

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Final appraisal determination

# Tivozanib for treating advanced renal cell carcinoma

## 1 Recommendations

- 1.1 Tivozanib is recommended as an option for treating advanced renal cell carcinoma in adults, only if:
- they have had no previous treatment and
  - the company provides tivozanib with the discount agreed in the patient access scheme.
- 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 in the NHS for untreated advanced renal cell carcinoma is usually sunitinib or pazopanib. There is no evidence to suggest that tivozanib is more effective than pazopanib and sunitinib in extending overall and progression-free survival. At best, tivozanib may have a similar effect to sunitinib or pazopanib. Also, the evidence does not clearly show that people tolerate the adverse effects of tivozanib better than those of sunitinib or pazopanib.

The cost of treating renal cell carcinoma with tivozanib is likely to be lower than the cost of treating it with sunitinib or pazopanib, but tivozanib is also likely to be less effective. The estimated cost savings are high enough to

compensate for the estimated lower effectiveness. Also, there is a need to be able to offer tivozanib to people who do not tolerate existing treatments. Therefore, tivozanib is recommended as an option for treating advanced renal cell carcinoma in adults who have had no previous treatment.

## 2 Information about tivozanib

<b>Marketing authorisation</b>	Tivozanib (Fotivda, EUSA Pharma) is indicated for 'the 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'.
<b>Dosage in the marketing authorisation</b>	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 4 weeks. The treatment schedule should be continued until disease progression or unacceptable toxicity.
<b>Price</b>	A 21-pack of 1,340 microgram hard capsules (that is, the pack size needed for 1 treatment cycle) costs £2,052 excluding VAT.  The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of tivozanib, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

## 3 Committee discussion

The appraisal committee (section 6) 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 significantly affect quality of life. So, some people would benefit from being able to switch to a different treatment, which they may tolerate better. The committee concluded that people with advanced renal cell carcinoma would welcome a new treatment option.

## ***Clinical management***

### **Tivozanib would be used only in untreated disease in the NHS**

3.2 Tivozanib has a marketing authorisation 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 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 untreated 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. Other treatments such as [bevacizumab](#), [sorafenib](#), and [temsirolimus](#) have a marketing authorisation for previously untreated advanced renal cell carcinoma, but they are not recommended by NICE and are not used in the NHS. The committee concluded that pazopanib and sunitinib were the relevant comparators in this appraisal.

## ***Clinical evidence***

### **The comparator and location of the pivotal trial, TIVO-1, has limited how generalisable the results are to clinical practice in England**

3.4 The main clinical evidence for tivozanib came from TIVO-1, an open-label randomised controlled trial that primarily investigated whether tivozanib (n=260) prolongs time to disease progression compared with sorafenib (n=257). At disease progression, patients in the sorafenib group could switch (cross over) to treatment with tivozanib. Patients in the tivozanib group could also have subsequent treatment if their disease progressed. The committee considered whether this trial was relevant to clinical practice in England:

- Comparator: the comparator in TIVO-1 was sorafenib, which is not used in the NHS and was not considered a comparator in this appraisal (see section 3.3).
- Outcome: the primary outcome was progression-free survival, but the trial also measured overall survival and health-related quality of life.
- Baseline characteristics: the clinical experts generally considered the baseline characteristics of patients in the trial to be similar to those of people who would be offered tivozanib in the NHS:
  - Most patients in the trial (88%) were enrolled in Central or Eastern Europe. The committee was concerned that these patients 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.
  - Patients in the sorafenib group had a better average performance status than those in the tivozanib group. In the sorafenib group, 54% had an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 (meaning that they did not have any symptoms and were able to carry out usual activities unrestricted) compared with 45% in the tivozanib group. This means that the results may underestimate the effectiveness of tivozanib.

The committee concluded that the comparator and location of TIVO-1 limited the generalisability of the results.

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

3.5 In TIVO-1, 70% of patients had not had previous treatment and 30% had already had 1 systemic treatment. Because tivozanib would be used only for untreated disease in NHS clinical practice (see section 3.2), the committee considered that patients in the trial who had not been treated represented the most relevant population in this appraisal. It was concerned that focusing on a subgroup of patients in TIVO-1 reduced the size of the population (n=362), and the statistical power of the study to detect differences between treatment groups. However, the committee concluded that, despite this, the group of patients not previously treated provided the most relevant evidence.

***Progression-free survival***

**Tivozanib increases progression-free survival compared with sorafenib**

3.6 The primary outcome in TIVO-1 was progression-free survival (assessed by reviewers blinded to patients' treatments). 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] 0.76, 95% confidence intervals [CI] 0.58 to 0.99). The company used a Cox proportional hazards model to estimate the hazard ratio for progression-free survival. However, both the company and the ERG acknowledged that the proportional hazard assumptions underlying the Cox proportional hazards model may not hold. To address this, the company used a fractional polynomial method for the network meta-analysis (used to compare tivozanib with sunitinib and pazopanib, see section 3.8) and for cost-effectiveness modelling (see section 3.13).

## ***Overall survival***

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

3.7 Among the previously untreated population in TIVO-1, 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, in TIVO-1, patients could switch from sorafenib to tivozanib when their disease progressed and 62.6% of patients in the sorafenib group switched. The committee acknowledged that the amount of crossover confounded the results for overall survival. This was likely to make tivozanib appear less effective 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 that tivozanib and sorafenib had a similar effect on overall survival (HR 1.02, 95% CI 0.67 to 1.55). It also noted that the company carried out the IPCW adjustment only 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 the approach 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 the company carried out this adjustment 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, which assumes that the treatment benefit with tivozanib is the same whether

patients take 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 had 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 presented by the company showed that, at best, tivozanib may be similar to sorafenib in extending overall survival. However, in the only analysis in the relevant population (that is, people who had not had previous treatment), patients randomised to tivozanib did not live as long as those randomised to sorafenib.

### ***Network meta-analysis***

#### **The structure of the amended network used by the company and ERG and the trials included in it are appropriate**

3.8 The company carried out a network meta-analysis to compare tivozanib with the comparators in the scope, pazopanib and sunitinib. The company submitted different approaches to the network meta-analysis, including a broad network of trials and several approaches to extrapolating beyond the end of the trials. However, the company's final network provided at the clarification stage of this appraisal was based on the ERG's suggested network of 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 that the baseline characteristics were broadly similar in the included trials, and that the ERG had also based its analyses on this network. In response to consultation, the company argued that the ERG should have excluded the Cross-J-RCC trial from the simplified network because it was small (n=124), it was carried out in a Japanese population, and its results were available only in poster form. However, the committee noted that the company had not provided the results based on the network without Cross-J-RCC. It concluded that the structure of the network provided by

the company after clarification, and the trials included in it, were appropriate.

**The results of the network meta-analyses are uncertain because they are not adjusted for crossover**

3.9 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 ERG corrected an error in the company's modelling of the fractional polynomial curves. It also presented its own preferred network meta-analysis (see table 1 for results) using fractional polynomial curves different to the ones chosen by the company, and taking into account clinical plausibility. In the ERG's network meta-analysis, median progression-free survival and overall survival were lower for tivozanib than for sunitinib and pazopanib. Neither the company nor the ERG adjusted for crossover in TIVO-1, Cross-J-RCC and SWITCH, in which patients switched to other treatments when their disease progressed. The committee concluded that not adjusting for crossover meant that the results of the network meta-analysis were likely to be confounded with the direction of bias unknown.

**Table 1 Overall and progression-free survival results from the pivotal trials and network meta-analyses with fractional polynomial modelling**

	Median progression-free survival (months)	Median overall survival (months)
<b>Trial results</b>		
Tivozanib (TIVO-1)	12.7	Not reported
Sunitinib (COMPARZ)	9.5	29.3
Pazopanib (COMPARZ)	8.4	28.4
<b>Company's results – error corrected</b>		
Tivozanib	9.3	25.0
Sunitinib	7.7	35.7
Pazopanib	7.5	27.8
<b>Evidence review group's results</b>		
Tivozanib	6.1	25.0
Sunitinib	6.8	27.5
Pazopanib	8.4	29.2

**At best, tivozanib may have a similar effect to sunitinib or pazopanib**

3.10 The committee had concerns about the company's and ERG's network meta-analyses. The clinical experts commented that some of the fractional polynomial curves in the company's network meta-analysis did not lead to clinically plausible results because the difference in overall survival between pazopanib and sunitinib (7.9 months in favour of sunitinib) contradicted the direct results from COMPARZ (0.9 months in favour of sunitinib). In the ERG's network meta-analysis, the results also contradicted the COMPARZ trial results, showing that pazopanib led to longer overall and progression-free survival than sunitinib. Moreover, the ERG estimated a median progression-free survival for tivozanib that was much lower than that seen in TIVO-1 (6.1 months compared with 12.7 months), despite this outcome not being affected by crossover. The ERG explained that this was because sorafenib provided the link between tivozanib and the comparators, and because all curves were adjusted to this baseline. Nonetheless, the committee had reservations about using an analysis that estimated a median progression-free survival which was shorter than half the duration seen in the trial. The committee also noted

that the choice of fractional polynomial model had a large effect on the estimates of progression-free and overall survival, and that the 95% credible intervals around the curves were wide, reflecting substantial uncertainty in the results. The committee considered that neither the company's nor the ERG's results were plausible or robust. This meant that the effectiveness of tivozanib compared with current treatments in the NHS (sunitinib and pazopanib) was unclear. The committee concluded that it had seen no evidence to suggest that tivozanib was more effective than sunitinib or pazopanib in extending overall and progression-free survival. What evidence there was suggested that, at best, tivozanib may have a similar effect to sunitinib or pazopanib.

## ***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 safety profiles between treatments. In response to consultation, the company provided data that it argued showed adverse events such as fatigue and diarrhoea to be less frequent with tivozanib than with sunitinib and pazopanib. The data came from a naive comparison of the incidence rates of all-grade adverse events from the TIVO-1 and COMPARZ trials including previously treated and untreated patients. The results of the ERG's network meta-analyses for grades 3 to 4 fatigue and diarrhoea in patients who had not had previous treatment favoured tivozanib, but the difference for fatigue were not statistically significant ( $p > 0.05$ ). The committee noted the company's comments about the limitations of the ERG's analysis, notably the small number of studies included, the perceived poor quality of the Cross-J-RCC study and the reliance on patient-reported adverse events from randomised controlled trials to synthesise the evidence.
- Nevertheless, the committee agreed that it was more appropriate to

consider results from network meta-analyses than from naive comparisons of clinical trials to maintain the benefits of randomisation and reflect uncertainty in credible intervals. 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, although it does not capture the health effects of subsequent treatments**

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 in 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 The company based the treatment effects it used in the cost-effectiveness modelling on the network meta-analysis using fractional polynomials. The committee agreed that the uncertainties in clinical effectiveness (see sections 3.10) carried over to the estimates of cost effectiveness. For example, changing the fractional polynomial curve used in the model had a large impact on the incremental cost-effectiveness ratios (ICERs). The committee concluded that the uncertainty in the clinical effectiveness results meant that the ICERs were also uncertain.

### ***Utility values in the economic model***

#### **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 data on health-related quality of life from EQ-5D questionnaires given to patients in TIVO-1. The company assumed the same utility values for each treatment. 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 utility decrements for adverse effects in its base case because the values were estimated from a sample of the UK general population, rather than from people with renal cell carcinoma. Moreover, the ERG considered that, by including decrements, the company could have double-counted the impact of adverse effects on quality of life because the questionnaires in the trial were likely to have captured this. The committee noted that removing the decrements for adverse effects negligibly affected the ICER.

### ***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 the costs of clinical appointments and CT scans. The ERG corrected an error in the company's calculation converting costs from monthly to weekly. The committee noted that, in its base-case model, the ERG included the costs of monthly blood tests and for managing adverse effects that differed from the company's, but that these had a limited effect on the ICER.

**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 the 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 modelling reflects the impact on outcomes of differences in adherence to the intended treatment regimen**

3.17 In its response to consultation, the company presented data showing that a lower proportion of people taking tivozanib interrupt or stop treatment, or reduce their dose, because of adverse events compared with people taking sunitinib or pazopanib. The company argued that this means tivozanib is better tolerated and leads to better outcomes and quality of life. The ERG stated that it was difficult to compare trials because of the differing definitions of dose interruptions and reductions. In addition, the results of the trials reflect the actual dose taken, which takes into account any variation in the scheduled dose. The committee concluded that the company's and ERG's modelling already captured any benefits from differences in adherence.

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

3.18 The committee discussed the subsequent therapies (that is, second line and beyond) 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 take 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 were 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 the ERG adjust for both the costs and benefits of subsequent treatments.

## ***End of life***

### **Tivozanib is not considered a life-extending treatment for people with a short life expectancy**

3.19 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 company had not provided estimates for mean overall survival with tivozanib. 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 means generally exceed medians, and because of the life-extending therapies now offered by the NHS that were 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.

## ***Results of the cost-effectiveness analyses***

### **The main difference between the company and ERG base cases is the choice of progression-free and overall survival curves**

3.20 The committee noted at its first meeting that the ERG's base-case model incorporated its preferred assumptions, including those about relative dose intensities (see section 3.16) and those modelling subsequent therapies (see section 3.18). In addition, 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 response to consultation, the company submitted a patient access scheme and updated its base case to reflect most of the above assumptions. The main difference between the company and ERG base cases was in the choice of the fractional polynomial curves used to model progression-free and overall survival.

### **Tivozanib can be recommended as a cost-effective use of NHS resources**

3.21 The company's revised results submitted in response to consultation and the ERG base-case results, including all patient access schemes for tivozanib and subsequent therapies, showed that tivozanib was cheaper and less effective than pazopanib and sunitinib. The company subsequently revised the patient access scheme for tivozanib, but did not provide updated results, agreeing that the ERG could provide them. The committee noted that, in situations in which an ICER is estimated for a technology that is less effective and less costly than its comparator, the commonly assumed decision rule of accepting ICERs below a given threshold is reversed. The ERG estimated ICERs greater than £30,000 saved per QALY lost for tivozanib compared with pazopanib, and greater than £50,000 saved per QALY lost compared with sunitinib. Because the subsequent therapies (axitinib, everolimus and nivolumab) included in the model are associated with confidential patient access schemes, the exact estimates of cost effectiveness cannot be reported here. The committee considered that, although the ICERs were within the range normally considered to represent cost-effective technologies, they were associated with a high degree of uncertainty. This was mainly because they did not account for the crossover in TIVO-1 or any of the other trials in the network meta-analysis. The committee acknowledged comments from the Cancer Drugs Fund clinical lead suggesting that clinicians view tivozanib as being broadly similar in effectiveness as pazopanib and possibly having a better safety profile. This could benefit people that clinicians think would not be able to tolerate pazopanib. The committee agreed that

extending treatment choices in this disease area would benefit both clinicians and patients. Taking into account the estimated cost effectiveness of tivozanib, the clinicians' views and unmet need, the committee recommended tivozanib as an option for treating advanced renal cell carcinoma in adults who have had no previous treatment.

### ***Other factors***

#### **No other factors were identified that could affect the recommendation**

3.22 The company did not provide evidence that tivozanib was an innovative treatment. However, the committee recognised that patient groups noted that tivozanib targets 3 vascular endothelial growth factor receptors. The committee was not 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 Implementation**

4.1 Section 7(6) of the [National Institute for Health and Care Excellence \(Constitution and Functions\) and the Health and Social Care Information Centre \(Functions\) Regulations 2013](#) requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal determination.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This

means that, if a patient has advanced renal cell carcinoma and the doctor responsible for their care thinks that tivozanib is the right treatment, it should be available for use, in line with NICE's recommendations.

- 4.4 The Department of Health and EUSA Pharma have agreed that tivozanib will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to **[NICE to add details at time of publication]**

## 5 Review of guidance

- 5.1 The guidance on this technology will be considered for review 3 years after publication. 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  
February 2018

## 6 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), technical advisers and a project manager.

#### **Kirsty Pitt and Ross Dent**

Technical Leads

#### **Jasdeep Hayre and Ahmed Elsada**

Technical Advisers

#### **Jeremy Powell**

Project Manager

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