Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ripretinib for treating advanced gastrointestinal stromal tumour after 3 or more treatments (review of TA881) [ID6496]

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of ripretinib within its marketing authorisation for treating advanced gastrointestinal stromal tumours after 3 or more treatments, including imatinib.

Background

Gastrointestinal stromal tumours (GIST) are a rare type of soft tissue sarcoma (a rare cancer of mesenchymal origin), which develops in the digestive tract (most frequently in the stomach and small intestine but can arise anywhere along the gastrointestinal tract). GIST are aggressive tumours and in advanced GIST the tumours will have begun to spread to other parts of the body (such as the liver or peritoneum). In over 85% of cases, the cancer cells associated with GIST are found with an activating mutation in either the tyrosine kinase (KIT) CD117 or platelet derived growth factor receptor alpha (PDGFRA) gene.[1] There are around 900 new cases of GIST each year in the UK.[2] Although GIST can occur at any age, the median age at diagnosis is around 60 to 65 years.[3]

The first treatment method used for GIST is surgery to remove the tumour. However drugs known as tyrosine kinase inhibitors can be used to treat tumours that are too large to be removed safely, or those that have already spread to other parts of the body. There are several pharmacological options for advanced GIST.

NICE technology appraisal guidance 86 recommends imatinib as first-line management of people with KIT (CD117)-positive unresectable and/or KIT (CD117)-positive metastatic GIST. This guidance notes that approximately 16% of patients will experience primary resistance to imatinib, and most patients will develop a reduced response at a later stage. However, NICE technology appraisal guidance 209 does not recommend imatinib at an increased dose for people with unresectable and/or metastatic GISTs whose disease has got worse after treatment with imatinib at the standard dose of 400 mg a day. NICE technology appraisal guidance 179 recommends sunitinib as a treatment option for people with unresectable and/or metastatic GISTs whose treatment with imatinib has failed due to resistance or intolerance.NICE technology appraisal guidance 488 recommends regorafenib as a treatment option (third-line) for people with unresectable or metastatic GIST whose disease has progressed on, or who are intolerant to, prior treatment with imatinib and sunitinib, but only if their Eastern Cooperative Oncology Group (ECOG) performance status is 0 to 1.

There are currently no lines of pharmacological therapy recommended specifically for the treatment of patients with GIST whose disease has progressed after treatment with third-line therapy. NICE technology appraisal guidance 881 does not recommend repritinib for treating advanced gastrointestinal stromal tumour (GIST) in adults after 3 or more kinase inhibitors. This scope is for a review of TA881.

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The technology

Ripretinib (Qinlock, Deciphera Pharmaceuticals) has a marketing authorisation in the UK for 'the treatment of adult patients with advanced gastrointestinal stromal tumour (GIST) who have received prior treatment with three or more kinase inhibitors, including imatinib'.

Intervention(s)	Ripretinib
Population(s)	Adults with advanced gastrointestinal stromal tumour who have received prior treatment with three or more kinase inhibitors, including imatinib
Subgroups	If the evidence allows the following subgroups will be considered: • people whose disease progressed after previous treatment with tyrosine kinase inhibitors • people whose disease is resistant or intolerant to tyrosine kinase inhibitors
Comparators	Established clinical management without ripretinib.
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rate (including partial response rate and duration of response) • adverse effects of treatment • 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. 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.

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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	**Related technology appraisals:** Ripretinib for treating advanced gastrointestinal stromal tumour after 3 or more treatments (2023) NICE technology appraisal guidance 881. Regorafenib for previously treated unresectable or metastatic gastrointestinal stromal tumours (2017) NICE technology appraisal guidance 488. Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (2014) NICE technology appraisal guidance 326. Imatinib for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours (2010) NICE technology appraisal guidance 209. Sunitinib for the treatment of gastrointestinal stromal tumours (2009) NICE technology appraisal guidance 179. Imatinib for the treatment of unresectable and/or metastatic gastro-intestinal stromal tumours (2004) NICE technology appraisal guidance 86. **Related interventional procedures:** Endoscopic full thickness removal of gastrointestinal stromal tumours of the stomach (2022) NICE interventional procedures guidance 717. **Related quality standards:** Sarcoma (2015) NICE quality standard QS78.

Questions for consultation

Please identify any new evidence that has become available since NICE technology appraisal guidance 881 was published?

Where do you consider repritinib will fit into the existing care pathway for advanced gastrointestinal stromal tumours?

Please select from the following, will ripretinib 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.

Would ripretinib be a candidate for managed access?

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Do you consider that the use of ripretinib 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.

Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.

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 ripretinib is 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. Oppelt P J, Hirbe A C, Van Tine B A (2017) Gastrointestinal stromal tumors (GISTs): point mutations matter in management, a review. Journal of Gastrointestinal Oncology 8 (3) 466- 473
2. GIST Cancer UK (2024) About GSTs. Available at: About GISTs – GIST Cancer UK
3. Judson I, Bulusu R, Seddon B, Dangoor A Mudan S (2017) UK clinical practice guidelines for the management of gastrointestinal stromal tumours (GIST). Clinical Sarcoma Research 7(6)