NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Axitinib for the treatment of advanced renal cell carcinoma after failure of prior systematic treatment

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of axitinib within its licensed indication for the treatment of advanced renal cell carcinoma after failure of prior systematic treatment.

Background

Renal cell carcinoma (RCC) is a type of kidney cancer that usually originates in the lining of the tubules of the kidney and contains many blood vessels. American Joint Committee on Cancer (AJCC) tumour node metastases (TNM) 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 or IV. Metastatic RCC, in which the tumour has spread beyond the regional lymph nodes to other parts of the body, is also 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. Others non-specific symptoms include fever, night sweats, malaise and weight loss.

In 2006, 6,906 new kidney cancers were diagnosed in England and Wales, of which an estimated 85 - 90% were RCC. In 2006, of people presenting with RCC in England and Wales for whom staging information was available, an estimated 17% had stage IV disease. The 5-year survival rate for metastatic RCC is approximately 10%.

The primary objectives of medical intervention are relief of physical symptoms and maintenance of function. Metastatic and/or advanced RCC is largely resistant to chemotherapy, radiotherapy and hormonal therapy. Current NICE guidance recommends sunitinib as a first-line treatment for people with advanced and/or metastatic RCC for whom immunotherapy is suitable and have an Eastern Cooperative Oncology Group status of 0 or 1 (technology appraisal 169). Pazopanib is recommended as a first-line treatment for people with advanced RCC have an Eastern Cooperative Oncology Group status of 0 or 1 (Technology appraisal 215). An alternative treatment option for advanced and/or metastatic RCC is cytokine-based immunotherapy, including interleukin-2 (IL-2) (sometimes called aldesleukin) or interferon alfa

2-a (IFN-alfa). Current NICE guidance does not recommend bevacizumab, sorafenib or temsirolimus as first-line treatments, or sorafenib or sunitinib as second-line treatments for people with advanced and/or metastatic RCC (Technology appraisal 178). Current NICE guidance does not recommend everolimus as second-line treatment for people with advanced RCC (Technology appraisal 219). There is no standard treatment for people with metastatic RCC in whom first-line immunotherapy has failed, or is unsuitable.

The technology

Axitinib (Pfizer) is an oral multi-targeted kinase receptor inhibitor with anti-tumour activity. Axitinib inhibits vascular endothelial growth factor receptor (VEGFR) -1, -2 and -3, platelet-derived growth factor receptor (PDGFR), and c-kit, which may result in inhibition of angiogenesis in tumours.

Axitinib does not have a UK marketing authorisation for use in advanced RCC after failure of prior systematic treatment. Axitinib has been studied in clinical trials compared with placebo or sorafenib. These trials include adults with metastatic or advanced RCC who have received prior systemic treatment with either sunitinib, bevacizumab, temsirolimus, or cytokine-based treatment; or whose disease is refractory to cytokine-based treatment.

Intervention	Axitinib
Populations	Adults with advanced renal cell carcinoma who have received prior systemic treatment
Comparators	• 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.

Other considerations	If evidence allows subgroups according to the following will be considered: • resected versus unresected primary tumour • performance status. Guidance will only be issued in accordance with the marketing authorisation
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal, No. 178, August 2009. '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'. Expected date of review October 2011. Technology Appraisal, No. 169, March 2009. 'Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma'. Expected date of review October 2011. Technology Appraisal, No. 215, February 2011. 'Pazopanib for the first-line treatment of advanced renal cell carcinoma''. Expected date of review December 2013. Technology Appraisal, No. 219, April 2011. 'Everolimus for the second-line treatment of advanced renal cell carcinoma'. Expected date of review February 2013. Related Interventional Procedures: Interventional Procedure No. 344, January 2007, 'Cryotherapy for renal cancers' NICE Interventional Procedure Guidance No. 91, September 2004, 'Percutaneous radiofrequency ablation of renal cancer' Related Cancer Service Guidance: NICE Cancer service guidelines CSG, September 2002, 'Improving outcomes in urological cancer', Related Guidelines:

Questions for consultation

Have the most appropriate comparators for the treatment of advanced RCC after failure of prior systematic treatment been included in the scope?

How should best supportive care be defined?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology 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 the technology 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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)