NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ripretinib for treating advanced gastrointestinal stromal tumours after 3 therapies [ID3805]

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ripretinib within its marketing authorisation for people with advanced gastrointestinal stromal tumours (GIST) who have had at least 3 prior therapies.

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] Public Health England estimate the annual incidence of all GIST to be approximately 800 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.[3]

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 after 3 prior targeted therapies.

Intervention(s)	Ripretinib
Population(s)	• Adults with advanced GIST who have had at least 3 prior therapies or have documented intolerance to any of these treatments
Comparators	• Established clinical management without ripretinib including best supportive care
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 of any managed access arrangement for the intervention will be taken into account. The economic modelling should include the costs associated with diagnostic testing in people with advanced GIST who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals'.
Other considerations	If the evidence allows the following subgroups will be considered • previous treatment with tyrosine kinase inhibitors whose disease has progressed • resistance or intolerance to tyrosine kinase inhibitors The availability and cost of biosimilar and generic products should be taken into account. 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:** 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 **Appraisals in development (including suspended appraisals):** Avapritinib for treating unresectable or metastatic gastrointestinal stromal tumours [ID1626] In development. Publication date to be confirmed Gastrointestinal stromal tumours (unresectable, metastatic) - masitinib (after progression with imatinib) [ID622] Suspended. Publication date to be confirmed. **Related Quality Standards:** Sarcoma (2015) NICE quality standard QS78 **Related NICE Pathways:** NICE pathway Gastrointestinal cancers
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105: specialist cancer services (adults). NHS England (2016) Robotic assisted surgery for oesophago-gastric cancers. Clinical Commissioning Policy. Reference: 16006/P. NHS England (2013) Oesophageal and Gastric (adult). 2013/14 NHS Standard Contract for Cancer. Reference: B11/S/a. NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Chemotherapy (adult).D 2013/14 NHS Standard Contract for Cancer. Reference: B15/S/a. 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

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 Detailed Statistics from the 'Get Data Out' programme NHS [online; accessed 11 February 2021]

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)