csas
Commissioning Support
Appraisals Service

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18 December 2012

National Institute for Health and Clinical Excellence

Dear [redacted],

RE: Axitinib for the treatment of advanced renal cell carcinoma after failure of prior systemic treatment

On behalf of Commissioning Support, Appraisals Service (CSAS), Solutions for Public Health, I would like to submit our comments on the appraisal consultation document for axitinib for the treatment of advanced renal cell carcinoma after failure of prior systemic treatment. We are in agreement with the recommendation in the ACD not to recommend axitinib for this indication as on the basis of the evidence considered it is unlikely that this treatment can be considered clinically and cost effective in real life clinical practice.

- **Axitinib for this population group is not a cost effective use of NHS resources.** The ICER of £65,000 per QALY (in the subgroup who had received prior cytokine therapy) is likely to have been an over-estimate. However, other uncertainties in the economic models mean that the most plausible ICER (for both prior-cytokine and prior-sunitinib populations) is still likely to exceed £50,000 per QALY gained and could not be considered a good use of NHS resources for this population.
- **A patient access scheme agreed with the Department of Health has already been taken into account in the ICER.** The size of the discount is commercial in confidence but was taken into account in the estimate of an ICER of £65,000 per QALY gained.
- **Although it fulfills the criteria for a life-extending treatment for people previously treated with sunitinib, axitinib could still not be considered a good use of NHS resources for this population.** Due to value of the ICERs and the uncertainty around the ICERs.
- **No trials have compared axitinib with best supportive care, which is the most appropriate and only scoped comparator for this appraisal.** There are no second-line drugs currently approved for people who have become resistant to first-line treatment and no trials have directly compared axitinib with best supportive care.
- **Axitinib improved progression-free survival, but not overall survival, compared to sorafenib in one good quality trial, but interpretation is difficult due to lack of information on appropriate comparators**. All models required indirect comparisons. Sorafenib is not approved by NICE as cost-effective for use in the NHS. The well conducted AXIS trial found that, compared to sorafenib, axitinib improved progression-free survival in people who had received prior cytokine treatment. However, there were serious limitations with the simulated treatment comparisons performed for the prior-sunitinib population; and also no comparison of axitinib with pazopanib or sunitinib for the prior-cytokine population.
- **The treatment pathway for patients with advanced renal cell carcinoma is changing**. The Committee heard from experts that fewer patients now receive first-line cytokines, and that most people receive first-line treatment with pazopanib or sunitinib. The prior-pazopanib group would be a relevant population for treatment with second-line axitinib; and also

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pazopanib and sunitinib are available as second-line treatments for people who have received first-line cytokines.

- **Axitinib has a manageable adverse effects profile compared with other treatments for advanced renal cell carcinoma.** Diarrhoea occurred in over half of patients in both arms of the AXIS trial. Hypertension, dysphonia, nausea and hypothyroidism occurred more frequently with axitinib than sorafenib.

If you require any further information please contact me directly: Phone: [redacted], email [redacted]

Yours sincerely

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