NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Cabozantinib for previously treated metastatic renal cell carcinoma

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of cabozantinib within its marketing authorisation for previously treated 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 (approximately 90% of the cases).[1] There are several different types of RCC, with the main ones divided into 5 categories: clear cell, papillary (types 1 and 2), chromophobe, oncocytic and collecting duct carcinoma. Clear cell is the most common form of RCC accounting for approximately 80–90% of cases.[2]

The tumour node metastases system is used to grade RCC into stages I to IV. Advanced RCC, in which the tumour is either locally advanced and/or has spread to regional lymph nodes, is generally defined as stage III. Metastatic RCC, in which the tumour has spread beyond the regional lymph nodes to other parts of the body, is generally defined as stage IV.

Early, small RCC tumours are usually asymptomatic; the diagnosis of early RCC is usually incidental after abdominal scans for other indications. The most common presenting symptoms of metastatic and/or 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 curative resection for earlier stages of the disease develop advanced and/or metastatic disease later on.

In 2012, 8638 new kidney cancer cases were diagnosed in England.[3] In 2013, approximately 46% of people diagnosed with kidney cancer had stage III or IV disease and 27% had stage IV disease.[3] The 5-year survival rate for metastatic RCC is approximately 10%.[4]

The aim of treatment is to stop the growth of new blood vessels within the tumour. After failure of prior systemic treatment with a tyrosine kinase inhibitor or cytokine, NICE technology appraisal guidance 333 recommends axitinib. Because the remit referred to NICE by the Department of Health for axitinib only includes adults who have been previously treated with sunitinib, the use

of axitinib after treatment with other tyrosine kinase inhibitors is not subject to statutory funding. This recommendation will be reviewed within the ongoing multiple technology appraisal of 'axitinib, everolimus, nivolumab, sorafenib and sunitinib for previously treated advanced or metastatic RCC'. Everolimus, sorafenib and sunitinib are not recommended after initial therapies had failed in NICE guidance (NICE technology appraisal guidance 178 and 219); however, everolimus is available in England for metastatic RCC through the Cancer Drugs Fund for some patients. The recommendations in technology appraisal guidance 219, and those in technology appraisal 178 on sorafenib and sunitinib for previously treated advanced or metastatic RCC, will also be reviewed within the ongoing multiple technology appraisal.

The technology

Cabozantinib (brand name unknown, Exelixis) inhibits multiple receptor tyrosine kinases implicated in tumour growth and angiogenesis, pathologic bone remodeling, and metastatic progression of cancer. It is orally administered.

Cabozantinib does not currently have a marketing authorisation in the UK for previously treated RCC. It has been studied in a clinical trial compared with everolimus in adults with metastatic RCC that has progressed after Vascular Endothelial Growth Factor Receptor (VEGFR) tyrosine kinase inhibitor therapy.

Intervention(s)	Cabozantinib
Population(s)	People with previously treated metastatic renal cell carcinoma
Comparators	• axitinib • everolimus (not recommended by NICE but funded via the Cancer Drugs Fund) • best supportive care
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. 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	If the evidence allows the following subgroups will be considered. These include: • previous treatment • prognostic score (for example, ECOG or Motzer). 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: 'Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment' (2015). NICE technology appraisal 333. Review ongoing. 'Everolimus for the second-line treatment of advanced renal cell carcinoma' (2011). NICE technology appraisal guidance 219. Review ongoing. '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 guidance 178. Part review ongoing. Appraisals in development 'Axitinib, everolimus, sorafenib and sunitinib for previously treated advanced or metastatic renal cell carcinoma (incl. review of TA333 and TA219, and part review of TA178)'. NICE technology appraisals guidance [ID897]. Publication expected April 2017. 'Pazopanib for the second line treatment of metastatic

	renal cell carcinoma (discontinued)' NICE technology appraisals guidance [ID70]. Related Guidelines: 'Referral guidelines for suspected cancer' (2005). NICE guideline 27 Review date June 2015. 'Improving outcomes in urological cancers' (2002). NICE guideline CSGUC. Review date to be confirmed. Related Interventional Procedures: 'Irreversible electroporation for treating renal cancer' (2013). NICE interventional procedures guidance 443. 'Laparoscopic cryotherapy for renal cancer' (2011). NICE interventional procedures guidance 405. 'Percutaneous cryotherapy for renal cancer' (2011). NICE interventional procedures guidance 402. 'Percutaneous radiofrequency ablation for renal cancer' (2010). NICE interventional procedures guidance 353. Related NICE Pathways: Renal cancer (2015) NICE pathway
Related National Policy	NHS England (January 2014) Manual for prescribed specialised services. Section 105. http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf NHS England: B14. Specialised Urology. NHS Care and Clinical Reference Groups. Link accessed: 26th February 2015 http://www.england.nhs.uk/commissioning/spec-services/npc-crg/group-b/b14/ Department of Health (2014) The national cancer strategy: 4th annual report https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report

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 previously treated metastatic renal cell carcinoma?

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 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 pathway, 'renal cancer'?

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.

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)

References

1. American Cancer Society (2014) Kidney Cancer (Adult) - Renal Cell Carcinoma. Accessed October 2015.

2. Patient.co.uk: Renal Cancer. Accessed October 2015.

3. Cancer Research UK (2012) Kidney cancer incidence statistics. Accessed February 2016

4. GP Notebook - Clear Cell Cancer. Accessed February 2016