NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Cabozantinib for untreated locally advanced or metastatic renal cell carcinoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of cabozantinib within its marketing authorisation for untreated locally advanced or metastatic renal cell carcinoma.

Background

Renal cell carcinoma (RCC) is a cancer that usually originates in the lining of the tubules of the kidney (the smallest tubes inside the nephrons) that help filter the blood and make urine. RCC is the most common type of kidney cancer (more than 80% of the cases)[1]. There are several types of RCC. The main ones are clear cell (accounting for approximately 75% of cases)[1], papillary and chromophobe.

The tumour node metastases system is used to classify RCC into stages I to IV. Stage III denotes disease that is locally advanced and/or has spread to regional lymph nodes. Metastatic RCC, in which the tumour has spread beyond the regional lymph nodes to other parts of the body, is defined as stage IV. Early, small RCC tumours are usually asymptomatic; the diagnosis of early RCC is often incidental after abdominal scans for other indications. The most common presenting symptoms of advanced RCC are blood in the urine (haematuria), a palpable mass in the flank or abdomen and abdominal pain. Other non-specific symptoms include fever, night sweats, malaise and weight loss. Nephron sparing surgery may be curative in people with localised tumours. However, around half of those who have surgery develop advanced disease later on.

In 2015, 10,507 new kidney cancer cases were diagnosed in England[2]. In 2014, approximately 44% of people diagnosed with kidney cancer had stage III or IV disease and 25% to 31% had metastases[3]. The 5-year relative survival rate for stage IV RCC is approximately 6%[4].

The aim of treatment is to stop the growth of new blood vessels within the tumour. In untreated RCC, NICE technology appraisal guidance 169 recommends sunitinib as a 'first-line treatment option for people with advanced and/or metastatic renal cell carcinoma who are suitable for immunotherapy and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.' NICE technology appraisal guidance 215 recommends pazopanib as a 'first-line treatment option for people with

advanced renal cell carcinoma who have not received prior cytokine therapy and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1'.

The technology

Cabozantinib (Cabometyx, Ipsen) inhibits multiple receptor tyrosine kinases implicated in tumour growth and angiogenesis, pathologic bone remodelling, and metastatic progression of cancer. It is administered orally.

Cabozantinib does not currently have a marketing authorisation in the UK for untreated locally advanced or metastatic RCC. It has been being studied in a clinical trial, compared with sunitinib, in adults with untreated locally advanced or metastatic RCC.

Cabozantinib has a marketing authorisation in the UK for the treatment of advanced RCC in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy.

Intervention(s)	Cabozantinib
Population(s)	People with untreated locally advanced or metastatic renal cell carcinoma
Comparators	• Pazopanib • Sunitinib • Tivozanib (subject to ongoing NICE appraisal)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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 patient access schemes for the intervention or comparator technologies will be taken into account.
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 and NICE Pathways	Related Technology Appraisals: 'Pazopanib for the first-line treatment of advanced renal cell carcinoma' (2011). NICE Technology Appraisal 215. Static list. 'Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma' (2009). NICE Technology Appraisal 169. Static list. 'Bevacizumab (first-line), sorafenib (first- and second-line), sunitinib (second-line) and temsirolimus (first-line) for the treatment of advanced and/or metastatic renal cell carcinoma' (2009). NICE Technology Appraisal 178. Static list. Appraisals in development: 'Tivozanib for treating renal cell carcinoma' NICE technology appraisal guidance [ID591]. Publication expected December 2017. 'Cabozantinib for previously treated advanced renal cell

	carcinoma' NICE technology appraisal guidance [ID931]. Publication expected August 2017. 'Nivolumab in combination with ipilimumab for untreated advanced or metastatic renal cell carcinoma'. Proposed NICE technology appraisal [ID1182]. Publication date to be confirmed. Related NICE Pathways: Renal cancer (2017) NICE pathway http://pathways.nice.org.uk/pathways/renal-cancer
Related National Policy	NHS England (May 2016) Manual for prescribed specialised services. Section 105. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health (April 2016) NHS Outcomes Framework 2016-2017. Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 http://www.cancerresearchuk.org/about-us/cancer-strategy-in-england Department of Health (2014) The national cancer strategy: 4th annual report https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report NHS England (2013) B14. Cancer: Specialised kidney, bladder and prostate cancer services (Adult). NHS Standard Contract. https://www.england.nhs.uk/wp-content/uploads/2013/06/b14-cancr-kidney-blad-pros.pdf

Questions for consultation

Have all relevant comparators for cabozantinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for untreated locally advanced or metastatic RCC?

Are the outcomes listed appropriate?

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

Where do you consider cabozantinib will fit into the existing NICE renal cancer pathway?

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.

Do you consider cabozantinib 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 cabozantinib 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. We welcome comments on the appropriateness and suitability of the cost comparison methodology to 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 technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Cancer Research UK (2016) Types of kidney cancer. Accessed July 2017.

2. Office for National Statistics (2017) Cancer Registration Statistics. Accessed July 2017.

3. Cancer Research UK (2017) Kidney cancer incidence statistics. Accessed July 2017.

4. Cancer Research UK (2016) Kidney cancer survival statistics. Accessed July 2017.

