NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

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 the pancreas. Extra-pancreatic NETs refers to NETs which are found outside the pancreas, including in the stomach, lungs, small and large bowel and thyroid.

NETs may be 'functioning', where cells produce and release higher than normal levels of hormones or non-site specific hormones, or 'non-functioning', where normal levels of hormones are released. Specific symptoms vary by tumour location and whether the tumours are functioning or non-functioning. NETs can also be categorised based on how similar the cancer cells look to normal cells (well-, moderately- or poorly- differentiated), how many cells are dividing (Ki-67 index) and whether the tumour cells have somatostatin receptors.

The incidence of NETs in England was 8.8 per 100,000 of the population per year in 2018, but the incidence and prevalence 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 potentially curative treatment for NETs, if undertaken at an early stage of the disease. 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 site, symptoms, stage of disease, grading and patient choice.

Somatostatin analogues, such as octreotide and lanreotide, may be used to reduce the symptoms caused the tumour and slow down tumour growth. Other options for treating NETs include radiotherapy, interventional radiology procedures (such as ablation and embolisation), chemotherapy regimens (including monotherapy or combinations of streptozocin, 5-fluorouracil, temozolomide, etoposide, cisplatin, carboplatin, doxorubicin, and capecitabine) and interferon alfa. There are also treatment options recommended by NICE for treating certain types of 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.

- NICE IPG786 recommends the use of selective internal radiation therapy as an option for NETs that have metastasised to the liver

The treatment pathway for people with NETs which have progressed after systemic treatment is unclear. This is largely because NETs are a heterogeneous group of tumours and numerous factors, including site, stage of disease and grade, impact treatment decisions. Best supportive care includes disease-specific dietetic support and palliation of hormone-specific and/ or treatment-related symptoms.

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) • Other characteristics of NETs (for example, functioning status, differentiation status, Ki-67 index and somatostatin receptor expression)
Comparators	Established clinical management without cabozantinib, including but not limited to: • Best supportive care • Chemotherapy • Other systemic treatments

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

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.