

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Cabozantinib for previously treated advanced renal cell carcinoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of cabozantinib within its marketing authorisation for previously treated advanced 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 2013, 9,900 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. Sorafenib, sunitinib and everolimus are not recommended after initial therapies have failed in NICE guidance (NICE technology appraisal guidance 178 and 219). Everolimus is available in England for metastatic RCC through the Cancer Drugs Fund (at the time the final scope was written) for people who have had prior treatment with only one previous tyrosine kinase inhibitor. Everolimus is also available for second or third line treatment of metastatic RCC where disease has progressed on or after treatment with VEGF-targeted therapy through the Cancer Drugs Fund. Everolimus is subject to ongoing NICE CDF transition review [ID1014]. An ongoing NICE technology appraisal is in development for nivolumab for previously treated advanced or metastatic RCC [ID853].

The technology

Cabozantinib (brand name unknown, Ipsen) 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 received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) for ‘the treatment of advanced renal cell carcinoma (RCC) in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy’.

Intervention(s)	Cabozantinib
Population(s)	People who have received previous VEGF-targeted therapy for advanced renal cell carcinoma
Comparators	<ul style="list-style-type: none"> • axitinib • everolimus • nivolumab (subject to ongoing NICE appraisal [ID 853]) • best supportive care
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression free survival • response rates • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.</p>
<p>Other considerations</p>	<p>If the evidence allows the following subgroups will be considered. These include:</p> <ul style="list-style-type: none"> • previous lines of treatment • prognostic score <p>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.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>‘Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment’ (2015). NICE technology appraisal 333. Review date to be confirmed.</p> <p>‘Everolimus for the second-line treatment of advanced renal cell carcinoma’ (2011). NICE technology appraisal guidance 219. Everolimus subject to ongoing NICE CDF transition review [ID1014], expected date of publication February 2017.</p> <p>‘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. Review date to be confirmed.</p> <p>Appraisals in development:</p> <p>‘Nivolumab for previously treated advanced or metastatic renal cell carcinoma’. NICE technology appraisal guidance [ID853]. Publication expected October 2016.</p>

	<p>‘Pazopanib for the second line treatment of metastatic renal cell carcinoma (discontinued)’ NICE technology appraisals guidance [ID70].</p> <p>Related Guidelines:</p> <p>‘Referral guidelines for suspected cancer’ (2005). NICE guideline 27 Review date June 2015.</p> <p>‘Improving outcomes in urological cancers’ (2002). NICE guideline CSGUC. Review date to be confirmed.</p> <p>Related Interventional Procedures:</p> <p>‘Irreversible electroporation for treating renal cancer’ (2013). NICE interventional procedures guidance 443.</p> <p>‘Laparoscopic cryotherapy for renal cancer’ (2011). NICE interventional procedures guidance 405.</p> <p>‘Percutaneous cryotherapy for renal cancer’ (2011). NICE interventional procedures guidance 402.</p> <p>‘Percutaneous radiofrequency ablation for renal cancer’ (2010). NICE interventional procedures guidance 353.</p> <p>Related NICE Pathways:</p> <p>Renal cancer (2015) NICE pathway</p>
<p>Related National Policy</p>	<p>NHS England, National Cancer Drugs Fund List, Feb 2016.</p> <p>NHS England (May 2016) Manual for prescribed specialised services. Section 105.</p> <p>https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf</p> <p>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013.</p> <p>https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf</p> <p>NHS England: B14. Specialised Urology. NHS Care and Clinical Reference Groups. Link accessed: 26th February 2015</p> <p>http://www.england.nhs.uk/commissioning/spec-services/npc-crg/group-b/b14/</p> <p>Department of Health (2014) The national cancer strategy: 4th annual report</p> <p>https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report</p>

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](#) (2013) Kidney cancer incidence statistics. Accessed March 2016.
4. GP Notebook - [Clear Cell Cancer](#). Accessed February 2016.