NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Tivozanib for treating advanced renal cell carcinoma

The Department of Health has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using tivozanib in the NHS in England. The appraisal committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts and patient experts.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the consultees and commentators for this appraisal and the public. This document should be read along with the evidence (see the committee papers).

The appraisal committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: August 2017

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The appraisal committee will meet again to consider the evidence, this appraisal consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final appraisal determination.
- Subject to any appeal by consultees, the final appraisal determination may be used as the basis for NICE's guidance on using tivozanib in the NHS in England.

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 4 September 2017

Second appraisal committee meeting: 20 September 2017

Details of membership of the appraisal committee are given in section 5.

1 Recommendations

1.1 Tivozanib is not recommended, within its anticipated marketing authorisation, for treating advanced renal cell carcinoma in adults who have had no previous treatment, or who have had 1 treatment with a cytokine.

1.2 This recommendation is not intended to affect treatment with tivozanib that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Current treatment for untreated advanced renal cell carcinoma is usually sunitinib or pazopanib. The evidence on whether tivozanib increases the overall length of time people live, compared with current treatment, is very uncertain. At best, tivozanib may have a similar effect to sunitinib or pazopanib, but it may not be as good. The evidence does not clearly show that the side effects with tivozanib are better tolerated than those with sunitinib or pazopanib.

Tivozanib is not recommended because the cost of treating renal cell carcinoma with tivozanib is likely to be higher than the cost of treating it with sunitinib or pazopanib, and it may not be as effective.

More information about how long people live while taking tivozanib is needed. However, it would not be useful to have data on tivozanib without being able to compare it with pazopanib and sunitinib, and it is not currently possible to collect the information for pazopanib and sunitinib through the Cancer Drugs Fund.

2 The technology

Tivozanib (Fotivda, EUSA Pharma)	
Anticipated marketing authorisation	On 22 June 2017, the Committee for Medicinal Products for Human Use recommended the granting of a marketing authorisation for tivozanib. In it, tivozanib is indicated for 'first line treatment of adult patients with advanced renal cell carcinoma (RCC) and for adult patients who are VEGFR and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for advanced RCC'.
Recommended dose and schedule	1,340 micrograms taken orally once daily for 21 days, followed by a 7-day rest period to make up 1 complete treatment cycle of 4weeks. The treatment schedule should be continued until disease progression or unacceptable toxicity.

3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by EUSA Pharma and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

New treatment option

People with renal cell carcinoma would welcome a new treatment option

3.1 The patient and clinical experts explained that the adverse effects of current treatments for advanced renal cell carcinoma, such as extreme fatigue, hand and foot syndrome, and chronic diarrhoea, can have a significant effect on quality of life. The committee understood that some people cannot tolerate these treatments and would benefit from being able to switch to a different treatment, which they may be able to tolerate better. It concluded that people with advanced renal cell carcinoma would welcome a new treatment option.

Clinical management

Tivozanib would only be used in untreated disease in the NHS

3.2 The anticipated marketing authorisation for tivozanib is for treating advanced renal cell carcinoma in adults who have had no previous treatment, or who have had 1 previous treatment with a cytokine (see section 2). The committee noted that the company had not submitted evidence for people who had been treated with cytokines. It heard from the clinical experts that cytokines are rarely used in the NHS for treating untreated renal cell carcinoma. The committee agreed that tivozanib would be used in the NHS only for people who have had no previous treatment.

Sunitinib or pazopanib are the current treatments for untreated advanced renal cell carcinoma

3.3 The clinical experts confirmed that most people in the NHS with newly diagnosed advanced renal cell carcinoma would be offered 1 of 2 tyrosine kinase inhibitors (TKIs), pazopanib or sunitinib, as recommended in NICE's technology appraisal guidance. If the disease progresses with pazopanib or sunitinib, and the person is fit enough to have further treatment, axitinib (a TKI), nivolumab (a PD-1 inhibitor) or everolimus (an mTOR inhibitor) are usually offered as second-line treatment, also as recommended in NICE guidance. If the disease progresses again on 1 of axitinib, nivolumab or everolimus, people are usually offered 1 of the 2 alternatives as a third-line treatment. The final appraisal determination for cabozantinib (a TKI) recommends it for advanced renal cell carcinoma in adults after vascular endothelial growth factor (VEGF)-targeted therapy (which includes pazopanib and sunitinib). Sorafenib, the comparator in the main trial for tivozanib, is not used in the NHS. The committee concluded that pazopanib and sunitinib were relevant comparators for this appraisal.

Clinical evidence

The pivotal trial, TIVO-1, has limited relevance to clinical practice in England

3.4 The main evidence for tivozanib came from TIVO-1, an open-label randomised controlled trial that investigated whether tivozanib (n=260) prolongs time to disease progression compared with sorafenib (n=257). At disease progression, patients in the sorafenib group of the trial were offered free treatment with tivozanib. Patients in the tivozanib group could also switch to a subsequent treatment if their disease progressed, but this was not provided as part of the trial. The committee considered whether this trial was relevant to clinical practice in England:

- Comparator: the committee noted that the comparator in TIVO-1 was sorafenib, which is not used in the NHS and was not considered a comparator for this appraisal (see section 3.3). The committee was aware that the company provided estimates of clinical effectiveness for tivozanib compared with the relevant comparators (sunitinib and pazopanib) using a network meta-analysis (see section 3.8).
- Outcome: the committee was aware that the primary outcome was progression-free survival, but that the trial also measured time to death and quality of life.
- Baseline characteristics: the clinical experts considered that the baseline characteristics of the patients in the trial were similar to those of people who would be offered tivozanib in the NHS in England. The committee noted that most patients in the trial (88%) were enrolled in Central or Eastern Europe. It was not concerned that these patients would respond less well to tivozanib than people in the NHS in England, but rather that they may have poorer access to second-, third- and fourth-line life-extending therapies. This would mean that the survival times in TIVO-1 might be shorter than those in England.

The committee concluded that TIVO-1 had some relevance to NHS clinical practice in England, but agreed that the comparator and location of the study limited the generalisability of the results.

The most relevant subgroup is patients who have not had previous treatment

3.5 70% of the TIVO-1 trial population had not had previous treatment and 30% had already had 1 systemic treatment. The committee recognised that tivozanib would only be used for untreated disease in NHS clinical practice, so it considered that the data from patients in the trial who had not been treated were the most relevant for this appraisal. It was concerned that focusing on a subgroup of patients in TIVO-1 reduced the size of the population (n=362). However, the committee concluded that, despite this, the population not previously treated was the most relevant population.

Progression-free survival

Tivozanib increases progression-free survival compared with sorafenib

3.6 The primary outcome measure in TIVO-1 was progression-free survival (assessed by reviewers blinded to patients' treatments). The committee noted that tivozanib increased median progression-free survival compared with sorafenib among patients who had not had previous treatment from 9.1 months to 12.7 months (hazard ratio [HR] 0.756, 95% confidence intervals [CI] 0.580 to 0.985). The committee was aware the company used a Cox proportional hazards model to estimate the hazard ratio for progression-free survival. It noted that, after the ERG requested clarification on the company's submission, the company presented a log-cumulative hazard plot for patients in TIVO-1 who had not had previous treatment that showed the curves representing progression-free survival for tivozanib and sorafenib crossed. Both the company and the ERG acknowledged that this indicated that the proportional hazard assumptions underlying the Cox proportional hazards model may not hold. The committee recognised that the company tried to address this by using a fractional polynomial method for the network meta-analysis (see section 3.10) and for cost-effectiveness modelling (see section 3.13). On balance, the committee concluded these results showed that tivozanib increased progression-free survival compared with sorafenib.

Overall survival

Results for overall survival were confounded by treatment switching in TIVO-1

3.7 The committee noted that people in the sorafenib group of TIVO-1 had a more favourable average performance status than people in the tivozanib group. It recognised that this may have affected the observed times to death. The committee also noted that, for the previously untreated population in TIVO-1, the results showed that patients randomised to tivozanib did not live as long as those randomised to sorafenib (HR 1.23, 95% CI 0.90 to 1.67). However, the committee knew that, in TIVO-1, patients could switch from sorafenib to tivozanib when their disease progressed and that 62.6% of patients in the sorafenib group had switched. It acknowledged that the amount of crossover confounded the results for overall survival because patients in the sorafenib group were more likely to have more therapies than patients in the tivozanib group. The committee appreciated that this was likely to make tivozanib appear less effective than it may be compared with sorafenib. The company carried out 2 analyses to adjust for the crossover:

- The inverse probability of censoring weights (IPCW) method: the committee noted that the results from this method showed tivozanib and sorafenib had a similar effect on overall survival (HR 1.021, 95% CI 0.671 to 1.553). It also noted that the IPCW adjustment was carried out for the full trial population and that it was the company's preferred method of adjusting for crossover. The committee was aware of the limitations of this approach, including the weight it gave to the small number of patients who did not crossover to another treatment.
- The rank preserving structural failure time (RPSFT) method: the committee noted that the results from this method showed the median overall survival for tivozanib (27.1 months) was lower than for sorafenib (32.3 months to 38.7 months depending on the type of analysis used). The committee noted that this adjustment was carried out for patients in TIVO-1 who had not had previous treatment, which the committee

considered more appropriate than using the whole trial population (see section 3.5). It also noted that the RPSFT method was the ERG's preferred method of adjusting for crossover. However, it acknowledged that there were limitations with this approach because the treatment benefit with tivozanib was assumed to be the same whether patients took it instead of sorafenib or after sorafenib. The committee considered that patients who took tivozanib after sorafenib (in effect second line) may not respond as well as if had they taken it earlier.

The committee agreed that both methods of adjusting for crossover had limitations and that the adjusted results for overall survival were inconsistent. It concluded that the evidence showed that, at best, tivozanib may be similar to sorafenib in extending overall survival. However, the committee was concerned that overall survival could be shorter with tivozanib than sorafenib.

Network meta-analysis

The structure of the network and the trials included are appropriate

3.8 The company carried out a network meta-analysis to compare tivozanib with the comparators in the scope, pazopanib and sunitinib, because there were no trials that compared them directly. The committee appreciated that the company had submitted different approaches to the network meta-analysis, including a broader network of trials and several extrapolation approaches. The final network was based on 4 trials: COMPARZ, which compared pazopanib with sunitinib; Cross-J-RCC, which compared sunitinib with sorafenib; SWITCH, which compared sorafenib with sunitinib; and TIVO-1, which compared tivozanib with sorafenib. The committee understood from the ERG that the baseline characteristics were broadly similar in the included trials. It concluded that the structure of the network and the trials included were appropriate.

Without adjustment for crossover in the trials, the results of the network meta-analysis are uncertain

3.9 The committee was concerned that, in the network meta-analysis, the company did not adjust for crossover in TIVO-1 or in any of the other trials, and notably so for Cross-J-RCC and SWITCH, in which patients also crossed over to other treatments when their disease progressed. The company said that it had not had the individual patient-level data for these trials to be able to make similar adjustments as it had done for TIVO-1. The committee understood that the imbalance in subsequent therapies was greater in TIVO-1 than in the other trials in the network. It appreciated that adjusting for crossover in all the trials in the network without the individual patient-level data could have made the results more uncertain. The committee discussed the ERG's suggestion of comparing the tivozanib group of the TIVO-1 trial with the COMPARZ trial via a matched-adjusted indirect comparison, for which patient-level data are not needed. However, the committee rejected this method of adjusting for crossover because it would not resolve the committee's concerns about the clinical uncertainty in the results. The committee concluded that the results from the network meta-analysis were highly uncertain and unreliable.

The clinical benefit of tivozanib is uncertain

3.10 The committee understood that the company used fractional polynomial modelling, as described by Janssen et al. (2011), to fit overall and progression-free survival curves for tivozanib, pazopanib and sunitinib because the proportional hazards assumption did not hold for progression-free survival in TIVO-1 (see section 3.6). The committee noted that the ERG corrected an error in the company's calculation of the fractional polynomial curves, and also presented its own preferred network meta-analysis data (see table 1 for results).

Table 1 Overall and progression-free survival results from the network meta-analysis with fractional polynomial modelling

	Median progression-free survival (months)	Median overall survival (months)
Company's results		
Tivozanib	9.1	22.2
Sunitinib	8.9	35.2
Pazopanib	7.2	20.8
Company's results – error corrected		
Tivozanib	9.3	25.0
Sunitinib	7.7	35.7
Pazopanib	7.5	27.8
Evidence review group's preferred results		
Tivozanib	6.1	25.0
Sunitinib	6.8	27.5
Pazopanib	8.4	29.2

The clinical experts commented that some of the fractional polynomial curves in the network meta-analysis did not lead to clinically plausible results because the difference in overall survival between pazopanib and sunitinib contradicted the direct results from COMPARZ. In the COMPARZ trial, median overall survival was 28.4 months in the pazopanib group and 29.3 months in the sunitinib group. The committee noted that the ERG explored different fractional polynomial curves to the company, and the ERG chose its preferred curves using criteria including how clinically plausible the network meta-analysis results appeared. In the ERG's preferred network meta-analysis, the curves for tivozanib, pazopanib and sunitinib were similar, although median progression-free survival and overall survival were lower for tivozanib than for sunitinib and pazopanib. The committee agreed that the results from the ERG's network meta-analysis were more plausible than those from the company's, but recognised that the 95% credible intervals around the curves suggested that there was substantial uncertainty. The committee concluded that the results of the network meta-analyses using a fractional polynomial approach showed that, at best, tivozanib may be similar to pazopanib and sunitinib in extending overall and progression-free survival.

However, the committee was concerned that overall survival could be shorter with tivozanib compared with pazopanib and sunitinib.

Adverse effects

It is not clear if tivozanib is better tolerated than pazopanib or sunitinib

3.11 The clinical experts explained that different adverse effects affect a person's quality of life differently. For example, hypertension may not affect quality of life as much as skin problems, fatigue or diarrhoea. This makes it difficult to compare adverse effect profiles between treatments. The committee agreed that tivozanib is reasonably well tolerated, but that it was not clear whether it is better tolerated than pazopanib or sunitinib.

The company's economic model

The company's model is appropriate for decision-making

3.12 The company used a partitioned-survival economic model that included 3 health states: pre-progression, post-progression and death. The committee concluded that the model was appropriate and consistent with the approach used for other appraisals for renal cell carcinoma. The model included either tivozanib, sunitinib or pazopanib as the first treatment, followed by axitinib or best supportive care. The committee was concerned that the model did not capture the clinical benefits of subsequent treatments, and that these benefits may extend overall survival beyond the 10-year time horizon in the model.

Treatment effects in the economic model

Changing the fractional polynomial curve used in the model had a large impact on the cost-effectiveness results

3.13 Treatment effects used in the cost-effectiveness modelling were based on the network meta-analysis with the fractional polynomial approach. The committee was concerned that the treatment effects were uncertain:

- The 95% credible intervals around the network meta-analysis curves were wide (see section 3.10)
- The network meta-analysis curves used by the company lacked clinical validity (see section 3.10)
- The network meta-analysis did not adjust for crossover in the trials (see section 3.9)

The committee noted that changing the fractional polynomial curve used in the model had a large impact on the incremental cost-effectiveness ratio (ICER) results. It concluded that the uncertainty in the clinical effectiveness results made the ICERs highly uncertain and potentially unreliable.

Utility values in the economic model

Alternative methods of modelling adverse effects had a limited effect on the cost-effectiveness results

3.14 The company derived utility values for the pre-progression and post-progression health states from health-related quality-of-life data from EQ-5D questionnaires given to patients in TIVO-1, and assumed the same utility values for each treatment group. It adjusted the pre-progression utility values to incorporate decrements for adverse effects, which it derived from a published cost-effectiveness analysis of pazopanib. The committee understood that the ERG did not include the decrements in utility for adverse effects in its base case because they were estimated from a sample of the UK general population, rather than from people with renal cell carcinoma. The committee noted that the questionnaires in the trial were likely to have captured the impact of adverse effects on quality of life. So, by including decrements, the ERG considered that the company could have double-counted the impact of adverse effects. The committee noted that removing the decrements for adverse effects had a negligible effect on the ICER. The committee

concluded that the ERG's changes to the company's base case, including removing utility decrements for adverse effects, were acceptable.

Costs and resources in the company's economic model

Disease management costs had a limited effect on the cost-effectiveness results

3.15 The company included costs for services and monitoring in its economic model, such as costs of appointments and CT scans. The ERG corrected an error in the company's calculation that converted monthly costs to weekly costs. The committee noted that the ERG, in its base-case model, included costs of monthly blood tests and costs for managing adverse effects that were different from the company's, but that these changes had a limited effect on the ICER. The committee concluded that the ERG's adjustments were appropriate.

Including actual doses compared with intended doses had a large effect on the cost-effectiveness results

3.16 The company assumed the relative dose intensity (the dose of the drug delivered as a proportion of the intended dose) for all treatments was 100% in its base-case model. The ERG included mean relative dose intensities of 94% for tivozanib, taken from TIVO-1, and 86% for both pazopanib and sunitinib, taken from the pazopanib and sunitinib appraisals. The committee noted that including relative dose intensities made tivozanib substantially less cost effective compared with pazopanib and sunitinib. The clinical experts explained that doses which had been prescribed, but not taken by patients, were likely to be returned to pharmacy to be destroyed and, as such, were unlikely to reduce costs in practice. The committee was aware that unused vials of injectable medicines would likely be returned to pharmacy to be destroyed but that it was unclear whether this would also happen with tablets and capsules. The committee concluded that the relative dose intensity was likely to be between 100% and the ERG's estimates of 86% for pazopanib and

sunitinib and 94% for tivozanib, and was more likely to be closer to the ERG's estimates.

The health benefits and costs of subsequent therapies assumed by the company were not realistic

3.17 The committee discussed the subsequent therapies included in the economic model for patients whose disease progressed while taking tivozanib, sunitinib or pazopanib.

- Company's model:
  - 60% had axitinib, 40% had best supportive care
  - patients on axitinib continued taking it for the rest of their lives
  - costs were not discounted
  - benefits of subsequent therapy were not included.
- ERG's model:
  - 50% had axitinib, 10% everolimus, 30% nivolumab, 10% best supportive care
  - mean treatment durations for axitinib, everolimus and nivolumab came from published literature
  - costs were discounted
  - benefits of subsequent therapy were not included.

The committee agreed that the ERG's modelling of subsequent therapy costs better reflected the current treatment pathway (see section 3.3). However, the committee remained concerned that both the company and the ERG had included only the costs of subsequent therapies in the model, but not any benefits of subsequent therapies on progression-free or overall survival. It agreed that changing the modelling of subsequent therapies from the company's approach to the ERG's approach made tivozanib substantially less cost effective compared with pazopanib and sunitinib. The committee concluded that, although the ERG's assumptions were more appropriate than the company's assumptions, it would have

preferred to have seen an adjustment for both the costs and benefits of subsequent treatments.

Results of the cost-effectiveness analyses

The assumptions in ERG's base case were more appropriate than the company's

3.18 The committee noted that the ERG's base-case model incorporated its preferred assumptions:

- ERG's preferred fractional polynomial curves (see section 3.10)
- ERG's modelling of adverse effects (see section 3.14)
- ERG's approach to disease management costs (see section 3.15)
- including relative dose intensities for all treatments (see section 3.16)
- ERG's approach to modelling subsequent therapies (see section 3.17)

The committee concluded that the ERG's base case was more appropriate than the company's base case.

The cost-effectiveness results from the ERG's base case were more plausible than the company's

3.19 The committee noted that the total quality-adjusted life years (QALYs) gained for pazopanib and sunitinib were more similar in the ERG's base-case results (2.35 and 2.24 respectively) than in the corrected company's base-case results (1.78 and 2.42 respectively). The committee agreed that the similar QALY gains in the ERG's base case better reflected the results of the direct comparison of pazopanib and sunitinib in the COMPARZ trial. In the ERG's base-case results, both pazopanib and sunitinib dominated tivozanib, that is, they were more effective and less costly. Because the subsequent therapies (axitinib, everolimus and nivolumab) included in the model were associated with confidential patient access schemes, the estimates of cost effectiveness are confidential and cannot be reported here. The committee concluded that the results of the ERG's base-case analysis were more plausible than the company's, even

though it did not address the uncertainty in the treatment effects or capture the benefits of subsequent therapies.

Tivozanib is not a cost-effective use of NHS resources

3.20 The committee considered that the results of the network meta-analysis and the cost-effectiveness analysis were very uncertain (see sections 3.10 and 3.13). It recognised that neither of them accounted for the crossover in TIVO-1 or in the other trials in the network (see sections 3.9 and 3.13). The committee therefore considered the modelled costs of tivozanib compared with the costs of pazopanib and sunitinib. This included consideration of a scenario in which the ERG assumed that tivozanib, sunitinib and pazopanib were all equally effective in extending progression-free and overall survival. The committee appreciated that this analysis was likely to be optimistic because the results from the network meta-analysis suggested that overall survival could be shorter with tivozanib compared with pazopanib and sunitinib (see section 3.10). The committee noted that the results showed that tivozanib was more costly than pazopanib and sunitinib even when this optimistic approach was taken. The committee agreed that the modelled cost of tivozanib was not low enough to compensate for the uncertainty around the clinical effectiveness. It concluded that tivozanib was not a cost-effective use of NHS resources and did not recommend it.

End of life

Tivozanib should not be considered as a life-extending treatment for people with a short life expectancy

3.21 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's Cancer Drugs Fund technology appraisal process and methods, recognising that the company did not submit evidence to support tivozanib as an 'end of life' therapy. It noted that the estimates for mean overall survival were not provided. It noted that the estimated median overall survival for people taking

pazopanib or sunitinib in both the ERG's corrected company's network meta-analysis and the ERG's preferred network meta-analysis was more than 24 months. The committee noted that an average estimated survival was likely to be even longer, in part because of life-extending therapies now offered by the NHS but unlikely to have been available to patients in the trials of pazopanib or sunitinib. It also noted that tivozanib did not increase median overall survival by 3 months or more compared with pazopanib or sunitinib in either analysis. The committee concluded that tivozanib did not meet the criteria for being considered as a life-extending treatment for people with a short life expectancy.

Cancer Drugs Fund

Tivozanib is not suitable for use in the Cancer Drugs Fund

3.22 Having concluded that tivozanib could not be recommended for routine use, the committee then considered if it could be recommended within the Cancer Drugs Fund. The committee discussed the new arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting the addendum to the NICE process and methods guides. Because of the uncertainty about tivozanib's effect on overall survival, the committee discussed whether collecting observational data on overall survival with tivozanib via the Systemic Anti-Cancer Therapy dataset would address the clinical uncertainty. The NHS commissioning expert explained that, under the current arrangements for the Cancer Drugs Fund, it would not be possible to collect information about patient characteristics and overall survival among patients treated with pazopanib or sunitinib. The committee agreed that, without the comparison with pazopanib and sunitinib, collecting overall survival data about tivozanib would not be useful and would not adequately reduce the clinical uncertainty. The committee concluded that tivozanib did not meet the criteria for inclusion in the Cancer Drugs Fund.

Other factors

The committee did not identify any other factors that affected its recommendation

3.23 The Pharmaceutical Price Regulation Scheme (2014) payment mechanism was not relevant in considering the cost effectiveness of tivozanib.

3.24 The company did not provide evidence that tivozanib was an innovative treatment. However, the committee noted that patient groups considered tivozanib as a more specific treatment than other treatments for metastatic renal cell carcinoma because it targets 3 vascular endothelial growth factor receptors. The committee was not been presented with evidence about the extent to which these benefits were realised in practice. The committee concluded that it had not seen any additional evidence of benefits that were not captured in the measurement of QALYs.

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. This is because NICE is not aware of any ongoing research into tivozanib for untreated renal cell carcinoma. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Amanda Adler

Chair, Appraisal Committee

August 2017

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee B.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Kirsty Pitt
Technical Lead

Jasdeep Hayre
Technical Adviser

Jeremy Powell
Project Manager

ISBN: [to be added at publication]