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Worldwide Biopharmaceutical Businesses

15th April 2013

[redacted]

Chair, Appeal Committee

National Institute for Health and Clinical Excellence

MidCity Place

71 High Holborn

London WC1V 6NA

Dear [redacted]

Re: Final Appraisal Determination –

Axitinib for the treatment of advanced renal cell carcinoma after failure of prior systemic treatment [ID518]

Pfizer Ltd would like to appeal against the Final Appraisal Determination for the above mentioned single technology appraisal.

If you require any further information or clarification then please do not hesitate to contact us.

Yours Sincerely,

[redacted]

Head of Oncology Business Unit UK

APPEAL AGAINST THE FINAL APPRAISAL DETERMINATION FOR AXITINIB FOR THE TREATMENT OF ADVANCED RENAL CELL CARCINOMA AFTER FAILURE OF PRIOR SYSTEMIC TREATMENT

EXECUTIVE SUMMARY

Pfizer's appeal is brought under Ground 1 (procedural fairness) of NICE's processes.

- The lack of transparency in relation to a submission relied upon for the purposes of the guidance is procedurally unfair
- The fact that Pfizer had no adequate opportunity to respond to the additional matters raised by the pharmaceutical industry commentator in response to the ACD, is unfair
- The Scope for this appraisal produces results that inevitably lack certainty
- The Appraisal Committee's refusal to find that use of axitinib in post-cytokine patients satisfied the "end of life" criteria on the basis that no comparison with sunitinib or pazopanib had been provided was inconsistent with the Scope for this appraisal
- The Committee's approach to the assessment of QALY gains occurring in the post-sunitinib group following disease progression and its conclusion that the post-progression model outputs lacked "clinical plausibility" was not transparent
- While the Committee found explanations for post progression QALY gains "clinically implausible", they failed to request attendance by the clinical specialist at the second Appraisal Committee meeting so that any concerns could be discussed
- The Appraisal Committee's final conclusions in relation to the cost-effectiveness of axitinib are not stated and its reasons for failing to recommend second-line treatment in patients with advanced or metastatic RCC are therefore unclear, in circumstances where the ICER values appear to fall within the range generally regarded as acceptable in other appraisals.

INTRODUCTION

Axitinib (Inlyta) is a second generation oral vascular endothelial growth factor receptor (VEGFR) inhibitor which acts through inhibition of the protease enzyme, tyrosine kinase. Axitinib selectively inhibits VEGFRs 1, 2 and 3, with greater potency and selectivity than currently available, first generation VEGFR-TKIs (sunitinib and pazopanib). VEGF is a crucial mediator of angiogenesis (the development of new blood vessels) a process required for tumours to develop the blood supply they require to grow and metastasise. By inhibiting VEGFR, axitinib acts to reduce tumour growth and metastases and to produce tumour regression.

Axitinib is the subject of a marketing authorisation granted by the European Commission under the centralised procedure on 3 September 2012.

The authorisation was based on the pivotal Phase III AXIS Study which compared axitinib with sorafenib in patients with advanced renal cell carcinoma after failure of prior treatment with any of the first-line treatment options licensed at the time of the study. These first-line treatments comprised: sunitinib; cytokines; bevacizumab with interferon-alpha; and temsirolimus - but not pazopanib, which was authorised subsequently. Based on data from the AXIS trial, Pfizer applied for an authorisation "*for the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of prior systemic treatment*". However, the clinical data in the temsirolimus and bevacizumab subgroups, were considered insufficient to draw any firm conclusions and the CHMP adopted a positive opinion for the narrower indication *"treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with sunitinib or a cytokine"*.

PROCEDURAL HISTORY OF THE APPRAISAL

February 2012:	Axitinib referred to NICE for single technology appraisal
June 2012:	Final scope issued
13 August 2012:	Submission of evidence by Pfizer
16 October 2012:	ERG report prepared by Kleijnen Systematic Reviews Limited in collaboration with Erasmus University Rotterdam and Maastricht University
24 October 2012:	Pfizer's comments on the factual accuracy of the ERG Report submitted
13 November 2012:	The first meeting of the Appraisal Committee
2 December 2012:	Appraisal Consultation Document (ACD) issued to consultees and commentators
11 January 2013:	Comments by Pfizer and other stakeholders on the ACD, submitted to NICE
13 February 2013:	Second meeting of the Appraisal Committee
23 March 2013:	Final Appraisal Determination (FAD) issued to consultees and commentators.

ADVANCED RENAL CELL CARCINOMA: BACKGROUND INFORMATION

Renal cell carcinoma (RCC) and its treatment is considered in detail in Pfizer's original submission to NICE in the context of this appraisal, dated 13 August 2012.

The term "RCC" incorporates all the malignancies that originate in the kidney within the epithelia of the renal tubules. It is a rare cancer and accounts for 3% of male cancers and 2% of female cancers in the UK.

Approximately 4456 patients are diagnosed with advanced or metastatic RCC in the UK, each year. The prognosis of such patients is poor; there is no cure and the goals of medical

intervention are to extend life, prevent worsening of disease, relieve symptoms and maintain physical function.

At the advanced or metastatic stage, RCC is largely unresponsive to chemotherapy, radiotherapy and hormonal therapy. Prior to targeted therapies, systemic treatment of advanced or metastatic RCC principally comprised use of cytokines (interleukin -2 and interferon-alpha). However, these treatments are associated with limited efficacy and high toxicity.

In recent years, the management of advanced or metastatic RCC has undergone substantial change, with the development of targeted therapies, including those directed towards the VEGFR pathway targeted by tyrosine kinase inhibitors (TKIs) such as sunitinib and pazopanib, currently recommended by NICE for first-line systemic treatment.

However, the majority of patients initially respond to first-line therapy but subsequently develop disease progression. NICE does not currently recommend any treatment for advanced or metastatic RCC following failure of first-line systemic therapy, although both everolimus and sorafenib are licensed second line treatments and are used widely in this indication. Second-line treatment for patients who have progressed following cytokine therapy generally comprises sunitinib or pazopanib. It is worth noting that at the time of the pivotal axitinib PhIII study being set up, sorafenib was the most commonly used second line therapy and consequently the regulators agreed with Pfizer that this should be the active comparator.

Axitinib is a second generation oral VEGFR-TKI, with greater potency and selectivity than the first generation products, indicated for second line treatment of advanced renal cell carcinoma (RCC) after failure of prior treatment with sunitinib or a cytokine. In circumstances where no second line treatment is currently recommended by NICE, the scope for the appraisal of axitinib indicated that the appropriate comparator was best supportive care (BSC) rather than any active therapy.

The AXIS trial however constitutes a comparison of axitinib with sorafenib, licensed for second line treatment of RCC when AXIS was commenced. In view of the availability of sorafenib a placebo control to the AXIS study would have been unethical. Any comparison of axitinib with BSC for the purposes of this appraisal accordingly required an indirect comparison or other method involving data collected from other trials.

GROUNDS OF APPEAL

1. Ground 1: Procedural Fairness

1.1. The lack of transparency in relation to a submission relied upon for the purposes of the guidance is procedurally unfair

At paragraph 4.8 of the FAD, the Appraisal Committee relies on a submission made by "a commentator" on the appraisal consultation document (ACD) relating to axitinib. The submission appears to be one received from the public through the NICE website and attributed in the "Comments on the ACD Received from the Public through the NICE Website" document ("the Comments from the Public Document") to a "pharmaceutical industry" commentator. The Comments from the Public Document states that no conflict of interest arises in relation to this submission.

The submission from the pharmaceutical industry commentator, as summarised at paragraph 4.8 of the FAD and reported in the Comments from the Public Document, provides extensive criticism of Pfizer's comparison of axitinib with BSC, using a simulated treatment comparison approach. We believe the Appraisal Committee's reliance on this evidence lacks transparency and is procedurally unfair, for the following reasons:

- The identity of the person who submitted the comments relied upon by the Appraisal Committee at paragraph 4.8 of the FAD, has not been disclosed to stakeholders, even though the identity of the commentator affects the interpretation of any criticisms made by them and the weight that should properly be attached. (The FAD does not even specify that the comments were made by a "pharmaceutical industry" commentator; that fact is taken from the Comments from the Public Document, which will not be considered by most persons reading the guidance.)

- The detailed criticisms made by the pharmaceutical industry commentator suggest that this may, in fact, have been one of Pfizer's competitors. If that is the case, the fact that the commentator is presented as having no conflict of interest would have been misleading to the Appraisal Committee and to any stakeholders during their consideration of the issues raised. (Pfizer notes that the declaration required from commentators who are members of the public, does not request disclosure of conflicts from competitor companies and is therefore not adequate in this respect.)

- While certain information is provided in the Comments from the Public Document and the facts relied upon by the Appraisal Committee are set out in the FAD, it is unclear whether these submissions are set out in their entirety or whether they have been summarised. If the summary of the submission from the pharmaceutical industry commentator, as set out in the Comments from the Public Document is in any way incomplete, then this represents a further lack of transparency and procedural unfairness.

This lack of transparency in relation to the identity of the commentator and its submission in response to the ACD for axitinib, prejudices Pfizer in its ability to understand and respond to the issues raised by the commentator and also potentially taints the consideration of this submission by the Appraisal Committee.

1.2. The fact that Pfizer had no adequate opportunity to respond to the additional matters raised by the pharmaceutical industry commentator in response to the ACD, is unfair

As indicated at paragraph 1.1 above, at paragraph 4.8 of the FAD, the Appraisal Committee placed reliance on substantive criticisms advanced by a pharmaceutical industry commentator in response to the ACD. The first occasion upon which Pfizer became aware of these criticisms was during the second meeting of the Appraisal Committee on 13 February 2013 and therefore, Pfizer had no opportunity to consider the issues raised by the pharmaceutical industry commentator or to provide any proper response to such matters.

The difficulties comparing outcomes in patients treated with axitinib and those who received BSC, in circumstances where comprised the central issues in this appraisal. In these circumstances, the introduction of new criticisms of the methodologies used by Pfizer to

model relative benefits, only at the FAD stage, giving Pfizer no opportunity to respond to such matters during the appraisal, was procedurally unfair. Pfizer does not agree with the criticisms advanced by the pharmaceutical industry commentator and would have provided a substantive response refuting the matters raised, had it been given the opportunity to do so.

In these circumstances, Pfizer contends that it should have been provided with the criticisms made by the pharmaceutical industry commentator in advance of the second Appraisal Committee meeting and invited to respond to such matters prior to any consideration by the Appraisal Committee or, alternatively, a second ACD should have been issued following the second Appraisal Committee meeting, allowing a second period of consultation in which to consider these matters.

1.3. The Scope for this appraisal produces results that inevitably lack certainty.

While several products are authorised for the second line treatment of advanced or metastatic RCC and used within the NHS, none of these have been recommended by NICE. As a result of this situation, when the Scope for the appraisal was finalised, the only comparator approved for consideration was BSC.

However, as several products are authorised for second line treatment of advanced or metastatic RCC any trial investigating axitinib had to compare the effects of treatment against an alternative active therapy; any trial comparing a new treatment (such as axitinib) with BSC (essentially placebo) would be unethical and would not be permitted to recruit patients.

In circumstances where there is no direct comparison between the new therapy under consideration and BSC, the comparison required by NICE demands complex modelling of data between several studies. Inevitably, any such approach raises questions of uncertainty greater than those present when data from a head to head study are available. These same problems, identified by the Appraisal Committee in relation to the current appraisal of axitinib will apply to any appraisal of any new second line therapy for advanced or metastatic RCC.

It is Pfizer's position that, in circumstances where second line treatments are available and a placebo (BSC) controlled study is ethically impossible, if the Appraisal Committee wishes to base guidance on a comparison with BSC, it must, as a matter of fairness, adopt a pragmatic approach to uncertainty, recognising that this is attributable to a conflict between regulatory requirements (including those of ethics committees) and the appraisal comparison which NICE itself has imposed on stakeholders.

1.4. The Appraisal Committee's refusal to find that use of axitinib in post-cytokine patients satisfied the "end of life" criteria on the basis that no comparison with sunitinib or pazopanib had been provided was inconsistent with the Scope for this appraisal

At paragraph 4.18 of the FAD, the Appraisal Committee criticised the axitinib submission on the basis that no comparison with sunitinib or pazopanib was provided in relation to the post-cytokine group and, seemingly for this reason, declined to find that axitinib had been shown to be a life-extending end-of-life treatment for the purposes of the end of life advice.

However sunitinib and pazopanib are not listed as comparators in the Scope for this appraisal, approved by the Secretary of State before axitinib was formally referred for appraisal. They are explicitly not recommended by NICE for use as second-line systemic therapy in patients who have received first-line therapy with a cytokine. In these circumstances, there is no basis for requiring a comparison with sunitinib or pazopanib and neither Pfizer nor the ERG considered that a comparison of axitinib with these products was appropriate.

Therefore, if, despite the negative recommendations by NICE and the wording of the Scope, the Appraisal Committee wished to consider comparisons of axitinib with sunitinib and pazopanib, procedural fairness requires that reasons for selecting these two products should have been provided, the Scope amended and Pfizer given adequate time in which to carry out the necessary work. This was not however done.

In these circumstances, the criticism of Pfizer for failing to provide a comparison of axitinib with sunitinib and pazopanib at paragraph 4.18 and the conclusion that axitinib should not be viewed as a life-extending end-of-life treatment as a result of the absence of a comparison that was not requested, is procedurally unfair.

Pfizer refers to the decision of the Appeal Panel who heard the appeal against the FAD for vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract. In that case, the Appeal Panel was asked to consider a situation where vinflunine had been compared with products not envisaged by the appraisal scope and concluded:

"*…it was unfair to the manufacturer for vinflunine to be compared with comparators outside the scope. The manufacturer had not directed submissions to such comparisons*" (paragraph 42).

1.5. The Committee's approach to the assessment of QALY gains occurring in the post- sunitinib group following disease progression and its conclusion that the post-progression model outputs lacked "clinical plausibility" was not transparent

At paragraph 4.13 of the FAD, the Appraisal Committee considered the plausibility of the survival gains estimated for the post-sunitinib group of patients and commented that "*an implausibly high proportion of the total QALY gains with axitinib (compared with best supportive care) in the post-sunitinib group was observed after progression when active treatment with axitinib has stopped.*" The Appraisal Committee expressed the view that these results "*should be interpreted with caution because they lacked clinical plausibility*". The Appraisal Committee's reasons for doubting the QALY benefits following disease progression were:

- that the median survival gain difference between axitinib and BSC estimated directly from the clinical trials was increased by 63% when modelled in the post-sunitinib group, although no such modelling increase was estimated in the post-cytokine group;
- that an "implausibly high" proportion of the total QALY gain with axitinib (compared with BSC) in the post-sunitinib group was observed after disease progression, when treatment with axitinib had been discontinued; this was not a feature in the prior-cytokine analysis or the AXIS trial results; and

- that the Committee concluded it was "implausible" for a high proportion of QALY gains to be present when active treatment with axitinib had been discontinued.

Some similar concerns had been expressed in the ACD and, accordingly, Pfizer addressed these in its response to the ACD. Further submissions also supporting QALY benefits deriving from the post-progression period, were provided by the clinical specialist, Professor Hawkins. By way of example he stated

> "*Post-axitinib it is certainly plausible that there will be a QALY gain as well as while on axitinib.*"and
> *"Thus I feel it is inappropriate to assume no benefit post progression as in section 4.13 of ACD."*

However, the Appraisal Committee provided no reasons for rejecting the explanations provided by Pfizer and the clinical experts in relation to these matters

i. The results obtained from the modelling conducted in this appraisal are consistent with the results of data from other phase III clinical trials in second line advanced or metastatic RCC comparing active treatments with BSC, including the demonstration of additional survival gains compared with BSC during the post-progression period

   - Data from the TARGET trial, which investigated sorafenib, produced a 1.3 month gain in OS for every 1 month gain in PFS (despite inadequate adjustment for patient cross-over to the sorafenib arm of the trial which artificially reduced the apparent survival benefits associated with sorafenib treatment).

   - Data from the RECORD-1 trial, which investigated everolimus, produced a 1.6 month gain in OS for every 1 month gain in PFS

   - For completeness, the Appraisal Committee refers at paragraph 4.15 of the ACD to the updated results of the Delea meta-analysis[1-2], in which the relationship between PFS and OS reported by Pfizer had been weakened by the inclusion of more studies in which cross-over from one treatment to another occurred. Clearly the inclusion of studies in which such cross-over is present requires adjustment and, in the absence of appropriate correction, the results may not be relied upon.

ii. In other appraisals the Appraisal Committee has found that an increased survival gain arising following second line treatment for advanced or metastatic RCC during the post-progression period is plausible (see NICE guidance for everolimus paragraph 4.5). While Pfizer does not suggest that the Committee considering axitinib is bound to reach the same conclusions as the Committee considering another product in a different appraisal, the fact of a different conclusion being reached on similar facts, enhances the obligation placed on the Committee in this case to provide adequate reasons to explain its decision.

iii. An increased survival benefit arising during the post-progression period following treatment of advanced or metastatic RCC, is entirely consistent with use of an active targeted therapy compared to BSC and is therefore clinically plausible. Evidence submitted by Pfizer in response to the ACD for this appraisal showed that a greater duration of progression free survival following treatment resulted in a higher period of

overall survival. Use of an active targeted therapy prevents worsening of disease and may achieve reduction in tumour burden, compared with patients who receive BSC, who are likely to experience more rapidly progressive disease, with associated clinical deterioration.

iv. The Appraisal Committee's conclusion that the median survival gain difference between axitinib and BSC estimated directly from the clinical trials was increased by 63% when modelled in the post-sunitinib group is unexplained and Pfizer has been unable to replicate this figure.

v. A post-progression survival advantage was not modelled for the post-cytokine group in Pfizer's base case analysis because the survival gain associated with axitinib compared with BSC in this patient population was artificially low as a result of patient cross-over in the TARGET trial (which provided the BSC comparator data) from the BSC arm to active therapy.

vi. Comparative OS data relating to axitinib and sorafenib from the AXIS trial are affected by the fact that the comparison is between two active therapies rather than with BSC.

While the Appraisal Committee referred, at paragraph 4.15 of the FAD, to comments provided by Pfizer in relation to QALY gains in the post-progression period, its conclusions are unclear. By way of example, the FAD suggests that the Committee considered it implausible that axitinib would be associated with survival benefits in patients who had previously failed to respond to sunitinib as both products are tyrosine inhibitors. Significantly, there is no indication that the Committee recognised that axitinib's superior potency translated into enhanced clinical benefits for patients.

In particular, the Committee failed to provide any explanation of its conclusions in relation to the matters set out at (i) - (v) above, its reasons, if any for rejecting the explanations provided by Pfizer and by the clinical specialist or, save for saying that the "*progression-free survival and overall survival relationship for the prior-sunitinib group was likely to lie between the manufacturer's estimate and the ERG's estimate, although probably closer to the ERG's estimate*" (i.e. a 1:1 relationship), reached no determination as to the QALY benefits arising in the post-progression period and the reasons for that conclusion. '

No reference is made in the FAD to the comments submitted by the clinical specialist or to the fact that he supported Pfizer's position in this respect and it is therefore unclear whether the Committee was even aware of his position.

This lack of clarity surrounding the Committee's decision in relation to this key aspect of its appraisal of axitinib, has prejudiced Pfizer in its ability to understand the conclusions reached by the Committee and is therefore procedurally unfair.

1.6. While the Committee found explanations for post progression QALY gains "clinically implausible", they failed to request attendance by the clinical specialist at the second Appraisal Committee meeting so that any concerns could be discussed

As explained above, the measure of survival benefits associated with axitinib, including those arising during the post-progression period, compared with BSC, represents a key issue in this appraisal and, therefore, the view of the Committee that Pfizer's modelling is "clinically implausible" is particularly important.

The issue of plausibility of survival benefit occurring during the post-progression period was not discussed during the first meeting of the Appraisal Committee when the clinical specialists were present. When the issue arose during consultation on the ACD, the Committee did not seek the views of the clinical specialists, despite the significance of this aspect of the appraisal and the fact that they seemingly did not accept the explanations provided by stakeholders in response to the ACD, confirming that survival benefit arising during the post-progression period is plausible., Instead they favoured the perspective of the ERG (even though this was apparently presented without any expert clinical advice) that no additional survival benefit arose during the post-progression period .

Paragraph 3.5.39 of the STA Process Guide indicates that, "*if clarification of issues raised during the consultation period is required, the Chair of the Appraisal Committee can, at their discretion, invite one or more of the clinical specialists…. to attend* [the second Appraisal Committee meeting]". In this case, the clinical specialists were not invited to attend the meeting of the Appraisal Committee on 13 February 2013, even though important new clinical evidence had been submitted.

While the Chair of the Appraisal Committee has a discretion whether to invite the clinical specialists to attend the second meeting of the Committee, that discretion must be exercised fairly. Pfizer strongly believes that, in view of the additional information provided in response to the ACD, the controversial conclusions of the Appraisal Committee (including their rejection of the views of the clinical specialist and the inconsistency with the conclusions of Committees in other appraisals) fairness required that the Chair should invite the clinical specialist to attend the meeting in order to provide further opportunity for advice and discussion in relation to these issues.

1.7. The Appraisal Committee's final conclusions in relation to the cost-effectiveness of axitinib are not stated and its reasons for failing to recommend second-line treatment in patients with advanced or metastatic RCC are therefore unclear, in circumstances where the ICER values appear to fall within the range generally regarded as acceptable in other appraisals.

While the Appraisal Committee has not recommended use of axitinib for the second line treatment of metastatic RCC in either post-cytokine or post-sunitinib patients, its reasons are unclear. In particular the bases for its conclusions that the ICER values for axitinib do not fall within the range of values recommended by NICE in accordance with the end of life criteria, are inconsistent with the conclusions reached in other appraisals. This is unfair to patients and to other stakeholders, including Pfizer.

Pfizer refers to the decision of the NICE Appeal Panel, which considered the appeal in relation to TA257. In that case, the Panel ruled that there should be a) clear and convincing reasons for any differences in treatment between appraisals; and b) that clinicians should be able to explain these reasons to patients.

(a) Conclusions of the Committee in relation to the post-cytokine population

The Appraisal Committee accepted that Pfizer's base case ICER of £55,300 per QALY gained for axitinib in the post-cytokine population was the highest potential value in that group of patients (paragraph 4.16 of the FAD), recognising that this may have been over-estimated as a result of patient cross-over in the TARGET trial. The Committee also commented that other factors may have resulted in a higher ICER, although there is no clarity as to the factors to which the Committee referred or how these could impact cost-effectiveness in either direction. The Committee provided no explanation of where it concluded the most plausible ICER in fact lay and how it had weighed the various factors which could affect this value.

While the Committee declined to find that axitinib satisfied the end of life criteria in post-cytokine patients (for reasons which Pfizer believes are flawed), if the end of life criteria apply, the ICER for axitinib is, on any view around the £50,000 threshold value accepted by NICE as acceptable in other cases. This is unsatisfactory and unfair; Pfizer has not been informed by how much, if at all, axitinib has missed the £50,000 threshold or which factors have resulted in a negative recommendation for post-cytokine patients.

(b) Conclusions of the Committee in relation to the post-sunitinib population

The Appraisal Committee concluded that the ICER for axitinib in the post-sunitinib population fell between £33,500 and £52,900 per QALY gained (paragraph 4.19 of the FAD), but that "*the most plausible valuations were at the higher end of this range*".

The Committee accepted that axitinib in post-sunitinib patients satisfied the end of life criteria (paragraph 4.18). In general for , products which fall within the end of life criteria, ICER values of around £50,000 per QALY gained have been viewed as acceptable by NICE. This threshold value is very close to the top of the range of ICERs calculated by the AC for axitinib in post-sunitinib patients and substantially above the bottom of the range calculated by the Committee. Furthermore the Appraisal Committee has found that the ERG's assessment of survival benefit associated with axitinib, which resulted in the ICER of £52,900 per QALY gained, based on an assumption of a 1:1 relationship between PFS and OS is likely to be an underestimate (paragraph 4.15). The consequence of this finding is that the Committee accepts that the most plausible ICER for axitinib in this population will fall below £52,900 per QALY gained.

In these circumstances, where the most plausible ICER is, on any view, at or below the threshold value for positive recommendations under the end of life criteria, it is unclear why the Committee has chosen not to recommend axitinib in the post-sunitinib population.

The fact that the Appraisal Committee has concluded that the most likely ICER value for axitinib in both the post-cytokine and post-sunitinib populations falls at or below the threshold value for products which satisfy the end of life criteria (which the Committee accepts should apply to post-sunitinib patients and Pfizer believes should apply to both

populations) enhances the general obligation of transparency, to provide reasons to patients and stakeholders why axitinib has not been recommended, when other products with similar ICERs have been recommended for use in the NHS.

THE DETERMINATION OF THIS APPEAL

Pfizer requests an oral hearing for the determination of this appeal.

REFERENCES

1. Delea, T.E., Khuu, A., Kay, A., Zheng, J. & Baladi, J.F. Association between treatment effects on disease progression (DP) endpoints and overall survival (OS) in patients with metastatic renal cell carcinoma (mRCC). J Clin Oncol 27(Suppl), Abstract 5105 (2009)
2. Delea TE, Khuu A, Heng DY, Haas T, Soulières D. Association between treatment effects on disease progression end points and overall survival in clinical studies of patients with metastatic renal cell carcinoma. J Cancer. 2012 Sep 25;107(7):1059-68. doi: 10.1038/bjc.2012.367. Epub 2012 Aug 30.