# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Appraisal

## Ripretinib for treating advanced gastrointestinal stromal tumours after 3 therapies

## Draft scope

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ripretinib within its marketing authorisation for advanced gastrointestinal stromal tumours (GIST) who have received previous treatment with tyrosine kinase inhibitors (TKI).

### 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-protein kinase KIT, CD117 (KIT) or platelet derived growth factor receptor alpha (PDGFRA) gene.[1] The annual incidence of GIST is estimated to be around 900 total cases (approximately 650 new diagnoses) per year in the UK.[2] Although GIST can occur at any age, the median age at diagnosis is around 60 to 65 years.[2]

The first treatment method used for GIST is surgery to remove the tumour, however drugs known as growth (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 and 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.

## The technology

Ripretinib (Qinlock, Deciphera Pharmaceuticals) is a switch-control tyrosine kinase inhibitor (TKI). It works by blocking the KIT and PDGFRA enzymes, slowing down the growth of the cancer cells and tumours. It is administered orally. Ripretinib does not currently have a marketing authorisation in the UK. It has been studied in clinical trials for the treatment of adults who have advanced GIST which has progressed despite receiving at least two prior targeted therapies.

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| **Intervention(s)** | Ripretinib |
| **Population(s)** | • Adults with advanced GIST who have received at least two TKI therapies or have documented intolerance to any of these treatments |
| **Comparators** | • Regorafenib (for adults whose disease has progressed on, or who are intolerant to, prior treatment with imatinib and sunitinib)<br>• Established clinical management without ripretinib including best supportive care |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression free survival<br>• response rate (including partial response rate and duration of response)<br>• adverse effects of treatment<br>• health-related quality of life. |

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| **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><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><br>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 of any managed access arrangement for the intervention will be taken into account. |
| **Other considerations** | If the evidence allows the following subgroups will be considered<br><br>• previous treatment with tyrosine kinase inhibitors whose disease has progressed<br><br>• resistance or intolerance to tyrosine kinase inhibitors<br><br>The availability and cost of biosimilar and generic products should be taken into account.<br><br>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 and NICE Pathways** | Related Technology Appraisals:<br><br>Regorafenib for previously treated unresectable or metastatic gastrointestinal stromal tumours (2017) NICE technology appraisal guidance 488<br><br>Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (2014) NICE technology appraisal guidance 326<br><br>Imatinib for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours (2010) NICE technology appraisal guidance 209<br><br>Sunitinib for the treatment of gastrointestinal stromal tumours (2009) NICE technology appraisal guidance 179 |

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| | Imatinib for the treatment of unresectable and/or metastatic gastro-intestinal stromal tumours (2004) NICE technology appraisal guidance 86<br><br>Appraisals in development (including suspended appraisals):<br><br>Avapritinib for treating unresectable or metastatic gastrointestinal stromal tumours [ID1626]<br><br>In development. Publication date to be confirmed<br><br>Gastrointestinal stromal tumours (unresectable, metastatic) - masitinib (after progression with imatinib) [ID622]<br><br>Suspended. Publication date to be confirmed.<br><br>Related Quality Standards:<br><br>Sarcoma (2015) NICE quality standard QS78Related NICE Pathways:<br><br>NICE pathway Gastrointestinal cancers<br><br>http://pathways.nice.org.uk/gastrointestinalcancers |
| **Related National Policy** | The NHS Long Term Plan, 2019. NHS Long Term Plan<br><br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105: specialist cancer services (adults).<br><br>NHS England (2016) Robotic assisted surgery for oesophago-gastric cancers. Clinical Commissioning Policy. Reference: 16006/P.<br><br>NHS England (2013) Oesophageal and Gastric (adult). 2013/14 NHS Standard Contract for Cancer. Reference: B11/S/a.<br><br>NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Chemotherapy (adult).D 2013/14 NHS Standard Contract for Cancer. Reference: B15/S/a.<br><br>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 |

**Questions for consultation**

Have all relevant comparators for ripretinib been included in the scope? How should best supportive care be defined?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom ripretinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider ripretinib will fit into the existing NICE pathway, Gastrointestinal cancers?

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 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.

Do you consider ripretinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of ripretinib can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's

Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

**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 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)