Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Cabozantinib for treating advanced neuroendocrine tumours that have progressed after systemic treatment ID6474

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of cabozantinib within its marketing authorisation for treating advanced pancreatic or extra-pancreatic neuroendocrine tumours that have progressed after systemic treatment.

Background

Neuroendocrine tumours (NETs) are a heterogeneous group of rare tumours which develop from neuroendocrine cells. Some types of NETs are also called carcinoid tumours. Pancreatic NETs are found in pancreas. Extra-pancreatic NETs refers to NETs which are found outside the pancreas, including in the stomach, lungs, bowel and thyroid.

Tumours may be 'functioning', where cells produce and release higher than normal levels of hormones or 'non-functioning', where normal levels are released. Specific symptoms vary by tumour location and whether the tumours are functioning or non-functioning.

The incidence of NETs in England was 8.8 per 100,000 of the population per year in 2018, but the incidence is increasing over time.[1] Approximately 50% of NETs occur in the digestive system, including the stomach, small and large bowel, pancreas and rectum, and 20% occur in the lungs.[2]

Surgery is the only curative treatment for NETs. For people who are unable to have surgery, where surgery has been unsuccessful, or where curative surgery is not an option because of the advance stage of the disease, the choice of treatment depends on the symptoms, stage of disease, and histological features of the tumour. Options for treating the tumour include interferon alfa, radiotherapy, ablation therapies and chemotherapy regimens (using combinations of streptozocin, 5-fluorouracil, temozolomide, etoposide, cisplatin, carboplatin, doxorubicin, and capecitabine). There are also several treatment options recommended by NICE for treating unresectable or metastatic NETs in adults with progressive disease:

- NICE TA449 recommends everolimus and sunitinib for treating well- or moderately differentiated unresectable or metastatic NETs of pancreatic origin in adults with progressive disease.

- NICE TA449 also recommends everolimus for treating well-differentiated (grade 1 or grade 2) non-functional unresectable or metastatic NETs of gastrointestinal or lung origin in adults with progressive disease.

- NICE TA539 recommends lutetium (177Lu) oxodotreotide for treating unresectable or metastatic, progressive, well-differentiated (grade 1 or grade 2), somatostatin receptor-positive gastroenteropancreatic NETs in adults.

Somatostatin analogues, such as octreotide and lanreotide, may also be used to reduce the symptoms caused the tumour and slow down tumour growth. The treatment pathway for people with NETs which have progressed after systemic treatment is unclear.

The technology

Cabozantinib (Cabometyx, Ipsen) does not currently have a marketing authorisation in the UK for advanced pancreatic or extra-pancreatic NETs that have progressed after systemic treatment. It is being studied in a clinical trial in people with advanced NETs after progression on prior therapy.

Intervention(s)	Cabozantinib
Population(s)	Adults with advanced pancreatic or extra-pancreatic NETs that have progressed after systemic treatment
Subgroups	If the evidence allows the following subgroups will be considered: • Pancreatic NETs • Extra-pancreatic NETs (including by tumour location)
Comparators	• Chemotherapy regimens • Best supportive care without cabozantinib
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • symptom control • 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.

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:** Lutetium (177Lu) oxodotreotide for treating unresectable or metastatic neuroendocrine tumours (2018) NICE technology appraisal guidance 539. Everolimus and sunitinib for treating unresectable or metastatic neuroendocrine tumours in people with progressive disease (2017) NICE technology appraisal guidance 449 **Related technology appraisals in development:** Lutetium oxodotreotide with octreotide for newly diagnosed unresectable or metastatic gastroenteropancreatic neuroendocrine tumours. Technology appraisal guidance [6315]. Expected publication date: TBC **Related interventional procedures:** Selective internal radiation therapy for neuroendocrine tumours that have metastasised to the liver. [IPG786] Published: May 2024
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017 NHS Digital (2022) NHS Outcomes Framework England, March 2022 Annual Publication

Questions for consultation

Where do you consider cabozantinib will fit into the existing care pathway for advanced pancreatic or extra-pancreatic NETs that have progressed after systemic treatment? Would cabozantinib be used after everolimus, sunitinib and lutetium (177Lu) oxodotreotide?

Please select from the following, will cabozantinib 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.

Are interferons a relevant comparator for cabozantinib for advanced pancreatic or extra-pancreatic NETs that have progressed after systemic therapy? Should any other comparators for cabozantinib be included in scope?

Are there any subgroups of people in whom cabozantinib is expected to more clinically effective or cost effective or other groups that should be examined separately?

Would cabozantinib be a candidate for managed access?

Do you consider that the use of cabozantinib 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.

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 cabozantinib 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.

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. White, B.E. et al. (2022) 'Incidence and survival of neuroendocrine Neoplasia in England 1995–2018: A retrospective, population-based study', The Lancet Regional Health - Europe, 23, p. 100510. doi:10.1016/j.lanepe.2022.100510.
2. Cancer Research UK (2024). Neuroendocrine tumours. Accessed October 2024.