NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Nirogacestat for treating desmoid tumours

Final scope

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 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:[5,7-10]

- Surgery, dependent on the tumour location. European consensus guidelines[1] suggest surgery is an option for sporadic DT located in the abdominal wall
- Chemotherapy or tyrosine kinase inhibitors (TKIs) (TKIs maybe available via compassionate use schemes).
- Local ablative therapy such as radiotherapy or cryoablation

Anti-hormonal therapies or non-steroidal anti-inflammatory drugs (NSAIDS) have been offered, but there is limited evidence of these being disease modifying treatments[5] , NSAIDs and pain medication may also be offered to control symptoms.

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.

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 • subgroups based on tumour site such as people with intra-abdominal or extra-abdominal DT • people with familial adenomatous polyposis
Comparators	• Established clinical management using medical therapies. ○ This may include chemotherapy, tyrosine kinase inhibitors • Best supportive care
Outcomes	The outcome measures to be considered include: • response rates (for example, partial or complete response) • duration of response • improvement in symptoms, including pain • adverse effects of treatment • health-related quality of life • progression-free survival • mortality

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. 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. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
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 **Related quality standards:** Sarcoma (2015) NICE quality standard 78

References

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

9. Kasper, Bernd, et al. "Current management of desmoid tumors: a review." JAMA oncology 10.8 (2024): 1121-1128.

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