A Guide to Proactively Managing Patients Treated With OGSIVEO

The first and only FDA-approved targeted therapy for adult patients with progressing desmoid tumors who require systemic treatment

OGSIVEO is the #1 prescribed systemic therapy for adults with desmoid tumors[1]

NCCN CATEGORY 1 PREFERRED

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).[2]

FDA, US Food and Drug Administration; NCCN, National Comprehensive Cancer Network® (NCCN®).

Learn more about 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 Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

Helping your patients start and stay on track with **OGSIVEO**

You play an important part in your patient's OGSIVEO journey.

A key aspect of patient care involves a thorough understanding of the safety profile of the drug and how to proactively manage potential side effects that may emerge.

This resource aims to support you and your patients during treatment by offering information regarding OGSIVEO safety considerations. It also provides strategies for helping patients stay on track with their therapy, including recommended dose modifications to help manage certain adverse reactions.

Table of Contents

Please see Important Safety Information throughout and click here for full Prescribing Information.

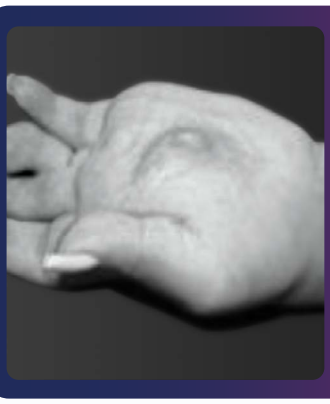
Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

Desmoid tumors are locally aggressive, potentially morbid soft tissue tumors that can infiltrate surrounding structures[3–5]

Examples of desmoid tumors and potential symptoms

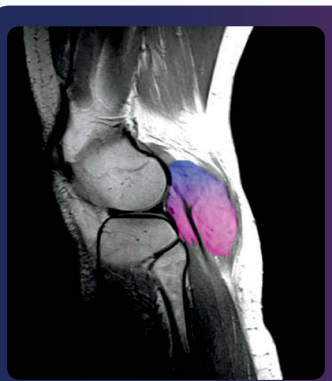
Back

Large desmoid tumor (15 cm x 10 cm) proximal to the spine[6,*]



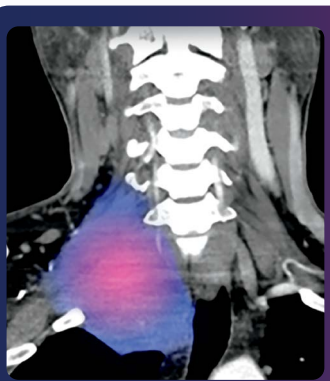
Hand

Desmoid tumor causing severe restriction in the flexion of the hand[7,†]



Knee

MRI scan showing desmoid tumor behind the right knee associated with electric paresthesias and reduced flexion[8,‡]



Neck

CT scan showing desmoid tumor in the right upper neck involving the brachial plexus associated with pain, numbness, and weakness in the right arm[9,§]

Surgery is no longer recommended by guidelines as first-line treatment for most clinical situations[2,10]

Up to 77% recurrence rates after surgical resection of desmoid tumors[11,12,‖]

*Image adapted from Cohen S, et al. *World J Surg Oncol.* 2008;6:28. Reused under Creative Commons License 2.0 (https://creativecommons.org/licenses/by/2.0). Image background changed to gray.

†Image reproduced from Scaramussa FS, et al. *SM J Orthop.* 2016;2(3):1036. Reused under Creative Commons License 4.0 (https://creativecommons.org/licenses/by/4.0).

‡Image adapted from Weschenfelder W, et al. *Case Rep Surg.* 2015;2015:262654. Reused under Creative Commons License 3.0 (https://creativecommons.org/licenses/by/3.0). False color added.

§Image adapted from Styring E, et al. *Am J Med Case Rep.* 2019;7(3):36-40. Reused under Creative Commons License 4.0 (https://creativecommons.org/licenses/by/4.0). False color added.

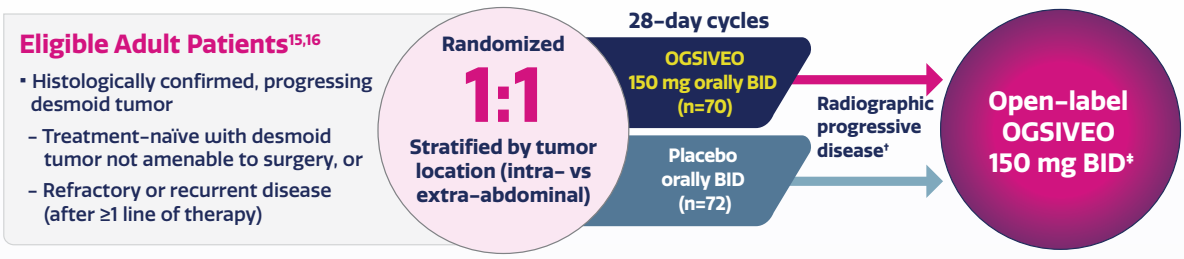
‖Based on retrospective, observational data. Factors associated with local recurrence postsurgery include tumor location, age of the patient, tumor size, margin status, and prior recurrence.[13,14]

CT, computed tomography; MRI, magnetic resonance imaging.

OGSIVEO was evaluated in the landmark DeFi trial—the largest completed* Phase 3 study in adult patients with desmoid tumors

The primary analysis from the landmark DeFi study was published in *The New England Journal of Medicine*

DeFi: An international, multicenter, randomized (1:1), double-blind, placebo-controlled, Phase 3 study of OGSIVEO in patients with progressing desmoid tumors not amenable to surgery. Patients had treatment-naïve, refractory, or recurrent disease (N=142).[15,16]



- All patients had histologically confirmed desmoid tumors that had progressed ≥20% by RECIST v1.1 within 12 months before screening[15]
- If patients had multiple target tumors that were located in the intra- and extra-abdominal locations, they were classified as intra-abdominal[15]
- Patients were randomized to receive 150 mg OGSIVEO or placebo orally twice daily until disease progression or unacceptable toxicity[16]
- Tumor imaging occurred every 3 months[16]

Primary End Point	Key Secondary Efficacy End Points§
▪ **Progression-Free Survival:** Progression-free survival was defined as the time from randomization until the date of imaging-based or clinical progression or death. Progression-free survival was based on RECIST v1.1 as assessed by blinded independent central review or on clinical progression by the investigator (and confirmed by independent review). Clinical progression required worsening of symptoms resulting in a global deterioration of health status causing the permanent discontinuation from trial treatment and the initiation of emergent treatment (e.g., radiotherapy, surgery, or systemic therapy including chemotherapy or tyrosine kinase inhibitors) for desmoid tumors.[15,16]	▪ **Objective Response Rate:** Objective response rate was defined as complete response or partial response according to RECIST v1.1. Assessed by blinded independent central review.‖ Partial response was defined as a ≥30% decrease in the sum of the longest diameters of target tumors. Complete response was defined as disappearance of all target and non-target tumors.[15,16] ▪ **Worst Pain Intensity (change from baseline at Cycle 10¶):** Patient-reported worst pain intensity was assessed daily using item 3 of the Brief Pain Inventory-Short Form (BPI-SF), an 11-point numerical rating scale ranging from 0 ("no pain") to 10 ("pain as bad as you can imagine") and averaged over 7 days prior to each visit.[15,16]

*Completed double-blind, randomized, Phase 3 trial in adult patients with desmoid tumors.[15,16]

†Imaging-based progression or completion of the primary analysis.[15]

‡Eligible patients were given the option to enroll in the open-label extension phase.[15]

§Additional secondary efficacy end points were evaluated in the DeFi study.[15]

‖Confirmed by repeat assessments that were performed no less than 4 weeks after the criteria for response were first met.[15]

¶Each cycle was 28 days.[15]

Long-term post-hoc analysis of the DeFi study: Patients from both the placebo and OGSIVEO treatment arms were eligible to enroll in the open-label extension phase and receive OGSIVEO 150 mg BID.[17]

A post-hoc analysis at annual milestones of 1 (n=46), 2 (n=40), 3 (n=33), and 4 (n=15) years for patients who initially received OGSIVEO was conducted.[17,#]

#Data cut-off date was August 13, 2024.[17]

BID, twice daily; DeFi, Desmoid Fibromatosis; RECIST, Response Evaluation Criteria in Solid Tumors.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

OGSIVEO demonstrated powerful efficacy in DeFi

71%

Significant PFS improvement

71% reduction in the risk of disease progression or death vs placebo (HR=0.29; 95% CI: 0.15, 0.55; *P*<0.001*,†).[15]

- Median PFS in the OGSIVEO arm was not reached (95% CI: NR, NR) compared with 15.1 months (95% CI: 8.4, NR) in the placebo arm[16,‡,§]
  - PFS events occurred in 12 patients (17%) in the OGSIVEO arm and 37 patients (51%) in the placebo arm[16]

41%

Statistically significant response vs placebo

41% objective response rate vs 8% with placebo

- CR: OGSIVEO (7%) vs placebo (0%)
- PR: OGSIVEO (34%) vs placebo (8%)

Reduced worst pain intensity

PFS results were supported by change from baseline in **patient-reported worst pain intensity favoring the OGSIVEO arm††**

Time to response (exploratory end point): Median time to objective response was 5.6 months with OGSIVEO (range: 2.6 to 19.4 months) vs 11.1 months with placebo (range: 2.8 to 16.4 months)[15,‡‡]

Analysis Limitations

- Time to objective response was an exploratory end point in the DeFi study
- This end point was not powered for statistical analysis and should be considered descriptive only
- Therefore, the results require cautious interpretation and could represent chance findings
- These data are not included in the OGSIVEO Prescribing Information

**P*-value was from a one-sided stratified log-rank test with placebo as reference.[16]

†Progression-free survival was defined as the time from randomization until the date of imaging-based or clinical progression or death. Progression-free survival was based on RECIST v1.1 as assessed by blinded independent central review or on clinical progression by the investigator (and confirmed by independent review). Clinical progression required worsening of symptoms resulting in a global deterioration of health status causing the permanent discontinuation from trial treatment and the initiation of emergent treatment (e.g., radiotherapy, surgery, or systemic therapy including chemotherapy or tyrosine kinase inhibitors) for desmoid tumors.[15,16]

‡Data cut-off as of April 7, 2022 for PFS.[15]

§Obtained using Kaplan-Meier methodology.[16]

‖Objective response rate was defined as complete response or partial response according to RECIST v1.1. Assessed by blinded independent central review. Partial response was defined as a ≥30% decrease in the sum of the longest diameters of target tumors. Complete response was defined as disappearance of all target and non-target tumors. PR and CR required confirmation by subsequent scans.[15,16]

¶Obtained using exact method based on binomial distribution.[16]

#*P*-value was from a two-sided Cochran-Mantel-Haenszel test.[16]

**Desmoid tumors can have an unpredictable course and may exhibit spontaneous regression.[4]

††Patient-reported worst pain intensity was assessed daily using item 3 of the BPI-SF, an 11-point numerical rating scale ranging from 0 ("no pain") to 10 ("pain as bad as you can imagine") and averaged over 7 days prior to each visit.[15,16]

‡‡Median time to objective response was calculated as time in months from first dose until date of the first documented response (CR or PR).[15]

BPI-SF, Brief Pain Inventory-Short Form; CI, confidence interval; CR, complete response; DeFi, Desmoid Fibromatosis; HR, hazard ratio; LS, least squares; OLE, open-label extension; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; TEAE, treatment-emergent adverse event.

OGSIVEO safety information

- Warnings and Precautions: diarrhea, ovarian toxicity, hepatotoxicity, non-melanoma skin cancers, electrolyte abnormalities, and embryo-fetal toxicity[16]
- The most common (≥15% with a difference between arms of ≥5% compared to placebo) adverse reactions that occurred in patients receiving OGSIVEO were diarrhea, ovarian toxicity, rash, nausea, fatigue, stomatitis, headache, abdominal pain, cough, alopecia, upper respiratory tract infection, and dyspnea[16]
- Most adverse events were Grade 1 or 2 and occurred within 1 month of starting OGSIVEO[15]

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

OGSIVEO offers convenient oral dosing[16]

The recommended dosage of OGSIVEO is 150 mg administered orally twice daily until disease progression or unacceptable toxicity

OGSIVEO may be taken **with or without food**

Instruct patients to **swallow OGSIVEO tablets whole** and not to break, crush, or chew prior to swallowing

Avoid concomitant use of OGSIVEO with **grapefruit products, Seville oranges, and starfruit**

If a patient vomits or misses a dose, instruct the patient to take the next dose at its scheduled time.

OGSIVEO is available in 150 mg and 100 mg tablets in blister packs

- Each blister pack contains a **7-day supply**
- Four blister packs provide a **28-day supply**

Blister packs may help simplify tracking of AM/PM dosing

OGSIVEO 150 mg BID
Recommended starting dose

150 mg tablet

Tablets shown are not actual size.

OGSIVEO 100 mg BID
Recommended for dose modifications for certain adverse reactions

100 mg tablet

Tablets shown are not actual size.

BID, twice daily.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

Adverse reactions in the DeFi trial

95% of adverse events were Grade 1 or 2 and first onset for most patients occurred within 1 month of starting OGSIVEO[15]

Adverse reactions (≥15%) in patients with desmoid tumor who received OGSIVEO with a difference between arms of ≥5% compared to placebo in DeFi[16]

		OGSIVEO (n=69)		Placebo (n=72)	
Adverse Reaction		**All Grades**	**Grade 3**	**All Grades**	**Grade 3**
Gastrointestinal	**Diarrhea**	**84%**	**16%**	35%	1.4%
	Nausea	**54%**	**1.4%**	39%	0
	Stomatitis*	**39%**	**4%**	4%	0
	Abdominal pain*	**22%**	**1.4%**	14%	1.4%
Reproductive system	**Ovarian toxicity*,†**	**75%‡**	**0**	0	0
Skin and subcutaneous tissue	**Rash***	**68%**	**6%**	14%	0
	Alopecia	**19%**	**0**	1.4%	0
General	**Fatigue***	**54%**	**2.9%**	38%	0
Nervous system	**Headache***	**30%**	**0**	15%	0
Respiratory	**Cough***	**20%**	**0**	6%	0
	Dyspnea	**16%**	**0**	6%	0
Infections	**Upper respiratory tract infection***	**17%**	**0**	2.8%	0

- In the DeFi trial, the median duration of exposure for OGSIVEO was 20.6 months (range: 0.3 to 33.6 months)[16]
- Clinically relevant adverse reactions occurring in <15% of patients receiving OGSIVEO in DeFi included non-melanoma skin cancers, epistaxis, hidradenitis suppurativa, folliculitis, and influenza-like illness[16]

- **Warnings and Precautions** associated with OGSIVEO include diarrhea, ovarian toxicity, hepatotoxicity, non-melanoma skin cancers, electrolyte abnormalities, and embryo-fetal toxicity[16]
- **The most common adverse reactions** (≥15%) in patients receiving OGSIVEO in the DeFi study 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%)[16]
- **Serious adverse reactions** occurred in 20% of patients who received OGSIVEO. Serious adverse reactions occurring in ≥2% of patients were ovarian toxicity (4%)[16]

*Includes multiple related composite terms.[16]

†Investigator assessment of ovarian toxicity included ovarian failure, premature menopause, amenorrhea, and menopause.[16]

‡The number of females of reproductive potential in each arm is used as the denominator (OGSIVEO N=36, placebo N=37).[16]

DeFi, Desmoid Fibromatosis.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

Proactive monitoring and management can help support patients receiving **OGSIVEO**

Effects of other drugs on OGSIVEO[16]

- **Strong or moderate CYP3A inhibitors:** OGSIVEO is a CYP3A substrate. Strong or moderate CYP3A inhibitors increase OGSIVEO exposure, which may increase the risk of OGSIVEO adverse reactions. Avoid concomitant use of OGSIVEO with strong or moderate CYP3A inhibitors, including grapefruit products, Seville oranges, and starfruit
- **Strong or moderate CYP3A inducers:** OGSIVEO is a CYP3A substrate. Strong or moderate CYP3A inducers decrease serum OGSIVEO exposure, which may reduce the effectiveness of OGSIVEO. Avoid concomitant use of OGSIVEO with strong or moderate CYP3A inducers
- **Gastric acid reducing agents:** OGSIVEO is poorly soluble at pH ≥6. Gastric acid reducing agents may decrease serum OGSIVEO exposure, which may reduce the effectiveness of OGSIVEO. 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)*,†
- For additional information about potential drug interactions with OGSIVEO, see Table 4 (Section 7.1) and Table 5 (Section 7.2) of the full Prescribing Information

*Gastric acid reducing agents include PPIs (e.g., omeprazole, lansoprazole, esomeprazole), H2 blockers (eg, cimetidine, famotidine, nizatidine), and antacids (e.g., Mylanta®, Rolaids®, Tums®). In accordance with the guidance in the OGSIVEO Prescribing Information, antacids should be administered either 2 hours before or 2 hours after OGSIVEO.

†Prior to use of any concomitant medication, please refer to Section 7 (Drug Interactions) of the OGSIVEO Prescribing Information.

Recommended dose modifications for adverse reactions[16]

Adverse Reaction	Severity	OGSIVEO Dosage Modifications
Diarrhea persisting for ≥3 days despite maximal medical therapy	**Grades 3 or 4**	Withhold OGSIVEO until resolved to Grade ≤1 or baseline, then restart at a dose of 100 mg twice daily.
ALT or AST increased	**Grade 2 (≥3 to 5 x ULN)**	Withhold OGSIVEO until ALT, AST, or both are resolved to <3 × ULN or baseline, then restart at a dose of 100 mg twice daily.
	Grades 3 or 4 (>5 x ULN)	Permanently discontinue.
Hypophosphatemia persisting for ≥3 days despite maximal replacement therapy	**Grades 3 or 4**	Withhold OGSIVEO until resolved to Grade ≤1 or baseline, then restart at a dose of 100 mg twice daily.
Hypokalemia despite maximal replacement therapy		

For other severe adverse reactions, life-threatening adverse reactions, or persistent intolerable Grade 2 adverse events, withhold drug until resolved to Grade ≤1 or baseline. Only restart at a dose of 100 mg twice daily after considering the potential benefit and likelihood of recurrence of the adverse reaction. Permanently discontinue OGSIVEO for recurrence of severe or life-threatening adverse reaction upon rechallenge at the reduced dose.[16]

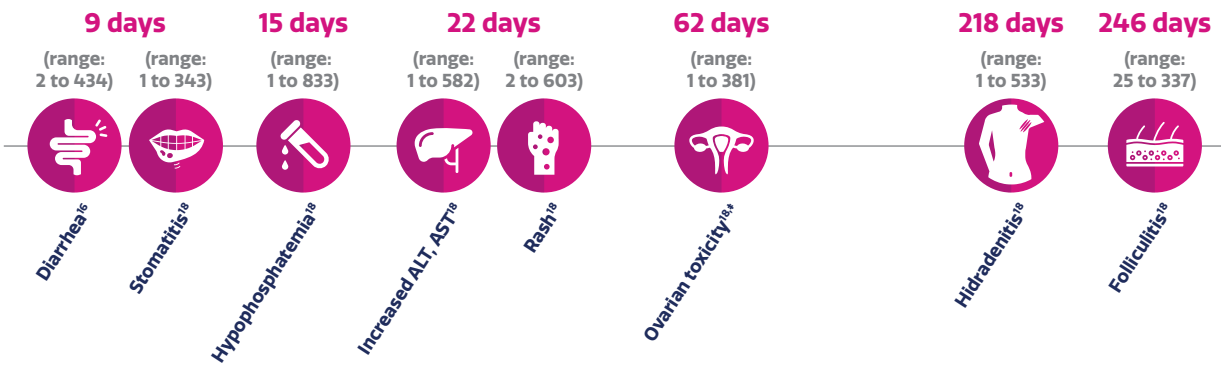
ALT, alanine aminotransferase; AST, aspartate aminotransferase; PPIs, proton pump inhibitors; ULN, upper limit of normal.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

Setting expectations at treatment initiation may help patients stay on track with therapy

Median time to onset of adverse reactions that led to dose reductions or discontinuations in ≥2% of patients receiving OGSIVEO in the DeFi study[16,18,*]

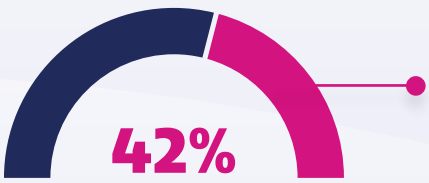


*In patients who received OGSIVEO in the DeFi trial, 42% had dose reductions, 51% had dose interruptions, and 20% permanently discontinued due to an adverse reaction. Adverse reactions that led to dose reduction, interruption, or discontinuation in ≥2% of patients receiving OGSIVEO included: diarrhea, ovarian toxicity, increased ALT/AST, rash, stomatitis, hypophosphatemia, fatigue, folliculitis, nausea, and hidradenitis.[16]

†In DeFi, ovarian toxicity was identified by investigators in females of reproductive potential based on abnormal reproductive hormone values or presence of perimenopausal symptoms (e.g., changes in menstrual cycle regularity), or both.[19]

These are not all the possible side effects of OGSIVEO. Patients should consult their doctor for medical advice about side effects.

150 mg BID → **until disease progression or unacceptable toxicity[16]**



In patients who received OGSIVEO in the DeFi trial:

42% had dose reductions due to an adverse reaction[16,‡]

51% had dose interruptions (median days interrupted per interruption: 8 days; range: 1 to 132 days) and 20% permanently discontinued due to an adverse reaction.[16,18,‡]

‡Adverse reactions that led to dose reduction, interruption, or discontinuation of OGSIVEO included: diarrhea, ovarian toxicity, increased ALT/AST, rash, stomatitis, hypophosphatemia, fatigue, folliculitis, nausea, and hidradenitis.[16]

For patients who were dose-reduced to 100 mg BID, no notable differences in PFS or ORR were observed[18]

Analysis Limitations

- Based on a post hoc analysis comparing PFS and ORR in patients treated with OGSIVEO in the DeFi study who dose-reduced versus those who did not
- DeFi was not powered to assess statistical differences between subgroups and this analysis should be considered descriptive only
- Therefore, the results require cautious interpretation and could represent chance findings
- These data are not included in the OGSIVEO Prescribing Information

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; DeFi, Desmoid Fibromatosis; ORR, objective response rate; PFS, progression-free survival.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

OGSIVEO can cause diarrhea, which may occur early and be severe

In the DeFi trial:

Adverse Reaction[16]	OGSIVEO (n=69)	
	All Grades	Grade 3
Diarrhea	84%	16%

- **Median time to first onset:** 9 days (range: 2 to 434 days)[16]
- **Median duration:** 26 days (range: 1 to 930 days)[18]
- **Investigator-reported resolution:** Resolution occurred in most patients who received treatment. Outcomes at time of analysis also included unresolved events and resolution with sequelae[18]

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
CTCAE Diarrhea[20]	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 – 6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of ≥7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated	Death

Counseling and intervention:

Advise patients that OGSIVEO can cause diarrhea, which may be severe, and to contact their care team for sustained diarrhea that does not respond to supportive care.[16]

Monitor and manage using antidiarrheal medications.[16]

In DeFi, 62% of patients experiencing diarrhea on OGSIVEO received concomitant medication.[18]

Dosage Modifications for Diarrhea Grades 3 or 4 Severity

Diarrhea persisting for ≥3 days despite maximal medical therapy, **withhold** OGSIVEO until resolved to Grade ≤1 or baseline, then **restart** at a dose of 100 mg twice daily.[16]

Permanently discontinue OGSIVEO for recurrence of severe or life-threatening adverse reaction upon rechallenge at the reduced dose.

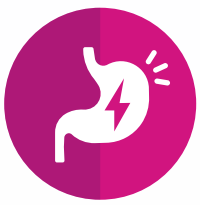
ADL, activities of daily living; CTCAE, Common Terminology Criteria for Adverse Events.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

Nausea and abdominal pain associated with **OGSIVEO**

In the DeFi trial:



Adverse Reaction[16]	OGSIVEO (n=69)	
	All Grades	Grade 3
Nausea	54%	1.4%
Abdominal pain*	22%	1.4%

*Includes multiple related composite terms.

	Grade 1	Grade 2	Grade 3
CTCAE Nausea[20,†]	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated
CTCAE Abdominal pain[20,†]	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self care ADL

†Grades 4 and 5 are not defined.

Counseling and intervention:

Advise patients to contact their care team for medical advice about side effects.[16]

Dosage Modifications for Abdominal Pain

For severe adverse reactions, life-threatening adverse reactions, or persistent intolerable Grade 2 adverse events, withhold drug until resolved to Grade ≤1 or baseline.

Only **restart** at a dose of 100 mg twice daily after considering the potential benefit and likelihood of recurrence of the adverse reaction.[16]

Permanently discontinue OGSIVEO for recurrence of severe or life-threatening adverse reaction upon rechallenge at the reduced dose.

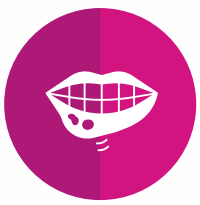
ADL, activities of daily living; CTCAE, Common Terminology Criteria for Adverse Events; TPN, total parenteral nutrition.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

Stomatitis (oral mucositis) with OGSIVEO

In the DeFi trial:



Adverse Reaction[16]	OGSIVEO (n=69)	
	All Grades	Grade 3
Stomatitis*	39%	4%

*Includes multiple related composite terms.

- **Median time to first onset:** 9 days (range: 1 to 343 days)[18]
- **Median duration:** 33 days (range: -28† to 993 days)[18]
- **Investigator-reported resolution:** Resolution occurred in most patients who received treatment[18]
- Most stomatitis events resolved, although 7 participants in the nirogacestat arm had not recovered at the time of database lock[18]

†Negative value due to imputation rule at time of the analysis.

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
CTCAE Mucositis Oral (stomatitis)[20]	Asymptomatic or mild symptoms; intervention not indicated	Moderate pain or ulcer that does not interfere with oral intake; modified diet indicated	Severe pain; interfering with oral intake	Life-threatening consequences; urgent intervention indicated	Death

Counseling and intervention:

Advise patients to contact their care team for medical advice about side effects.[16]

In DeFi, 67% of patients experiencing stomatitis on OGSIVEO received concomitant medication, typically oral rinses, topical anesthetics, and topical steroids.[18]

Dosage Modifications for Stomatitis

Withhold drug until resolved to Grade ≤1 or baseline for severe adverse reactions, life-threatening adverse reactions, or persistent intolerable Grade 2 adverse events.

Only **restart** at a dose of 100 mg twice daily after considering the potential benefit and likelihood of recurrence of the adverse reaction.[16]

Permanently discontinue OGSIVEO for recurrence of severe or life-threatening adverse reaction upon rechallenge at the reduced dose.

CTCAE, Common Terminology Criteria for Adverse Events.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

Monitor for laboratory abnormalities regularly

Laboratory abnormalities (≥15%) reported in DeFi[16]				
	OGSIVEO (n=69)		Placebo (n=72)	
Laboratory Abnormality	**All Grades**	**Grade 3 or 4**	**All Grades**	**Grade 3 or 4**
Decreased phosphate*,†	**65%**	**Not Applicable**	11%	Not Applicable
Increased urine glucose‡,§	**51%**	**Not Applicable**	0	Not Applicable
Increased urine protein‡	**40%**	**0**	25%	0
Increased aspartate aminotransferase*	**33%**	**2.9%**	18%	1.4%
Increased alanine aminotransferase*	**30%**	**6%**	21%	1.4%
Decreased potassium*	**22%**	**1.4%**	4.2%	0

*The denominator used to calculate the rate was 69 for nirogacestat and 72 for placebo based on the number of patients with a baseline value and at least one post-treatment value.

†CTCAE Version 5.0 does not include numeric thresholds for grading of hypophosphatemia; all grades represent patients with lab value < lower limit of normal (LLN).

‡The denominator used to calculate the rate was 68 for nirogacestat and 69 for placebo based on the number of patients with a baseline value and at least one post-treatment value.

§CTCAE Version 5.0 does not include numeric thresholds for grading of increased urine glucose.

- OGSIVEO can cause electrolyte abnormalities[16]
  - Monitor phosphate and potassium levels regularly and supplement as necessary. Modify dose as recommended
- OGSIVEO can cause elevation of liver transaminases ALT or AST[16]
  - Monitor liver function tests regularly and modify dose as recommended

Not an actual patient.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

Hypophosphatemia is common with **OGSIVEO**

In the DeFi trial:

Laboratory Abnormality	OGSIVEO (n=69)	
	All Grades	Grade 3 or 4
Decreased phosphate*,†	65%	NA

*The denominator used to calculate the rate was 69 for OGSIVEO and 72 for placebo based on the number of patients with a baseline value and at least one post-treatment value.

†CTCAE Version 5.0 does not include numeric thresholds for grading of hypophosphatemia; all grades represent patients with lab value < lower limit of normal (LLN).

- **Phosphate <2 mg/dL** occurred in 20% of patients who received OGSIVEO[16]
- **Median time to first onset:** 15 days (range: 1 to 833 days)[18]
- **Median duration:** 62.5 days (range: 2 to 764 days)[18]
- **Investigator-reported resolution:** Resolution occurred in most patients who received treatment. Outcomes at time of analysis also included unresolved events and resolution with sequelae[18]

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
CTCAE Hypophosphatemia[20]	Laboratory finding only and intervention not indicated	Oral replacement therapy indicated	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated	Life-threatening consequences	Death

Counseling and intervention:

Advise patients that OGSIVEO can cause hypophosphatemia, which may require phosphate supplementation.

Advise patients to contact their care team if they experience muscle pain or weakness.[16]

Monitor phosphate levels regularly and supplement as necessary.[16]

In DeFi, 72% of patients experiencing hypophosphatemia on OGSIVEO received concomitant medication, most commonly supplement formulations.[18]

Dosage Modifications for Hypophosphatemia Grades 3 or 4 Severity

Hypophosphatemia persisting for ≥3 days despite maximal replacement therapy, **withhold** OGSIVEO until resolved to Grade ≤1 or baseline, then **restart** at a dose of 100 mg twice daily.[16]

Permanently discontinue OGSIVEO for recurrence of severe or life-threatening adverse reaction upon rechallenge at the reduced dose.

CTCAE, Common Terminology Criteria for Adverse Events.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

Monitor for hypokalemia

In the DeFi trial:

Laboratory Abnormality	OGSIVEO (n=69)	
	All Grades	Grade 3 or 4
Decreased potassium*	22%	1.4%

*The denominator used to calculate the rate was 69 for OGSIVEO and 72 for placebo based on the number of patients with a baseline value and at least one post-treatment value.

- **Median time to first onset:** 15 days (range: 1 to 57 days)[18]
- **Median duration:** 14 days (range: 8 to 512 days)[18]
- **Investigator-reported resolution:** Resolution occurred in most patients who received treatment. Outcomes at the time of analysis also included unresolved events and resolution with sequelae[18]

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
CTCAE Hypokalemia[20]	<LLN – 3.0 mmol/L	Symptomatic with <LLN – 3.0 mmol/L; intervention indicated	<3.0 – 2.5 mmol/L; hospitalization indicated	<2.5 mmol/L; life-threatening consequences	Death

Counseling and intervention:

Advise patients that OGSIVEO can cause hypokalemia, which may require potassium supplementation.

Advise patients to contact their care team if they experience muscle pain or weakness.[16]

Monitor potassium levels regularly and supplement as necessary.[16]

Dosage Modifications for Hypokalemia Grades 3 or 4 Severity

Hypokalemia despite maximal replacement therapy, **withhold** OGSIVEO until resolved to Grade ≤1 or baseline, then **restart** at a dose of 100 mg twice daily.[16]

Permanently discontinue OGSIVEO for recurrence of severe or life-threatening adverse reaction upon rechallenge at the reduced dose.

CTCAE, Common Terminology Criteria for Adverse Events; LLN, lower limit of normal.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

Monitor liver enzymes

In the DeFi trial:

Laboratory Abnormality	OGSIVEO (n=69)	
	All Grades	Grade 3 or 4
Increased AST*	33%	2.9%
Increased ALT*	30%	6%

*The denominator used to calculate the rate was 69 for OGSIVEO and 72 for placebo based on the number of patients with a baseline value and at least one post-treatment value.

- **Median time to first onset:** 22 days (range: 1 to 582 days)[18]
- **Median duration:** 29 days (range: 2 to 747 days)[18]
- **Investigator-reported resolution**: Resolution occurred in most patients who received treatment. Outcomes at time of analysis also included unresolved events and resolution with sequelae[18]

	Grade 1	Grade 2	Grade 3	Grade 4
CTCAE Increased ALT/AST[20,†]	>ULN – 3.0 x ULN if baseline was normal; 1.5 – 3.0 x baseline if baseline was abnormal	>3.0 – 5.0 x ULN if baseline was normal; >3.0 – 5.0 x baseline if baseline was abnormal	>5.0 – 20.0 x ULN if baseline was normal; >5.0 – 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal

†Grade 5 is not defined.

Counseling and intervention:

Advise patients that OGSIVEO can cause ALT or AST elevations and that they will be monitored for this.[16]

Monitor liver function tests regularly and modify dose as recommended.[16]

Dosage Modifications for Increased ALT or AST
Grade 2 Severity

Withhold OGSIVEO until ALT, AST, or both are resolved to <3 × ULN or baseline, then **restart** at a dose of 100 mg twice daily.[16]

Permanently discontinue OGSIVEO for recurrence of severe or life-threatening adverse reaction upon rechallenge at the reduced dose.

Grade 3 or 4 Severity

Permanently discontinue.[16]

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; ULN, upper limit of normal.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

Skin and subcutaneous tissue side effects with **OGSIVEO**

In the DeFi trial:

Adverse Reaction	OGSIVEO (n=69)	
	All Grades	Grade 3
Rash	68%	6%
Alopecia	19%	0

- **Median time to first onset of skin rash:** 22 days (range: 2 to 603 days)[18]
- **Median duration of skin rash:** 37 days (range: 1 to 815 days)[18]
- **Investigator-reported resolution:** Resolution occurred in most patients who received treatment. Outcomes at time of analysis also included unresolved events and resolution with sequelae[18]

Rash included multiple related composite terms:[16,18]

- Rash maculopapular (32%)[15]
- Dermatitis acneiform (22%)[15]
- Rash papular
- Rash erythematous
- Rash pruritic
- Rash
- Eczema
- Dermatitis
- Palmar-plantar erythrodysesthesia

Counseling and intervention:

Dosage Modifications for Skin and Subcutaneous Tissue Adverse Reactions

Withhold drug until resolved to Grade ≤1 or baseline for severe adverse reactions, life-threatening adverse reactions, or persistent intolerable Grade 2 adverse events.[16]

Permanently discontinue OGSIVEO for recurrence of severe or life-threatening adverse reaction upon rechallenge at the reduced dose.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

Non-melanoma skin cancers in patients treated with **OGSIVEO**

New non-melanoma skin cancers can occur in patients treated with OGSIVEO

In the DeFi trial:

Non-melanoma skin cancer[16]	OGSIVEO (n=69)
Cutaneous squamous cell carcinoma	2.9%
Basal cell carcinoma	1.4%

Counseling and intervention:

Advise patients that OGSIVEO can cause new non-melanoma skin cancers and to contact their care team for any new or changing lesions on their skin.

Perform dermatologic evaluations prior to initiation of OGSIVEO and routinely during treatment.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

OGSIVEO can cause ovarian toxicity

In the DeFi trial:

Adverse Reaction	OGSIVEO (n=36)*	
	All Grades	Grade 3
Ovarian toxicity (including ovarian failure, premature menopause, amenorrhea, and menopause)	**75%**	**0%**

*The number of females of reproductive potential is used as the denominator (OGSIVEO N=36). Zero patients in the placebo arm experienced ovarian toxicity (N=37).

- **Median time to first onset:** 8.9 weeks[18]
- **Median duration:** 19.1 weeks[18]

Counseling and intervention:

Long-term effects of OGSIVEO on fertility have not been established.

Advise patients on the potential risk for ovarian toxicity before initiating treatment with OGSIVEO.[18]

Advise:

- Females of reproductive potential that OGSIVEO can cause ovarian toxicity and impair fertility, and that these effects may continue following discontinuation[18]
- Patients to contact their care team (which may also include an OBGYN, among others) if they experience symptoms of ovarian toxicity[16]

Monitor patients for changes in menstrual cycle regularity or the development of symptoms of estrogen deficiency, including hot flashes, night sweats, and vaginal dryness.[16]

OBGYN, obstetrician gynecologist.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

Important considerations for patients of reproductive potential

Category	Consideration	Guidance
Pregnancy[16]	Based on findings from animal studies and its MOA, OGSIVEO can cause fetal harm or loss of pregnancy	▪ Administer a **pregnancy test** to verify that female patients are not pregnant before starting OGSIVEO ▪ Advise females and males with female partners of reproductive potential to use **effective contraception** during treatment and for 1 week after the last dose ▪ Advise females of reproductive potential to inform their HCP of a known or suspected pregnancy and to stop taking OGSIVEO if they become pregnant
Lactation[16]	Potential for serious adverse reactions in breastfed children	▪ Advise **not to breastfeed** during treatment and for 1 week after the last dose
Infertility[16]	Based on animal studies, OGSIVEO can impair female and male fertility	▪ Advise patients of reproductive potential that OGSIVEO can impair fertility, which may continue following discontinuation ▪ Advise females of reproductive potential of the potential risk prior to treatment and monitor routinely ▪ Impact on fertility may depend on factors including the duration of therapy and the state of gonadal function at the time of treatment ▪ The long-term effects of OGSIVEO on fertility have not been established

Per the ASCO Clinical Practice Guideline Update on Fertility Preservation in Patients with Cancer, consider referring your patient to a reproductive specialist if they have any fertility questions or concerns.[21]

ASCO, American Society of Clinical Oncology; HCP, healthcare provider; MOA, mechanism of action.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

General Management Tips

American Cancer Society recommendations for diarrhea:[22]		
Consider	**Avoid**	**Additional tips**
▪ Clear liquids ▪ BRAT diet or easy-to-digest foods ▪ Drinking at least 1 cup of liquid after each loose bowel movement to replace lost fluids	▪ Caffeine ▪ Alcohol ▪ Spicy, high-fat, or high-sugar foods ▪ Acidic or carbonated drinks ▪ Tobacco ▪ Certain supplements (e.g., aloe)	▪ Track the number and frequency of bowel movements ▪ Baby wipes as well as petroleum ointment can help relieve soreness ▪ Warm water or a sitz bath can help reduce pain or discomfort

Encourage patients to contact you if they: have diarrhea for more than 24 hours, can't keep liquids down for more than 24 hours, notice any blood in their stool, or have a fever.[22] An example of a therapeutic intervention for cancer treatment–related diarrhea is OTC loperamide.[23,24]

American Cancer Society recommendations for stomatitis:[25]		
Consider	**Avoid**	**Additional tips**
▪ Soft toothbrush or foam swab to reduce injury risk ▪ Oral rinses such as baking soda, salt water, or other mouthwashes that may be prescribed ▪ Regular dental visits	▪ Mouthwashes with alcohol ▪ Hard, dry, or crusty foods ▪ Very salty, spicy, or sugary foods ▪ Acidic fruits and juices ▪ Alcohol ▪ Tobacco	▪ Keep lips moisturized ▪ Drink 2 to 3 quarts of fluids daily ▪ Eat chilled foods and fluids (e.g., popsicles, ice chips, frozen yogurt) ▪ Eat small, frequent meals of soft, moist, easy-to-swallow food ▪ Use a straw

Advise patients that good oral care can help reduce the risk or severity of mouth sores.[25]

These tips are based on general recommendations for oncology and are not specific to desmoid tumors.

BRAT, bananas, rice, applesauce, and toast; OTC, over-the-counter.

General Management Tips

Considerations for hypophosphatemia:[26]

Consult with healthcare team for management strategy; interventions for hypophosphatemia in the oncology setting may commonly include:

- A healthy, balanced diet high in phosphate-rich foods, such as meat, dairy, and nuts
- Treatment for hypophosphatemia involves treating the underlying cause and stabilizing blood phosphate levels

Additional considerations[27]

- Foods high in phosphate may help improve phosphate levels
- Phosphate replacement medication may be used

Considerations for rash and other skin side effects*

General Skin Rash Management[28]

- Patients should discuss rashes and management with their care team
- Mild soaps, lotions, moisturizers, and in some cases, medication may be recommended
- Skin can be cleaned with warm water and gentle soap; rinse skin carefully and pat dry
- Keep skin moisturized
- Protect affected areas from heat and cold
- Avoid sun exposure
- Wear loose-fitting, soft clothing

*Recommendations are from diverse sources, including the American Cancer Society.

Dermatitis Acneiform[29]	Folliculitis[30]	Hidradenitis
▪ Alcohol-free moisturizers ▪ Topical treatments ▪ Avoid over-the-counter acne medication	▪ Emollients and adapted skin cleansers or topical antibiotics and antiseptic soap ▪ Sun protection ▪ Hypoallergenic non-alcohol-based skin care products	▪ Topical treatments:[31] – Skin cleansers – Over-the-counter topical antibiotics ▪ Refer to a dermatologist[32]

These tips are based on general recommendations for oncology and are not specific to desmoid tumors.

General Management Tips

American Cancer Society general tips for premenopausal signs and symptoms:

Tips for hot flashes, sweating, and night sweats[33]

- Stay cool with light clothing and temperature regulation
- Dress in layers
- Use good personal hygiene
- Stay hydrated
- Maintain a healthy weight
- Avoid triggers like spicy food, caffeine, alcohol, and tobacco
- Practice relaxation techniques like deep breathing and meditation
- Consider complementary therapies such as acupuncture, yoga, or hypnosis
- Track symptoms

Estrogen may promote desmoid tumor growth.[4,34]

These tips are based on general recommendations for oncology and are not specific to desmoid tumors.

Monitoring considerations during patient journey on OGSIVEO†

	Baseline	OGSIVEO Treatment	
		Before treatment	Throughout treatment
Desmoid Tumor symptoms	✓	✓	✓
Potential adverse reactions of OGSIVEO, management recommendations, and dosing	✓	✓	✓
Laboratory values	✓	✓	✓
Dermatologic exam	✓	✓	✓

Monitoring patients during treatment with OGSIVEO may help support them during their treatment journey.

Follow the dose modifications for adverse reactions as presented in the PI.

In DeFi, the median duration of exposure to OGSIVEO was 20.6 months (range: 0.3 to 33.6 months).[16]

†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 see Important Safety Information throughout and click here for full Prescribing Information.

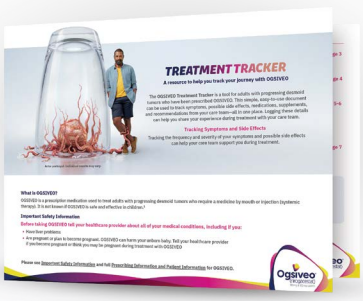
Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

Resources & Support

For healthcare professionals:

How to Order/Rx Guide

For patients:



OGSIVEO Treatment Tracker

Visit www.ogsiveo.com/hcp/practice-resources to find additional information and resources to support your patients.

Advocacy Groups

Desmoid Tumor Research Foundation	REIN IN SARCOMA Increase awareness. Increase survivors.	NORD®
dtrf.org	reininsarcoma.org	rarediseases.org
SARC a collaborative research group accelerating the cure for sarcoma	Global Genes® Allies in Rare Disease	NCCN® | NCCN FOUNDATION® PATIENT RESOURCES
sarctrials.org	globalgenes.org	nccn.org
NORTHWEST SARCOMA FOUNDATION HOPE • EDUCATION • SUPPORT	Sarcoma SFA Foundation of America finding the cure in our time	SARCOMA STRONG EST. 2014 UNITE THE FIGHT
nwsarcoma.org	curesarcoma.org	sarcomastrong.com

SpringWorks Therapeutics, Inc. is providing these links to help patients find more information about desmoid tumors, but inclusion on this list does not represent an endorsement or a recommendation from SpringWorks for any group or organization. The organizations listed are independent of SpringWorks Therapeutics.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

SpringWorks CareConnections™

Connections at Each Point of *Care*

SpringWorks CareConnections™ provides personalized support services and resources to help your patients start and stay on track with OGSIVEO

Live support is available by calling 844-CARES-55 (844-227-3755)
Monday–Friday 8 AM–10 PM ET

Coverage and Access Support

Resources and assistance to support timely access to OGSIVEO

Financial Assistance

Connecting patients to financial assistance options that may be available

Personalized Educational and Emotional Support

Dedicated Nurse Advocates provide personalized support and serve as a single point of contact for patients regardless of where they are in their treatment journey*

Field Access Manager (FAM) Capabilities

FAMs can provide in person or virtual support to help facilitate access to OGSIVEO by providing regional payer education and timely responses to questions

*SpringWorks CareConnections is not intended to replace healthcare providers. The team of Nurse Advocates cannot provide medical or clinical advice.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat)
150 mg & 100 mg tablets

References

1. Data on file. SpringWorks Therapeutics, Inc. Based on analysis of Komodo Sentinel patient claims data from March 1, 2024 through February 28, 2025.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma V.1.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed May 12, 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. 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.
4. Penel N, Chibon F, Salas S. Adult desmoid tumors: biology, management and ongoing trials. *Curr Opin Oncol.* 2017;29(4):268-274.
5. Sbaraglia M, Bellan E, Dei Tos AP. The 2020 WHO Classification of Soft Tissue Tumours: news and perspectives. *Pathologica.* 2021;113(2):70-84.
6. Cohen S, Ad-El D, Benjaminov O, Gutman H. Post-traumatic soft tissue tumors: case report and review of the literature a propos a post-traumatic paraspinal desmoid tumor. *World J Surg Oncol.* 2008;6:28.
7. Scaramussa FS, Castro UB. Desmoid tumor in hand: a case report. *SM J Orthop.* 2016;2(3):1036.
8. Weschenfelder W, Lindner R, Spiegel C, et al. Desmoid tumor of the popliteal fossa during pregnancy. *Case Rep Surg.* 2015;2015:262654.
9. Styring E, Ahlstrom M, Rissler P, et al. Desmoid fibromatosis in the brachial plexus mimicking an ulnar nerve entrapment. *Am J Med Case Rep.* 2019;7(3):36-40.
10. Kasper B, Baldini EH, Bonvalot S, et al; Desmoid Tumor Working Group. Current management of desmoid tumors: a review. *JAMA Oncol.* 2024;10(8):1121-1128.
11. Easter DW, Halasz NA. Recent trends in the management of desmoid tumors. Summary of 19 cases and review of the literature. *Ann Surg.* 1989;210(6):765-769.
12. Skubitz KM. Biology and treatment of aggressive fibromatosis or desmoid tumor. *Mayo Clin Proc.* 2017;92(6):947-964.
13. Crago AM, Denton B, Salas S, et al. A prognostic nomogram for prediction of recurrence in desmoid fibromatosis. *Ann Surg.* 2013;258(2):347-353.
14. Tsagozis P, Stevenson JD, Grimer R, Carter S. Outcome of surgery for primary and recurrent desmoid-type fibromatosis. A retrospective case series of 174 patients. *Ann Med Surg (Lond).* 2017;17:14-19.
15. Gounder M, Ratan R, Alcindor T, et al. Nirogacestat, a gamma-secretase inhibitor for desmoid tumors. *N Engl J Med.* 2023;388(10):898-912.
16. OGSIVEO. Prescribing Information. SpringWorks Therapeutics, Inc.
17. Ratan R, Kasper B, Schöffski P, et al. Nirogacestat treatment in adult patients with desmoid tumors: longterm efficacy and safety from the phase 3 DeFi trial. Oral presentation at: CTOS Annual Meeting; November 13-16, 2024; San Diego, CA.
18. Data on file. SpringWorks Therapeutics, Inc.
19. Loggers ET, Chugh R, Federman N, et al. Onset and resolution of ovarian toxicity with nirogacestat treatment in females with desmoid tumors: updated safety analyses from the DeFi phase 3 study. *Cancer.* 2024;130(16):2812-2821.
20. NCI. National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Accessed April 17, 2025. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf
21. Oktay K, Harvey BE, Partridge AH, et al. Fertility preservation in patients with cancer: ASCO Clinical Practice Guideline Update. *J Clin Oncol.* 2018;36(19):1994-2001.
22. American Cancer Society. Managing cancer-related side effects. Diarrhea. Accessed April 17, 2025. https://www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html
23. Kornblau S, Benson AB, Catalano R, et al. Management of cancer treatment-related diarrhea. Issues and therapeutic strategies. *J Pain Symptom Manage.* 2000;19(2):118-129.
24. Benson AB 3rd, Ajani JA, Catalano RB, et al. Recommended guidelines for the treatment of cancer treatment-induced diarrhea. *J Clin Oncol.* 2004;22(14):2918-2926.
25. American Cancer Society. Managing cancer-related side effects. Mouth soreness and pain. Accessed April 17, 2025. https://www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/mouth-sores.html
26. Cleveland Clinic. Accessed April 17, 2025. https://my.clevelandclinic.org/health/diseases/24040-hypophosphatemia
27. Adhikari S, Mamlouk O, Rondon-Berrios H, Workeneh BT. Hypophosphatemia in cancer patients. *Clin Kidney J.* 2021;14(11):2304-2315. Published 2021 April 15.
28. American Cancer Society. Accessed April 17, 2025. https://www.cancer.org/cancer/managing-cancer/side-effects/hair-skin-nails/skin-rash.html
29. Lacouture ME, Sibaud V, Gerber PA, et al. Prevention and management of dermatological toxicities related to anticancer agents: ESMO Clinical Practice Guidelines. *Ann Oncol.* 2021;32(2):157-170.
30. Bensadoun RJ, Humbert P, Krutman J, et al. Daily baseline skin care in the prevention, treatment, and supportive care of skin toxicity in oncology patients: recommendations from a multinational expert panel. *Cancer Manag Res.* 2013;5:401-408. Published 2013 December 9.
31. Alikhan A, Sayed C, Alavi A, et al. North American clinical management guidelines for hidradenitis suppurativa: A publication from the United States and Canadian Hidradenitis Suppurativa Foundations: Part II: Topical, intralesional, and systemic medical management. *J Am Acad Dermatol.* 2019;81(1):91-101.
32. American Academy of Dermatology Association. Accessed April 17, 2025. https://www.aad.org/public/diseases/a-z/hidradenitis-suppurativa-overview#
33. American Cancer Society. Accessed April 17, 2025. https://www.cancer.org/cancer/managing-cancer/side-effects/hair-skin-nails/hot-flashes-and-sweating.html
34. Constantinidou A, Scurr M, Judson I, Litchman C. Clinical presentation of desmoid tumors. In: Litchman C, ed. *Desmoid Tumors.* Springer; 2012:chap 2. Accessed April 17, 2025. https://www.researchgate.net/publication/226455135

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

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.

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 x 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.

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® (nirogacestat)
150 mg & 100 mg tablets

Please click here for full Prescribing Information.

Help Patients Stay on Track With OGSIVEO

The first and only FDA-approved targeted therapy for adult patients with progressing desmoid tumors who require systemic treatment

See the Data

Explore the data from DeFi and a long-term post-hoc analysis.

Empower Your Patients

Equip your patients with tools and resources to help monitor and manage potential side effects.

Support the Treatment Journey

Support your patients by proactively managing side effects, including recommended dose modifications to help them confidently navigate their treatment with OGSIVEO.

OGSIVEO safety information

- Warnings and Precautions: diarrhea, ovarian toxicity, hepatotoxicity, non-melanoma skin cancers, electrolyte abnormalities, and embryo-fetal toxicity[16]
- The most common (≥15% with a difference between arms of ≥5% compared to placebo) adverse reactions that occurred in patients receiving OGSIVEO were diarrhea, ovarian toxicity, rash, nausea, fatigue, stomatitis, headache, abdominal pain, cough, alopecia, upper respiratory tract infection, and dyspnea[16]
- Most adverse events were Grade 1 or 2 and occurred within 1 month of starting OGSIVEO[15]

Visit www.ogsiveo.com/hcp to learn more about OGSIVEO.

Please see Important Safety Information throughout and click here for full Prescribing Information.

Ogsiveo® (nirogacestat) 150 mg & 100 mg tablets

SpringWorks® THERAPEUTICS