NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology Appraisals and Guidance Information Services

Static List Review (SLR)

Title and TA publication number of static topic:	TA178: 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 TA169: Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma
Final decision:	The guidance will remain on the 'static guidance list'

1. Publication date:	August 2009 (TA178) March 2009 (TA169)
2. Date added to static list:	May 2012 (both TAs)
3. Date the last searches were run:	August 2011 (both TAs)
4. Current guidance:	**TA178**

	1.1 Bevacizumab, sorafenib and temsirolimus are not recommended as first-line treatment options for people with advanced and/or metastatic renal cell carcinoma. *1.2 Sorafenib and sunitinib are not recommended as second-line treatment options for people with advanced and/or metastatic renal cell carcinoma.* *1.3 People who are currently being treated with bevacizumab (first-line), sorafenib (first- and second-line), sunitinib (second-line) and temsirolimus (first-line) for advanced and/or metastatic renal cell carcinoma should have the option to continue their therapy until they and their clinicians consider it appropriate to stop.* **TA169** *1.1 Sunitinib is recommended as a first-line treatment option 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.* *1.2 When using ECOG performance status score, clinicians should be mindful of the need to secure equality of access to treatments for people with disabilities. Clinicians should bear in mind that people with disabilities may have difficulties with activities of daily living that are unrelated to the prognosis of renal cell carcinoma. In such cases clinicians should make appropriate judgements of performance status taking these considerations into account.* *1.3 People who are currently being treated with sunitinib for advanced and/or metastatic renal cell carcinoma but who do not meet the criteria in 1.1 should have the option to continue their therapy until they and their clinicians consider it appropriate to stop.*

5. Research recommendations from original guidance:	**TA178** *6.1 There are a number of ongoing trials which are actively recruiting participants and which are relevant to this appraisal. Some of these trials are investigating the optimum sequences of treatment. Full details of ongoing research can be found at the National Institute for Health Research Clinical Research Network, ClinicalTrials.gov and Current Controlled Trials.* *6.2 The Assessment Group considered that the following well-conducted RCTs reporting health-related utility values in accordance with the NICE methods guide could be of value:* • *RCTs to investigate the effectiveness of temsirolimus and sorafenib as first-line treatments (both as monotherapy) compared with best supportive care in people who are unsuitable or have contraindications for immunotherapy and who have a poor or intermediate prognosis.* • *RCTs of sunitinib as a second-line treatment in people in whom immunotherapy has failed.* • *RCTs of sorafenib as a second-line treatment in whom first-line non-immunotherapy treatment (including sunitinib) has failed and who are unsuitable or have contraindications to immunotherapy.* **TA169** *6.1 There are a number of ongoing trials that are actively recruiting participants and that are relevant to this appraisal. Some of these trials are investigating the*

	optimum sequences of treatment. Full details of ongoing research can be found at the National Institute for Health Research Clinical Research Network, ClinicalTrials.gov and Current Controlled Trials. *6.2 The Assessment Group considered that the following well-conducted RCTs reporting health-related utility values in accordance with the NICE methods guide could be of value:* • *RCTs to investigate the effectiveness of sunitinib compared with best supportive care in people who are unsuitable or have contraindications for immunotherapy and who have a poor or intermediate prognosis.* *6.3 The Committee considered that rigorous data collection is needed on the life-extending benefits of sunitinib when no second-line treatments are given.*
6. Current cost of technology/ technologies (taken from C+D data website unless otherwise stated, all sites accessed 20th June 2017)**:**	Bevacizumab – £924.40 for a 400 mg / 16 ml vial [C + D data] Interferon alfa (administered with bevacizumab) – 9 million units / 0.5ml solution for injection £42.57 [BNF online] Sorafenib – £3576.56 per pack of 200 mg tablets (112 tablets per pack) Sunitinib – £3138.80 per pack of 50 mg tablets (28 tablets per pack) Temsirolimus – £620 for a 30 mg / 1.2 ml vial [BNF online]
7. Cost information from the TA (if available):	Bevacizumab/interferon-α

	"The price for a 400-mg vial of bevacizumab is £924.40 and the price of IFN-α is £45.19 for 9 MIU (excluding VAT; 'British National Formulary' [BNF] edition 55)". Sorafenib *"The current price for a pack of 200-mg tablets (112 tablets per pack) is £2980.47 (excluding VAT)".* Subject to PAS Sunitinib *"The price for a pack of 50-mg capsules (30 capsules per pack) is £3363.00 (excluding VAT; BNF edition 55)".* Temsirolimus *"The net-price for a 30-mg vial of temsirolimus is £620 (excluding VAT; BNF edition 57)".* The TA notes that bevacizumab, sorafenib and sunitinib were all the subjects of patient access schemes agreed between the Department of Health and the manufacturers and so the quoted list prices may not reflect the true acquisition cost to the NHS.
8. Alternative company(ies):	None.
9. Changes to the original indication:	No change.
10. New relevant trials:	Temsirolimus Versus Sorafenib As Second-Line Therapy In Patients With Advanced RCC Who Have Failed First-Line Sunitinib (INTORSECT trial) NCT00474786 – completed January 2013

	A Study of Avastin (Bevacizumab) Added to Interferon Alfa-2a (Roferon) Therapy in Patients With Metastatic Renal Cell Cancer With Nephrectomy NCT00738530 – completed September 2008, last updated May 2016
11. Relevant NICE guidance (published or in progress):	*Published* Improving outcomes in urological cancers (2002) NICE guideline CSG2 Everolimus for advanced renal cell carcinoma after previous treatment (2017) NICE technology appraisal guidance 432 Nivolumab for previously treated advanced renal cell carcinoma (2016) NICE technology appraisal guidance 417 Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment (2015) NICE technology appraisal guidance 333 Pazopanib for the first-line treatment of advanced renal cell carcinoma (2011 updated 2013) NICE technology appraisal guidance 215 *In progress* Sunitinib for the adjuvant treatment of early renal cell carcinoma [ID1076]. NICE technology appraisal guidance [ID1076]. Publication expected April 2018 Cabozantinib for treating renal cell carcinoma. NICE technology appraisal guidance [ID931]. Publication expected August 2017 Tivozanib for treating renal cell carcinoma. NICE technology appraisal guidance [ID591]. Publication expected December 2017
12. Relevant safety issues:	No relevant Drug Safety Updates published since previous review proposal.

13. Any other additional relevant information or comments:	None of these drugs are on the latest (June 2017) Cancer Drugs Fund list for renal cell carcinoma indications.
14. Technical Lead comments and recommendation:	Most of the identified trials published since the previous review compare one of the treatments with a novel comparator (including drugs subsequently approved by NICE, such as axitinib). Other studies compared the sequencing of sunitinib and sorafenib, but did not include a control group. As neither drug is approved for both first and second line, these results would not be sufficient for a reversal of the recommendations in TA169 and TA178. One relevant study compared bevacizumab in combination with interferon alfa-2a (in accordance with the marketing authorisation for bevacizumab) and interferon alfa-2a monotherapy. However, given the committee's previous considerations on the high toxicity and poor tolerance of interferon alfa-2a, this will unlikely change the negative recommendation. Furthermore, the hazard ratio suggested worse effectiveness than considered in the appraisal (0.91 compared to 0.79, neither statistically significant). Another relevant study compared temsirolimus versus sorafenib as second-line therapy in patients who have failed first-line sunitinib. However, there was no control group and therefore the study does not address the recommendations for further research in TA178 (i.e. the comparison with best supportive care). In summary, no study was identified which could have an impact on the decisions in the previous TA guidance (169 and 178).

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Appendix 1 – explanation of options

Options	Consequence	Selected – 'Yes/No'
The guidance will remain on the 'static guidance list'	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes
The decision to review the guidance will be deferred to specify date or trial	NICE will consider whether a review is necessary at the specified date. NICE will actively monitor the evidence available to ascertain when a consideration of a review is more suitable.	No
A full consideration of a review will be carried out through the Review Proposal Process	There is evidence that could warrant a review of the guidance. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	No
The guidance will be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	No

The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. NICE will schedule a consideration of a review, including a consultation with relevant consultees and commentators.	No