy name	Disease State
Multi-Targeted Tyrosine Kinase Inhibitors (Multi-TKI)	Desmoid Tumor

Policy Implementation/Update:

Action and Summary of Changes	Date
Removed mutational analysis requirement from diagnosis of desmoid tumors	03/2024
Policy created	02/2024