**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

# Nirogacestat for treating desmoid tumours ID6453

**Draft scope**

## Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of nirogacestat within its marketing authorisation for treating desmoid tumours.

## Background

Desmoid tumours (DTs) are a type of soft tissue tumour DTs commonly present as a lump. They can be found in various parts of the body including the arms, legs, abdomen, head and neck. DTs can only spread locally and not to other parts of the body.[1,2] The symptoms and mortality are dependent on the site of the tumour. Some tumours may be asymptomatic but tumours within the abdominal cavity (intra-abdominal), behind the peritoneum or in the head and neck can be associated with significant morbidity (pain and loss of function) and mortality.[1-4] DTs are usually sporadic due to mutations in the CTNNB1 gene and in a small group of people (5-10%), DT is associated with a genetic condition called familial adenomatous polyposis.[1-4]

Around 3% of all soft tissue tumours are estimated to be DTs.[1,6] European and UK studies estimate that between 3 to 6 people per million per year are diagnosed with DTs.[5-7] There is a higher incidence in women and the risk of DTs increase in pregnancy and childbirth.[1-2,7]

Current clinical management of DTs depends on the tumour site and characteristics.[1-2,5] A 'watch and wait' active surveillance policy is taken for newly diagnosed cases.[8] If the condition stabilises or regresses a person would continue to be monitored. If the condition progresses treatment options may include:[5,7-8]

- Surgery, dependent on the tumour location. European consensus guidelines[1] suggest surgery is an option for sporadic DT located in the abdominal wall
- Medical therapies such as anti-hormonal therapies, non-steroidal anti-inflammatory drugs (NSAIDS), tyrosine kinase inhibitors (sorafenib, pazopanib or imatinib) or chemotherapy
- Local ablative therapy such as radiotherapy or cryoablation

Pain medication may also be offered.

## The technology

Nirogacestat (Ogsiveo, SpringWorks Therapeutics) does not currently have a marketing authorisation in the UK for treating desmoid tumours. It has been studied in clinical trials in which nirogacestat has been compared with placebo in adults with progressing desmoid tumours that are not amenable to surgery .

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| **Intervention(s)** | Nirogacestat monotherapy |
| **Population(s)** | Adults (aged 18 years and over) with desmoid tumours (DTs) |
| **Subgroups** | • people who have not had previous treatment and people whose DT is relapsed or refractory to treatment<br>• subgroups based on tumour site such as people with intra-abdominal or extra-abdominal DT<br>• people with familial adenomatous polyposis |
| **Comparators** | Established clinical management using medical therapies. This may include anti-hormonal therapies, non-steroidal anti-inflammatory drugs (NSAIDS), tyrosine kinase inhibitors or chemotherapy. |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rates<br>• improvement in symptoms, including pain<br>• adverse effects of treatment<br>• health-related quality of life |
| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.<br>The availability and cost of biosimilar and generic products should be taken into account. |

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| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. |
| **Related NICE recommendations** | None<br>**Related quality standards:**<br>Sarcoma (2015) NICE quality standard 78 |

**Questions for consultation**

Does the survival outcome vary depending on the site of the desmoid tumour (DT)? Are intra-abnominal and extra-abdominal DT distinct in terms of morbidity and prognosis?

Are there any outcome differences (quality of life and survival rate) for people with DT associated with familial adenomatous polyposis compared with sporadic DT?

Where do you consider nirogacestat will fit into the existing care pathway for DTs?

Please select from the following, will nirogacestat be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

What medical therapies (licensed or off-label) are used for treating DT? If anti-hormonal therapies, non-steroidal anti-inflammatory drugs, tyrosine kinase inhibitors or chemotherapy is used, what drugs within these groups are used in clinical practice in the NHS? Is there clinical evidence to suggest these treatments are disease modifying?

Would medical therapies ever be used as an alternative to surgery or local ablative therapy?

Would nirogacestat be a candidate for managed access?

Do you consider that the use of nirogacestat can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which nirogacestat will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

**References**

1. Orphanet (2013) Desmoid tumor. Accessed March 2025

2. Sarcoma UK (2025): Desmoid-type fibromatosis. Accessed March 2025

3. Shivaani, K, et al. Clinical Activity of the γ-Secretase Inhibitor PF-03084014 in Adults With Desmoid Tumors (Aggressive Fibromatosis). JCO 35, 1561-1569(2017).

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5. Alman, B, et al. "The management of desmoid tumours: a joint global consensus-based guideline approach for adult and paediatric patients." *European Journal of Cancer* 127 (2020): 96-107.

6. Borghi A, Gronchi A. Desmoid tumours (extra-abdominal), a surgeon's nightmare. Bone Joint J. 2023;105-B(7):729-734.

7. Bektas, M, et al. Desmoid Tumors: A Comprehensive Review. Adv Ther 40, 3697–3722 (2023).

8. Timbergen, M, et al. "Active surveillance in desmoid-type fibromatosis: a systematic literature review." European Journal of Cancer 137 (2020): 18-29.