NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Everolimus for the second-line treatment of advanced and/or metastatic renal cell carcinoma

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of everolimus, within its licensed indication, for the treatment of advanced and /or metastatic renal cell carcinoma.

Background

Renal cell carcinoma (RCC), also called renal adenocarcinoma or hypernephroma, is a cancer usually originating in the lining of the tubules of the kidney. The stage of RCC is usually reported using the tumour, node and metastasis (TMN) classification. This is based on the extent of the primary tumour (T), whether lymph nodes are affected (N) and whether metastases are present (M). Advanced and metastatic RCC fall within stages III and 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 usually 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. Others non-specific symptoms include fever, night sweats, malaise and weight loss.

Kidney cancer accounts for around 2% of all cancers in the UK. In 2004, 6,180 new kidney cancers were diagnosed in England and Wales, of which an estimated 85 - 90% were RCC. RCC is nearly twice as common in men, than in women, and most commonly affects adults aged 50-80 years old. In 2005, there were 3,134 registered deaths from kidney cancer in England and Wales.

Approximately 25% of RCC patients present with advanced and/or metastatic disease (stage III or IV). An estimated 50% of patients who have curative resection for earlier stages will develop recurrent and/or metastatic disease. Without treatment, these patients have a median survival rate of only 6-12 months and a two-year survival rate of 10-20%.

Surgical resection to remove the entire kidney (radical nephrectomy) or part of the kidney (partial nephrectomy) is the only accepted curative treatment for patients with non metastatic RCC (TNM stage I –III), and the success of

surgery depends on the stage of disease. Current standard treatment of metastatic RCC (stage IV) is immunotherapy with interleukin-2 (IL-2) (sometimes called aldesleukin) or interferon alfa (IFN-α) which may lead to tumour shrinkage. Palliative surgery, arterial embolisation or radiotherapy may also be considered in these patients. Bevacizumab plus IFN-α, sorafenib, sunitinib and temsirolimus all have UK marketing authorisations for use in the treatment of advanced and/or metastatic RCC. Current NICE guidance recommends sunitinib as a first-line treatment 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.There is a currently a technology appraisal underway of the use of bevacizumab (first-line), sorafenib (first- and second-line), sunitinib (second-line) and temsirolimus (first-line) for the treatment of advanced and/or metastatic RCC.

The technology

Everolimus (Afinitor, Novartis Pharmaceuticals) is an oral active inhibitor of the mammalian target of rapamycin (mTOR) protein, a central regulator of tumour cell division and blood vessel growth in cancer cells.

Everolimus does not have a UK marketing authorisation for use in advanced/metastatic RCC. In May 2009, the EMEA adopted a positive opinion, recommending everolimus for the treatment of patients with advanced RCC, whose disease has progressed on or after treatment with vascular endothelial growth factor (VEGF)-targeted therapy. Everolimus has a marketing authorisation for other indications in the EU.

Intervention(s)	Everolimus
Population(s)	Adults with advanced RCC whose disease has progressed on or after treatment with VEGF-targeted therapy
Comparators	• best supportive care * dependent on the outcome of the ongoing MTA: 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, sorafenib and/or sunitinib may be included as comparators.

Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rate • 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 the evidence allows the following subgroups will be considered: resected versus unresected primary tumour; clear cell versus non-clear cell; prognostic risk group; and prior therapy. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No.169, Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma (March 2009). Technology Appraisal in Preparation, 'Bevacizumab (first-line), sorafenib (first- and second-line), sunitinib (second-line) and temsirolimus (first-line) for the treatment of renal cell carcinoma', Earliest anticipated date of publication TBC Technology Appraisal in Preparation (pre-referral) 'Pazopanib for the treatment of advanced and/or metastatic renal cell carcinoma', date of publication TBC Related Cancer Service Guidance: NICE Cancer service guidelines CSG, September 2002, 'Improving outcomes in urological cancer'