National Institute for Health and Care Excellence

Health Technology Evaluation

Nirogacestat for treating desmoid tumours [ID6453]
Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	SpringWorks Therapeutics	[redacted] Given that there is a high unmet need for these patient as there are currently no licensed treatment options, evaluation by NICE is needed to provide recommendations on the use of nirogacestat by the NHS in England and Wales. Nirogacestat should be evaluated under the highly specialised technology route, given the rarity of the disease, low number of patients, disease impact on mortality and quality of life, and lack of recommended treatment alternatives. Further details are provided separately.	Thank you for your comment. Topic routing was discussed at the NICE Prioritisation Board in May 2025. The Board concluded that the topic was suitable for a Single Technology Appraisal. Please see project documents for further details.
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	No comment	No action needed

Section	Stakeholder	Comments [sic]	Action
Wording	SpringWorks Therapeutics	Wording is appropriate.	No action needed
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? If not, please suggest alternative wording. - Yes	No action needed
Timing Issues	SpringWorks Therapeutics	There is an urgent need for [redacted] as no licensed treatment options are currently available.	Thank you for your comment. This topic has been scheduled into NICE's work programme. For further details, please see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta11559
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	Given that few other effective treatments exist or are being developed for people diagnosed with Desmoid Tumours, which is a condition with impacts upon people' quality of life, it is urgent that an evaluation is undertaken into nirogacestat.	Thank you for your comment. This topic has been scheduled into NICE's work programme. For further details, please see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta11559

Section	Stakeholder	Comments [sic]	Action
Additional comments on the draft remit	SpringWorks Therapeutics	No additional comments	No action needed
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	No additional comments	No action needed

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	SpringWorks Therapeutics	Medical therapies such as anti-hormonal therapies and NSAIDS are not indicated, recommended, or routinely used in the treatment of [redacted]. Around 3% of all soft tissue tumours are estimated to be DTs. European and UK studies estimate that between 3 to 5 people per million per year are diagnosed with DTs (Anneberg et al., 2022; Nieuwenhuis et al., 2011; Orphanet, 2019; Reitamo et al., 1982; van Broekhoven et al., 2015). Rather, the NIHR Health Technology Briefing (Apr 2024) on nirogacestat for treating DT indicates in the UK: Management strategy for DT can incorporate periods of no treatment and active surveillance, which is the established standard approach, eventually followed by interventions including surgery, off-label cytotoxic chemotherapy, tyrosine kinase inhibitors, local ablation, or radiation therapy (Kingswell, 2023; Grounder et al., 2023; Alman et al., 2020, Kasper, 2023).	Thank you for your comment. The treatment options have been updated to reflect the anti-hormonal therapies and non-steroidal anti-inflammatory drugs have been offered but there is limited evidence of these being disease modifying treatments (Kasper 2024, Mercier 2024).
	Joint response on behalf of Sarcoma UK	Paragraph 2:	Thank you for your comment. The background section of

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	and Desmoid Aid UK	• It should be noted that very limited data is being recorded about the incidence and prevalence of desmoid tumours (DTs) in England and Wales, which limits the accuracy of the estimated incidence figures. • This is also the case for the noted higher of DTs amongst women, and particularly a high associated risk in pregnancy and childbirth. DT that are associated with pregnancy may be linked due to the normal increase in a woman's body of hormones during pregnancy. In many cases, the DT will subsequently shrink on its own as hormone levels fall after pregnancy; but this may not always be the case. Paragraph 3: The order of treatment for most patients is understood to be as follows: 1) Active surveillance with supportive management, e.g. physiotherapy and pain relief. 2) Chemotherapy, either Vinorelbine or Doxorubicin for large, symptomatic, rapidly progressive intra-abdominal DTs 3) Ablation is considered, but surgery is rarely considered as an option 4) Multi-kinase inhibitor, Sorafenib (however, individual requests for this treatment are only available on a compassionate-use basis to the pharmaceutical company which funds the treatment) 5) Radiotherapy, but this tends to be avoided because it has long-term impacts and there are risks it could lead to second tumours. However, radiotherapy it is sometimes considered for Head and Neck Fibrosis. It should be noted that anti-hormonal therapies and non-steroidal anti-inflammatory drugs (NSAIDS) are no longer considered disease-modifying agents, according to the most recent international consensus guidelines (*Current Management of Desmoid Tumors*, June 2024). NSAIDS may be prescribed for the control of symptoms.	the scope is intended to give a brief overview of the condition and treatment options. The treatment options have been updated to reflect the limited use of anti-hormonal therapies and non-steroidal anti-inflammatory (Kasper 2024, Mercier 2024).

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Population	SpringWorks Therapeutics	Population should align with anticipated marketing authorisation: [redacted]	Thank you for your comment. As the anticipated marketing authorisation wording is still confidential, the population has been aligned with the remit of the scope and this has not been updated. No action required.
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	Is the population defined appropriately? - Yes	No action required.
Subgroups	SpringWorks Therapeutics	The subgroup populations identified by NICE in the scope are appropriate for investigation.	Thank you for your comment. No action required.
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	No comment	No action required.
Comparators	SpringWorks Therapeutics	The comparators considered to be the standard treatments currently used (off-label) in the NHS with which nirogacestat could be compared include TKIs and chemotherapy. However, please note that clinical advisors	Thank you for your comment. NSAID and anti-hormonal therapies

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		mentioned that TKIs (e.g., sorafenib) are only available for compassionate use in the UK and are, therefore, not an appropriate comparator as they are not widely funded by the NHS. Currently, the DTWG 2020 Consensus-based Guidelines, DTWG 2024 Guideline Update, SPAEN/EORTC/STBSG 2017 Consensus Guidelines, and ESMO-EURACAN-GENTURIS 2021 Clinical Practice Guidelines do not recommend use of antihormonal therapies and NSAIDs in the management of DT due to the lack of evidence establishing their efficacy and activity in patients with DT. **Clinical experts also noted that options like NSAIDs or anti-hormonal therapy are now rarely prescribed in clinical practice due to limited evidence-based efficacy.**	have been removed from the scope. The comparator list has been kept broad to include both chemotherapy and TKIs as potential medical therapy comparators. Best supportive care has also been added as a comparator in recognition that some people who may need [redacted] may not be receiving chemotherapy or TKIs in clinical practice. The company within its submission can include justification for non-inclusion of comparators.
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	As noted in comments above (on the 'Background') The order of treatment and therefore comparators for most patients are understood to be as follows: 1) Active surveillance with supportive management, e.g. physiotherapy and pain relief. 2) Chemotherapy, either Vinorelbine or Doxorubicin for large, symptomatic, rapidly progressive intra-abdominal DTs 3) Ablation is considered, but surgery is rarely considered as an option	Thank you for your comment. NSAID and anti-hormonal therapies have been removed from the scope. The comparator list has been kept broad to include both

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		4) Multi-kinase inhibitor, Sorafenib (however, individual requests for this treatment are only available on a compassionate-use basis to the pharmaceutical company which funds the treatment) 5) Radiotherapy – but this tends to be avoided because it has long-term impact and there are risks it could lead to second tumours. However, radiotherapy it is sometimes considered for Head and Neck Fibrosis. It should be noted that anti-hormonal therapies and non-steroidal anti-inflammatory drugs (NSAIDS) are no longer considered disease-modifying agents, according to the most recent international consensus guidelines (*Current Management of Desmoid Tumors*, June 2024). NSAIDS may be prescribed for the control of symptoms.	chemotherapy and TKIs as potential medical therapy comparators. Best supportive care has also been added as a comparator in recognition that some people who may need [redacted] may not be receiving chemotherapy or TKIs in clinical practice. The company within its submission can include justification for non-inclusion of comparators. No action required.
Outcomes	SpringWorks Therapeutics	The outcome measures are appropriate and are expected to capture the most important health related benefits (and harms) of the technology. It should be noted that from a cost-effectiveness perspective, the most important outcome is the level of tumour response as defined by the Response Evaluation Criteria in Solid Tumours [RECIST], version 1.1) that a patient with progressing DT will experience (e.g., stable disease, partial response, complete response, progression). Given the variability in patient experiences, and the variety of outcomes that can be experienced within the pre-progression state alone (each associated with different levels of morbidity and pain), it is important to consider additional response states beyond “pre-progression” and “post-progression”.	Thank you for your comment. Partial and complete response has been added as examples under response rates. Duration of response has been added as an outcome measure. Overall survival has been changed to mortality.The outcomes

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			list is intended to be non-exhaustive guide. In the submission the company can include further justification for inclusion of additional outcomes.
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	For people diagnosed with DTs, the disease has a significant impact upon their quality of life. The outcome measures should therefore be ranked as follows (i.e. 1 being the highest priority; 6 the lowest priority) to reflect both patients' and clinical priorities, with (1) and (2) being the most important: 1) Improvement in symptoms, including pain 2) Health-related quality of life Then followed by: 3) Response rates 4) Adverse effects of treatment 5) Progression-free survival, and Overall survival – being the least important, due to mortality from DTs being very low, except for familial adenomatous polyposis (FAP) associated DTs.	Thank you for your comment. The outcomes list includes all suggested options. Partial and complete response has been added as examples under response rates. Duration of response has been added as an outcome measure. Overall survival has been changed to mortality.
Equality	SpringWorks Therapeutics	No evidence.	Thank you for your comment. No action required.

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	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	The draft remit and scope need to ensure that particular attention and effort is made to seeking evidence about DTs with regards to people that are covered by three of the protected characteristics under the *Equality Act 2010*, for sex, pregnancy and maternity, and age, due to: • The higher incidence of DTs amongst women as noted in the background • The associated risk for women in pregnancy and childbirth as noted in the background, and • Given the relatively younger age profile of people diagnosed with DTs.	Thank you for your comment. This will be incorporated and considered in the equalities impact assessment form and will be considered by the committee during the appraisal.
Other considerations	SpringWorks Therapeutics	No suggestions for additional issues.	No action required.
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	No comments	No action required.
Questions for consultation	SpringWorks Therapeutics	**1. 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?** Based on the findings from the SLR, Bouhamama et al. (2023) reported that tumours located in the neck and trunk showed higher recurrence rates compared to those in the abdominal wall. Cates et al. (2014) reported that high (extremities, limb girdles, deep soft tissues of the chest wall and back, and head/neck region) vs. low risk (superficial soft tissues of the chest wall and back, abdominal wall and abdominal cavity) anatomic sites were the only statistically significant independent predictor of relapse-free survival. Additionally, Penel et al. (2023) reported that pain was more frequent in	Thank you for your comments. Survival and quality of life outcomes from these consultation comments were taken into consideration during the topic routing discussion at the NICE Prioritisation Board in May 2025. Please see project documents for further details.

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		tumours located in the neck and shoulder region compared to those in the abdominal wall or intra-abdominal locations. **2. Are there any outcome differences (quality of life and survival rate) for people with DT associated with familial adenomatous polyposis compared with sporadic DT?** Patients with DT associated with familial adenomatous polyposis (FAP) appear to have worse survival outcomes compared to those without FAP. Anneberg et al. (2022) reported that most deaths in a DT cohort occurred in patients with FAP, despite only representing 7% of the cohort. Similarly, Nathenson et al. (2022) reported that out of six patients who died from tumour-related complications, five had known FAP and mesenteric tumour location. Zhao et al. identified FAP as an independent risk factor for recurrence in a multivariate Cox regression analysis. **3. Where do you consider nirogacestat will fit into the existing care pathway for DTs?** [redacted] **4. 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):	The treatment pathway has been updated in the scope.

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		C. Prescribed in secondary care with routine follow-up in secondary care **5. For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** We do not anticipate any change in the setting for prescribing and routine follow-up for the intervention (e.g., nirogacestat) would differ from comparators and subsequent treatments. **6. 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?** The NIHR Health Technology Briefing (Apr 2024) on nirogacestat for treating DT indicates in the UK: • There is no treatment option recommended by NICE specifically for DT. • Management strategy for DT can incorporate periods of no treatment and active surveillance, which is the established standard approach, eventually followed by interventions including surgery, off-label cytotoxic chemotherapy (anthracyclines, low dose methotrexate plus vinblastine or vinorelbine), tyrosine kinase inhibitors (pazopanib, imamtinib, sorafenib), local ablation, or radiation therapy. The NIHR Health Technology Briefing was partly developed on the basis of the 2020 DTWG Guidelines from the Management of DT (other sources	

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		focused on nirogacestat). Importantly, while the 2020 DTWG guidelines list antihormonal therapies and NSAIDs as systemic therapies used to manage DT, guideline authors noted that 'there is no evidence to consider antihormonal therapies and NSAIDs in patients with DT,' citing the only prospective phase 2 study evaluating antihormonal therapy plus NSAIDs was in a pediatric patient population which showed limited response activity and PFS rates, and recent evidence showed no clear relationship between size, MRI signal changes, and symptom changes with tamoxifen treatment. The 2024 DTWG guideline update notes the low-quality evidence available for chemotherapies (low-dose and conventional) and pazopanib. Similarly, the SPAEN/EORTC/STBSG 2017 Guidelines and ESMO-EURACAN-GENTURIS 2021 Guideline do not recommend use of antihormonal therapies and NSAIDs in the management of DT due to the lack of evidence establishing their efficacy and activity in patients with DT. Based on clinical expert interviews, it was noted that current standard of care for DT is variable and may depend on tumour site and the centre's clinical practice. Clinicians identified chemotherapy and TKIs as the most frequently used (off-label) systemic treatments in the current treatment landscape for DT. It was also noted that previous options like NSAIDs or hormonal therapy (e.g., sulindac, tamoxifen, and raloxifene) are now rarely prescribed due to limited evidence-based efficacy. **7. Would medical therapies ever be used as an alternative to surgery or local ablative therapy?** The 2024 DTWG Guideline update incorporates new evidence for surgery, medical therapy, and local ablative techniques, and now recommends a clinical scenario-centric approach that considers the expected effectiveness and morbidity associated with the treatment. Primary treatment options depend on location of the tumor and/or whether the patient has FAP, and	

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		includes surgery, local ablative techniques, and medical therapy. Importantly, the authors provide guidance on when to consider surgery and local ablative techniques as primary therapy: • Surgery is only recommended as the 1L option for treatment when morbidity and risk of recurrence are low, in particular for abdominal wall DT, mesenteric (non-FAP) DT, and to treatment complications for mesenteric DT in patients with FAP, and retroperitoneal and pelvic DT • Medical therapy is recommended as one of the 1L treatment options for patients who require treatment for a DT in the abdominal wall, mesentery, retroperitoneum, pelvis, extremities, girdles, or chest wall, and is the only recommended 1L treatment for DT in the head, neck, or intrathoracic region. According to the 2024 DTWG consensus statement, medical therapies should be selected considering the safety profiles of the available agents in the context of the specific patient. The guidelines also state that nirogacestat is the first approved systemic therapy for DT. They do not mention use of anti-hormonal therapies or non-steroidal anti-inflammatory drugs as systemic medical therapies for DT. • For local ablative therapies, the 2024 DTWG Guideline update includes cryoablation, high-intensity focused ultrasonography (HIFU) treatment, other thermal ablative techniques such as radiofrequency and microwave, and chemical ablative techniques. ○ The guideline authors provide no recommendation on the use of cryoablative therapy in DT. Guidelines authors do note that the evidence suggest cryoablation may be ideal for treating smaller DTs, as tumor size was the only variable associated with treatment failure, and that the current indication for cryoablative therapy is a growing DT after 2 or more lines of systemic therapy or with functional symptoms or pain.	

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		○ Other local ablation therapies such as HIFU treatment, other thermal ablative techniques such as radiofrequency and microwave, and chemical ablative techniques should only be considered within the context of a randomized controlled study, and are not recommended. • While surgery remains a treatment option in certain contexts, as described above, it is often avoided because it can be associated with considerable and unnecessary morbidity and loss of function. Similarly, cryoablation use is limited when proximal vital structures may be impacted. Neither of these therapies achieve all of the treatment goals of patients with DT, which include progression free survival, objective response rate, pain management, control of DT symptoms, and improvements to physical functioning, role functioning, and quality of life. As such, there remains a large unmet need for treatment of patients with DT. In addition, it should be noted that surgery or local ablative therapy would not be considered a direct competitor, as nirogacestat is currently indicated for patients with [redacted]. **8. Would nirogacestat be a candidate for managed access?** Yes **9. 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.**	

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		The health-related benefits expected to be included in the QALY calculation include the impact of the response health state (stable disease, partial response, complete response, progressed disease) and adverse events. Nirogacestat may also offer some benefits to QALYs through improvement on physical functioning and role functioning, increasing the capacity for patients and caregivers to work, and improvements in overall quality of life in (particularly in patients with a best overall response of stable disease), allowing patients to have a long-term positive outlook on life; however, it is unlikely to capture these benefits in the QALY calculation. **10. 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.**	

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		No evidence. 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).** **4. Cojocaru, E, et al. Approach to screening for Familial Adenomatous Polyposis (FAP) in a cohort of 226 patients with Desmoid-type Fibromatosis (DF): experience of a specialist center in the UK. *Familial Cancer* 21, 69–74 (2022).** **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.**	

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		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.**	
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	**Q1. 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?** A1. Intra-abnominal (DTs) are rare, noncancerous growths in the connective tissue of the abdomen, often in the mesentery surrounding the intestines. They are intermediate tumours that can cause local damage due to being aggressive, and spreading beyond their original location and growing into surrounding healthy tissues Extra-abdominal DTs are intermediate, slow-growing, and locally aggressive tumors that grow in various locations outside the abdomen, e.g. the shoulders, upper arms, chest wall, upper legs, head, and neck, that can cause significant issues due to their location and potential to encase nerves. Survival outcomes do vary depending on the nature and size of the DT, and how and whether it is changing. Survival is worse for Head and Neck fibromatosis and intra-abdominal compared to other sites; they also differ in terms of morbidity and effects on quality of life.	Thank you for your comments. Survival and quality of life outcomes from these consultation comments were taken into consideration during the topic routing discussion at the NICE Prioritisation Board in May 2025. Please see project documents for further details. The treatment pathway has been updated in the scope.

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		Q2. Are there any outcome differences (quality of life and survival rate) for people with DT associated with familial adenomatous polyposis compared with sporadic DT? A2. Yes, there are known to be significant differences in outcomes for people with DT associated with familial adenomatous polyposis (FAP) compared with sporadic DT in outcomes. These include impacts on quality of life including severe and chronic pain. Also, lower survival rates and higher recurrence of the disease. DTs associated with FAPs tend to be larger, more multifocal (i.e. the presence of multiple distinct tumours), and have a more aggressive clinical behaviour, leading to a higher risk of recurrence and mortality compared to sporadic DTs. **Q3. Where do you consider nirogacestat will fit into the existing care pathway for DTs?** A3. It would be prescribed as follows: • At 'first line' after progression on active surveillance, and • At 'second line' after progression to the use of the chemotherapy drug Vinorelbine. **Q4. 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):** A4. Other – all patients with DTs must have their care overseen by a Sarcoma Multidisciplinary Team (MDT), which is a Highly Specialised Service and Quaternary-level service within the NHS. Sarcoma MDTs would therefore prescribe nirogacestat, as they are responsible for determining patients' care	

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		plans and are responsible for delivery in Specialist Sarcoma Centres or by designated practitioners in Local Sarcoma Units, in line with pathways agreed with the Sarcoma Advisory Group, NICE and British Sarcoma Group guidelines, and as mandated by NHS England's 2019 *Sarcoma Service Specification*. **Q5. For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** A5. No. **Q6. 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?** A6. We understand that: The Chemotherapy drugs Vinorelbine and Doxorubicin have limited evidence from a retrospective study. The multi-kinase inhibitor, Sorafenib has been subject to a randomised prospective trial which suggests that it is active as a disease modifier (however, as noted above, individual requests for this treatment are only available on a compassionate-use basis to the pharmaceutical company which funds the treatment). It should be noted that anti-hormonal therapies and non-steroidal anti-inflammatory drugs (NSAIDS) are no longer considered disease-modifying agents, according to the most recent international consensus guidelines (*Current Management of Desmoid Tumors*, June 2024). NSAIDS may be prescribed for the control of symptoms.	

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		Q7. Would medical therapies ever be used as an alternative to surgery or local ablative therapy? A7. Yes, chemotherapy, e.g. Vinorelbine or Doxorubicin, would normally be used as a first-line treatment. **Q8 Would nirogacestat be a candidate for managed access?** A8. Yes, nirogacestat should be a candidate for managed access, e.g. NICE can recommend a drug for use under the Cancer Drugs Fund giving early access to promising new treatments, via managed access arrangement, while further evidence is collected to address clinical uncertainty. The fund can also provide interim funding for all newly recommended cancer drugs, so that patients can access these treatments much earlier than they would otherwise be able to. **Q9. 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.** A9. It is important that the QALY calculation takes account of potential health-related benefits that may be gained from approving nirogacestat, specifically in terms of being able to modify the disease or mitigate its impacts upon patients. As noted above (in comments against the 'Outcomes'), the most important outcome measures for patients are: 1) Improvement in symptoms, including pain; and 2) Health-related quality of life.	

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		This is because DTs have significant impacts upon people's quality of life which can affect both physical and emotional health, including: pain, reduced mobility, fatigue, nausea and vomiting, change in appearance; as well as anxiety, social isolation, body image and self-esteem. The impact of dealing with a DT-diagnosis also varies according to an individual's life- stage and can be particularly difficult for people to deal with if they are of working age and/or who have children. The impact of a DT-diagnosis upon family and carers can also be significant. The Committee should consider the following evidence: • Husson O, Younger E, Dunlop A, Dean L, Strauss DC, Benson C, Hayes AJ, Miah A, van Houdt W, Zaidi S, Smith M, Williams J, Jones RL, van der Graaf WTA, *Desmoid fibromatosis through the patients' eyes: time to change the focus and organisation of care?* Support Care Cancer (March 2019), 27(3):965-980. • Schut AW, de Bruin LE, de Rooij BH, Lidington E, Timbergen MJM, van der Graaf WTA, van Houdt WJ, Bonenkamp JJ, Jones RL, Grünhagen DJ, Sleijfer S, Gennatas S, Verhoef C, Husson O. *Physical symptom burden in patients with desmoid-type fibromatosis and its impact on health-related quality of life and healthcare use.* Cancer Med. (June 2023), 12(12):13661-13674. • Timbergen MJM, van de Poll-Franse LV, Grünhagen DJ, van der Graaf WT, Sleijfer S, Verhoef C, Husson O. *Identification and assessment of health-related quality of life issues in patients with sporadic desmoid-type fibromatosis: a literature review and focus group study.* Qual Life Res (December 2018), 27(12):3097-3111. • In July 2025, Sarcoma UK will publish the *2025 National Sarcoma Survey*, which is a repeat five-year study of people's experiences of the impact of	

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		people affected by sarcoma including DTs, and the care and treatment they have received from the NHS. **Q10. 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.** A10. As noted above (in comments on 'Equality'), the draft remit and scope needs to ensure that particular effort is made to gather evidence about DTs with regards to people that are covered by three of the protected characteristics under the *Equality Act 2010*, for sex, pregnancy and maternity, and age, due to: • The higher incidence of DTs amongst women as noted in the background • The associated risk for women in pregnancy and childbirth as noted in the background, and • Given the relatively younger age profile of people diagnosed with DTs.	

Section	Consultee/ Commentator	Comments [sic]	Action
		The committee should consider the following evidence: • S. Otero, E.C. Moskovic, D.C. Strauss, C. Benson, A.B. Miah, K. Thway, C. Messiou, *Desmoid-type fibromatosis* Clinical Radiology, Volume 70, Issue 9, September 2015, Pages 1038-1045.	
Additional comments on scope	SpringWorks Therapeutics	No additional comments	
	Joint response on behalf of Sarcoma UK and Desmoid Aid UK	No additional comments	