



Worldwide Biopharmaceutical Businesses

National Institute for Health and Clinical Excellence
Level 1A, City Tower
Piccadilly Plaza
Manchester
M1 4BD

BY EMAIL

11th January 2013

RE: Revised patient access scheme (PAS) on Axitinib for the treatment of advanced renal cell carcinoma after failure of prior systemic treatment (ID 518)

Dear [REDACTED],

[REDACTED]

[REDACTED]

Yours sincerely,

[REDACTED]

For and on behalf of Pfizer Limited

Executive summary

As stated in our ACD response, we hold strong concerns about the analyses and assumptions used as the basis for the draft recommendation in the ACD. We do not believe that the ACD represents a sound and reliable assessment of the evidence and therefore appropriate guidance to the NHS. We are concerned that the NICE process has under-stated the value of axitinib. However, to ensure that UK patients get access to this innovative therapy we have revised the PAS.

In the updated cost-effectiveness analysis with the revised PAS, the base case incremental cost per QALY gained versus BSC in the prior sunitinib population is £33,538/QALY for axitinib. For the ERG scenario, even with the clinically implausible assumption of no QALY/survival gain post progression the ICER in the updated base case analysis and the revised PAS for the prior sunitinib population was £52,850 per QALY gain. In addition, in the updated analysis with the revised PAS and CIs for STC adjustment factors, the probability of axitinib being cost effective in the prior sunitinib population is 65%–90% at £50,000 threshold around and depending on the inclusion of the uncertainty around median cross-over adjusted OS for BSC in RECORD-1 trial.

As previously stated, no QALY/survival gain post progression was observed in the base case for the prior cytokine population which resulted in an ICER of £55,284 per QALY gain for axitinib vs. BSC in the updated base case analysis with the revised PAS. However, this is not the most plausible ICER for decision-making as the axitinib survival and cost-effectiveness is underestimated due to the unlikely high estimated OS for BSC. In fact, when a more clinically plausible scenario was used for the OS with BSC the ICER for the updated analysis with the revised PAS was £36,493.

In summary, to maximise the likelihood of UK patients getting access to this innovative therapy we have revised the PAS. In the prior sunitinib population who represent the vast majority of second-line mRCC patients in the UK, our base case ICER for axitinib is substantially lower than the accepted thresholds for other end-of-life treatments. Even with the clinically implausible assumption of no QALY/survival gain post progression in the ERG additional scenario, axitinib is cost-effective end of life treatment for second-line mRCC. Overall, we believe that axitinib is clinically- and cost- effective treatment and should be recommended for second-line mRCC patients where there is significant unmet need as there are no NICE approved treatments.

1. Updated Base Case and Revised Patient Access Scheme

Following the critique of our model by the ERG, where standard deviations (SD) were used instead of SE, in the revised model we replaced the SE for the base case progression free (PF) and progressed disease (PD) health state utilities (i.e. SD=0.275 for PF and SD=0.316 for PD, by SE=0.0035 and SE=0.0175) and for the relative dosing intensity (i.e. SD=35.2% by SE=1.86%). The SE of the cost of death has also been applied to the revised base case. Updated probabilistic sensitivity analysis (PSA) results (scatter plot and cost-effectiveness acceptability curves) include the changes above and the parameter variation of the adjustment factors.

The ERG also noted that the percentage of people with hypertension was less than 1% in the TARGET trial, whereas a value of 2% was applied in the model; therefore, the revised model applies a value of 0%. The ERG was also concerned that the lifetime time horizon of 10 years used in the base case model may not be in line with real-life expectancy and we, therefore, applied a 15 year time horizon for the revised base case in both the prior sunitinib and prior cytokine populations. Finally, we applied specific utility values and relative dose intensity (RDI) rates for the two subgroups rather than the estimates for the intention-to-treat (ITT) population.

During the preparation of response, a transcription error was identified that involved the timescale of the STC analyses and the OS data analysis. The statistical analyses for the STCs and the survival models for OS (but not for progression-free survival [PFS]) were based on a timescale of 28-day cycles, but were implemented in the model as if they had been calculated using months as the timescale. PFS was analysed and implemented with months so the PFS results have not been affected. The OS data have been amended by changing the time reference in the formulas (cycles as opposed to months) for these specific curves on the respective sheets for axitinib and BSC for the two populations. The estimated mean costs and QALYs were reduced in all cases for both arms. However, the error had only a marginal impact on ICERs for both the prior sunitinib and prior cytokine populations. The median PFS and OS estimates and Kaplan-Meier curves have also been adjusted.

In addition to the changes in the base case described above, a revised PAS has been submitted to the Department of Health. [REDACTED]

The updated cost-effectiveness results with the revised PAS are provided in the PAS template.