

## Social Values and Health Priority Setting Case Study

<b>Title of Case Study</b>	<b>Sunitinib as a first line treatment for advanced and/or metastatic renal cell carcinoma</b>
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<b>Case Summary (approx. 350 words)</b>  Please include information here about why the case is of particular interest	<p>Sunitinib was the first treatment assessed by NICE under its end of life criteria introduced in 2009. This end of life criteria give special consideration to life-extending treatments for patients with short life expectancy and where patient populations are small, in recognition of the higher costs and innovative nature of some such interventions which put them beyond the range of cost effectiveness ratios normally required for a treatment to be judged an acceptable use of NHS resources by NICE.</p> <p>Sunitinib was one of the cancer medicines involved in the ‘top up payments’ controversy in the UK in 2008, wherein patients were paying privately for expensive treatments not approved for use in the NHS, and being effectively forced out of NHS care by rules which prohibited the concurrent provision of private and NHS care, leaving those patients to pay not only for the costs of the drug in question but also for all associated care.</p> <p>The end of life criteria were developed and introduced by NICE in order to take account of the innovative and high cost nature of end of life drugs such as sunitinib, which would be refused for use on the NHS if assessed on the basis of existing ‘normal’ NICE rules on cost-effectiveness.</p>
<b>1. Facts of the case</b>	<b>Facts of the case</b>
Please include information on as many of the following as are relevant to the case: <ul style="list-style-type: none"> <li>• At what condition is the intervention, program or service aimed?</li> <li>• What are its effects? Eg. Is it curative, preventative, palliative, life-prolonging, rehabilitative?</li> <li>• Is there a relevant comparator? If so how does this intervention, service or program compare to the alternative? Include ICER estimates/QALY costs if relevant.</li> <li>• What are the significant features about the condition and/or about the patient population in this case? Eg. patient population is very young, very old, condition is rare, life-threatening, life-limiting etc.</li> <li>• How are the benefits of the intervention distributed across the</li> </ul>	<p>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. RCC accounts for 90% of kidney cancers and approximately 3% of all adult cancers. In England and Wales, kidney cancer is the 8th most common cancer in men and the 14th most common in women. In 2004, there were 5745 cases of newly diagnosed kidney cancer registered in England and Wales. The incidence of kidney cancer begins to rise after the age of 40 and is highest in people older than 65. In England and Wales the estimated overall 5-year survival rate for RCC is 44%, but there are large differences according to the stage of disease at the time of diagnosis. The worldwide incidence of kidney cancer among both men and women has been rising steadily since the 1970s (NICE, 2009a)</p> <p>In 2006, of people presenting with RCC in England and Wales for whom staging information was available, an estimated 26% and 17% had stage III and stage IV disease, respectively. About half of those who have curative resection for earlier stages of the disease also go on to develop advanced and/or metastatic disease. The prognosis following a diagnosis of advanced and/or metastatic RCC is poor. The 5-year survival rate for metastatic RCC is approximately 10%.</p>

<p>patient population and/or across time?</p> <ul style="list-style-type: none"> <li>• What is the cost or budget impact of the intervention/service/ programme?</li> <li>• What is the nature and strength of the evidence about the outcomes of the intervention, service or programme? Eg. randomized clinical trials, evidence on patient-related outcomes.</li> <li>• How did the issue about this case arise - for example, from clinical practice, from a policy setting, from a topic selection process?</li> </ul>	<p>Metastatic RCC is largely resistant to chemotherapy, radiotherapy and hormonal therapy. People with advanced and/or metastatic RCC are usually treated with either interferon alfa-2a (IFN-<math>\alpha</math>) or interleukin-2 immunotherapy or a combination of IFN-<math>\alpha</math> and interleukin-2. IFN-<math>\alpha</math> is the most commonly used immunotherapy and has a marketing authorisation for treatment of people with advanced RCC.</p> <p>Sunitinib is an inhibitor of a group of closely related tyrosine kinase receptors. It inhibits VEGF/PDGF receptors on cancer cells, vascular endothelial cells and pericytes, inhibiting the proliferation of tumour cells and the development of tumour blood vessels. Sunitinib has a UK marketing authorisation for the treatment of people with advanced and/or metastatic RCC.</p> <p>One randomised controlled trial (RCT) of 750 people assessed the effect of sunitinib (n = 375) compared with IFN-<math>\alpha</math> alone (n = 375). Median overall survival was found to be 26.4 months in the sunitinib arm and 20.0 months in the interferon alfa-2a (IFN-<math>\alpha</math>) arm. The median final progression-free survival was found to be 48 weeks (11 months) in the sunitinib arm and 22.3 weeks (5.1 months) in the IFN-<math>\alpha</math> arm</p> <p>Sunitinib is administered orally. The average daily cost of sunitinib is £74.74, with an average 6-week cycle costing £3139. The manufacturer of sunitinib agreed a patient access scheme in which the first treatment cycle of sunitinib is free to the NHS.</p> <p>Including the agreed patient access scheme, the final ICER estimates for Sunitinib were between £49,300 and £54,366 per QALY gained for sunitinib compared with IFN-<math>\alpha</math>. (NICE, 2009a; para. 4.3.9).</p>
<p><b>2. Policy decision: process</b></p>	<p><b>Policy decision: process</b></p>
<p>Please include information on as many of the following as are relevant to this case:</p> <ul style="list-style-type: none"> <li>• What stages/institutions were involved in the decision making process?</li> <li>• Is legal context important in this case? If so, in what way?</li> <li>• Who was involved? Eg. key stakeholders, the public, professionals, industry, patients, governmental or non-government policy actors.</li> <li>• How were they involved, and at what stages of the process?</li> <li>• Was there disagreement between any of the parties involved in the decision process?</li> <li>• Do any rules or frameworks exist to guide decision making? If so, were they followed in this instance?</li> <li>• Do mechanisms exist for challenging the decision at any stage of the process?</li> </ul>	<p>Sunitinib was appraised according to NICE's Single Technology Appraisal process (see NICE, 2010)</p> <p>Sunitinib was originally appraised by NICE along with three other drugs (bevacizumab, sorafenib and temsirolimus) in 2008 and rejected on the basis that, whilst they provided some benefits, they did not meet cost-effectiveness criteria and so could not be considered a good use of NHS resources.</p> <p>NICE then reconsidered sunitinib in 2009, using the then new End of Life criteria, and published guidance approving the drug for use in the NHS in March of that year. The decision also took into account the Patient Access Scheme proposed by Pfizer in which it offered to provide the first cycle of sunitinib free to NHS patients.</p>

<ul style="list-style-type: none"> <li>• How, if at all, is the decision process or the decision itself publicized?</li> </ul>	
<b>3. Policy decision: content</b>	<b>Policy decision: content</b>
<p>Please include information on as many of the following as are relevant to this case:</p> <ul style="list-style-type: none"> <li>• What decision was made about the intervention, service or program, if any?</li> <li>• What values were relevant in the case or in the decision itself? For example, values of cost-effectiveness, clinical effectiveness, justice/equity, solidarity or autonomy. How did they affect the decision itself?</li> <li>• Was the way in which these values were balanced affected by any specific features of the case? For example, end of life considerations, age of patients, impact on carers, disease severity, innovative nature of the intervention, social stigma or cultural sensitivity?</li> <li>• Did the case challenge established guidance or 'decision rules'? Eg. on cost-effectiveness, cost thresholds, age discrimination etc. If so, in what way?</li> <li>• Were any health system-wide considerations influential in the decision? For example, displacement of old technologies, professional practice issues, or infrastructure/feasibility considerations.</li> </ul>	<p>The following were included in NICE's decision to approve sunitinib for use in the NHS:</p> <p><i>Relevance of limited treatment alternatives</i></p> <p>The Committee heard from clinical specialists and patient experts that there are limited treatment options for people with advanced and/or metastatic RCC. The Committee noted that the only current standard first-line treatment is immunotherapy and there are no current treatment options for people whose condition had failed to respond to immunotherapy or who were considered unsuitable for immunotherapy. Moreover there are no current standard second-line treatment options. The Committee heard from people with RCC and patient experts that immunotherapy is associated with limited effectiveness and high toxicity. The Committee also heard that RCC does not respond well to conventional chemotherapies and that sunitinib represents a substantial improvement in first-line treatment for advanced and/or metastatic RCC. The Committee noted the comments received that some individual patients experienced clinical benefit from this drug and that lives of people with RCC had been extended for a number of years following treatment with sunitinib.</p> <p><i>Disease rarity and disease severity</i></p> <p>The Committee heard from people with RCC and patient experts that advanced and/or metastatic RCC is a relatively rare cancer and noted the views of both patient and clinical experts concerning the severity of the disease. The Committee also heard from clinical experts, the Assessment Group and the manufacturer that there is a paucity of data on the utility values associated with living with advanced and/or metastatic RCC. The Committee noted that it may be difficult to fully capture the effects of sunitinib on health-related quality of life. The Committee acknowledged the comments that were received from people with RCC and the public, and that were summarised in a report, stating that some people with RCC had experienced significant improvements in their quality of life as a result of using sunitinib.</p> <p><i>Clinical Effectiveness</i></p> <p>The Assessment Group concluded that for people who are suitable for immunotherapy sunitinib appears to offer benefits compared with IFN-<math>\alpha</math> alone in terms of overall survival, progression-free survival and tumour response. Therefore the Committee concluded that sunitinib is a clinically effective first-line treatment for advanced and/or metastatic RCC for patients with an ECOG performance status of 0 or 1.</p> <p><i>End of Life considerations</i></p> <p>The Committee was aware that the total number of people with advanced and/or metastatic RCC in England and Wales was approximately 4000. Although the Committee noted that sunitinib was to be aimed at more patient groups than just people with RCC, such as people with gastrointestinal stromal tumours, this was the first indication for which it was being appraised. It therefore considered that for this appraisal, sunitinib should be regarded as meeting this criterion for an end-of-life treatment.</p>

	<p>The Committee noted from the clinical trials that the normal life expectancy with IFN-<math>\alpha</math> treatment alone was unlikely to be greater than 24 months and was potentially as low as 12 months.</p> <p>The Committee also noted that evidence from the sunitinib trial suggested that sunitinib increased survival by more than 3 months in comparison with IFN-<math>\alpha</math> alone.</p> <p><i>Innovation</i></p> <p>The Committee was further persuaded that sunitinib provided a step-change in the first-line treatment of advanced and/or metastatic RCC and noted that more than 20% of the public and patients that responded in consultation highlighted this impressive benefit from sunitinib.</p> <p>In summary, the Committee was satisfied that sunitinib met the criteria for being a life-extending end-of-life treatment, and that the evidence presented for this consideration was sufficiently robust. Whilst the Committee concluded that although it might be at the upper end of any plausible valuation, with ICERs of between £49,300 and £54,366 per QALY, in this case there was a significant step-change in treating a disease for which there is only one current standard first-line treatment option. It concluded that sunitinib as a first-line treatment for advanced and/or metastatic RCC could be recommended as a cost-effective use of NHS resources, if a patient has an ECOG performance status of 0 or 1 and there are no further treatment options recommended by NICE after first-line sunitinib treatment.</p> <p>(NICE, 2009a)</p>
<p><b>4. Discussion</b></p>	<p><b>Discussion</b></p>
<p>Please use this space to reflect on, for example:</p> <ul style="list-style-type: none"> <li>• The reasons or values explicitly used in making the decision. Do these reflect any institutional decision rules or statements of value, for example commitments to equality, non-discrimination or fairness? Do they reflect wider social, moral, cultural, religious values, and if so how?</li> <li>• Considerations not explicitly taken into account in the decision, but which may nonetheless have been important ‘background’ factors. These might include, for example, public opinion, political sensitivity, moral sensitivity, and international reputation, as well as cultural, social, moral, religious or institutional norms.</li> <li>• The impact of the decision making process on the decision itself, if any.</li> <li>• Any issues relating to implementation. For example, whether access may be restricted by</li> </ul>	<p>Sunitinib was one of the first drugs to be approved using the end of life criteria introduced by NICE in early 2009.</p> <p>When NICE first rejected Sunitinib for use in the NHS in 2008, some patients were paying privately for the drug and there were numerous stories in the media about individuals having, for example, to sell their houses to pay for cancer medicines (see for example <a href="http://www.news.bbc.co.uk/1/hi/england/kent/8650765.stm">www.news.bbc.co.uk/1/hi/england/kent/8650765.stm</a>)</p> <p>This was part of the ‘NHS top ups’ controversy which developed in 2008 whereby patients were paying large sums of money privately for cancer drugs which had not been approved by NICE for use in the NHS, and then being excluded from <i>all</i> NHS care because of rules which stipulated that NHS and private care should not be provided concurrently. This controversy was the subject of the Richards Review into ‘top up payments’ which reported in November 2008 (see Richards, 2008; see also Weale and Clark, 2009).</p> <p>Also notable in this case is an issue about the small population size criterion in end of life cases, and the interpretation of that criterion as being about cumulative patient populations across all diseases for which the treatment has an indication, rather than about the single patient population in an individual appraisal. As noted above, the committee here expected that sunitinib would in the future be aimed at more patient groups than just those with renal cell cancer, and it foresaw that the <i>cumulative</i> patient population</p>

<p>capacity issues, even if the intervention, service or programme is provided on a 'universal' basis.</p> <ul style="list-style-type: none"> <li>• Anything else you think significant or interesting about the decision.</li> </ul>	<p>may increase. Indeed, Sunitinib was later approved for use in treating gastro-intestinal stromal tumours under the end of life criteria (NICE, 2009b) although the patient population in that case was very small - between 90 and 150 (see NICE, 2009b; 4.9).</p>
<p><b>5. References/Links to relevant documents</b></p>	
	<p>NICE (2009a) <i>Sunitinib for the treatment of advanced and/or metastatic renal cell carcinoma</i>. Available at:  <a href="http://guidance.nice.org.uk/TA169">http://guidance.nice.org.uk/TA169</a></p> <p>NICE (2009b) <i>Sunitinib for the treatment of gastro-intestinal stromal tumours</i>. Available at:  <a href="http://www.nice.org.uk/nicemedia/pdf/TA179Guidance.pdf">http://www.nice.org.uk/nicemedia/pdf/TA179Guidance.pdf</a></p> <p>Richards, M (2008) <i>Improving access to medicines for NHS patients</i> (London: Dept of Health). Available at:  <a href="http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_089952.pdf">http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_089952.pdf</a></p> <p>Weale, A and Clark, S (2010) 'Co-payments in the NHS: An Analysis of the Normative Arguments', <i>Health Economics, Policy and Law</i> 5:2 pp225-246. Available in pre-publication form at:  <a href="http://www.ucl.ac.uk/spp/research/social-contract-deliberative-democracy-and-public-policy">http://www.ucl.ac.uk/spp/research/social-contract-deliberative-democracy-and-public-policy</a></p>