

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Lenvatinib with everolimus for previously treated advanced renal cell carcinoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of lenvatinib with everolimus within its marketing authorisation for previously treated advanced renal cell carcinoma.

Background

Renal cell cancer (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 80% of the cases).¹ There are several types of RCC. The main ones are clear cell, papillary and chromophobe. Clear cell is the most common form of RCC accounting for approximately 75% of cases.²

The tumour node metastases system is used to grade RCC into stages I to IV. Stage III denotes disease that is locally advanced and/or has spread to regional lymph nodes and stage IV denotes that distant metastasis has occurred. 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 or metastatic 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 or metastatic disease later on.

In 2014, 9,123 new kidney cancer cases were diagnosed in England.³ In 2014, approximately 44% of people diagnosed with kidney cancer had stage III or IV disease and 25% had stage IV disease.⁴ The 5-year survival rate for metastatic RCC is approximately 10%.⁵

The aim of treatment is to stop the growth of new blood vessels within the tumour. After failure of prior systemic treatment with a cytokine or tyrosine kinase inhibitor 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, such as pazopanib (NICE technology appraisal guidance 215) is not subject to statutory funding. Nivolumab is also recommended as an option for previously

treated advanced renal cell carcinoma in adults (TA417). Everolimus is available in England for metastatic RCC through the Cancer Drugs Fund (at the time the scope was written) for people whose disease has progressed during or after treatment with vascular endothelial growth factor targeted therapy. Everolimus is subject to ongoing NICE CDF transition review [ID1015]. Cabozantinib is subject to ongoing NICE appraisal for previously treated advanced RCC.

The technology

Lenvatinib (Kisplyx, Eisai) is a multiple receptor tyrosine kinase inhibitor that selectively inhibits vascular endothelial growth factor (VEGF) receptors and other receptor tyrosine kinases that are involved in tumour proliferation. It is administered orally.

Lenvatinib has a marketing authorisation in the UK “in combination with everolimus for the treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF)-targeted therapy.”

Intervention(s)	Lenvatinib
Population(s)	Adults with advanced renal cell carcinoma who have had 1 prior VEGF-targeted therapy
Comparators	<ul style="list-style-type: none"> • Axitinib • Nivolumab • Everolimus (NICE guidance is in development, funded by the Cancer Drugs Fund in the interim) • Best supportive care • Cabozantinib (subject to ongoing NICE appraisal [ID931])
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.

Economic analysis	<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>
Other considerations	<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>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>‘Nivolumab for previously treated advanced renal cell carcinoma’ (2016). NICE technology appraisal 417. Review date November 2019.</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 [ID1015], 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>Terminated appraisals</p> <p>‘Pazopanib for the second line treatment of metastatic renal cell carcinoma (discontinued)’ NICE technology appraisals guidance [ID70].</p> <p>Appraisals in development (including suspended appraisals)</p>

	<p>'Cabozantinib for treating renal cell carcinoma'. NICE technology appraisals guidance [ID931]. Publication expected June 2017.</p> <p>'Tivozanib for the treatment of advanced renal cell carcinoma'. NICE technology appraisals guidance [ID591]. Publication expected December 2017.</p> <p>'Axitinib, everolimus, sorafenib and sunitinib for treated advanced or metastatic renal cell carcinoma'. NICE technology appraisals guidance [ID897]. Suspended appraisal.</p> <p>Related Guidelines:</p> <p>'Suspected cancer: recognition and referral' (2015) NICE guideline 12</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 (July 2016) National Cancer Drugs Fund List.</p> <p>https://www.england.nhs.uk/cancer/cdf/cancer-drugs-fund-list/</p> <p>NHS England (May 2016) Manual for prescribed specialised services. Section 15.</p> <p>https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf</p> <p>Department of Health (April 2016) NHS Outcomes Framework 2016-2017. Domain 1.</p> <p>https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p> <p>Independent Cancer Taskforce (2015) Achieving world-</p>

	<p>class cancer outcomes: a strategy for England 2015-2020</p> <p>http://www.cancerresearchuk.org/about-us/cancer-strategy-in-england</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> <p>NHS England (2013/14) B14. Specialised Urology. NHS Standard Contract.</p> <p>http://www.england.nhs.uk/commissioning/spec-services/npc-crg/group-b/b14/</p>
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References

- ¹ Cancer Research UK [Types of kidney cancer](#). Accessed November 2016.
- ² Cancer Research UK [Types of kidney cancer](#). Accessed November 2016.
- ³ Office for National Statistics [Cancer Registration Statistics](#). Access October 2016.
- ⁴ Cancer Research UK [Kidney cancer statistics](#). Accessed October 2016.
- ⁵ GP Notebook [Clear Cell Cancer](#). Accessed October 2016.