

**National Institute for Health and Clinical Excellence
Centre for Health Technology Evaluation**

Pro-forma Response

Executable Model

Bevacizumab, sorafenib, sunitinib and temsirolimus for the treatment of advanced and/or metastatic renal cell carcinoma

The economic model enclosed and its contents are confidential and are protected by intellectual property rights, which are owned by University of Exeter. It has been sent to you for information only. It cannot be used for any other purpose than to inform your understanding of the appraisal. Accordingly, neither the model nor its contents should be divulged to anyone other than those individuals within your organisation who need to see to them to enable you to prepare your response. Those to whom you do show the documents must be advised they are bound by the terms of the Confidentiality Acknowledgement and Undertaking Form that has already been signed and returned to the Institute by your organisation.

You may not make copies of the file and you must delete the file from your records when the appraisal process, and any possible appeal, are complete. You must confirm to us in writing that you have done so. You may not publish it in whole or part, or use it to inform the development of other economic models.

The model must not be re-run for purposes other than the testing of its reliability.

Please set out your comments on reliability in writing providing separate justification, with supporting information, for each specific comment made. Where you have made an alteration to the model details of how this alteration was implemented in the model (e.g. in terms of programme code) must be given in sufficient detail to enable your changes to be replicated from the information provided. Please use the attached pro-forma to present your response.

Please prepare your response carefully. Responses which contain errors or are internally inconsistent (for example where we are unable to replicate the results claimed by implementing the changes said to have been made to the model) will be rejected without further consideration.

Results from amended versions of the model will only be accepted if their purpose is to test robustness and reliability of the economic model. Results calculated purely for the purpose of using alternative inputs will not be accepted.

No electronic versions of the economic model will be accepted with your response.

Responses should be provided in tabular format as suggested below (please add further tables if necessary).

November 2008

Issue 1

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
Applying the hazard ratio to estimate the survival outcomes relating to Nexavar results in an inaccurate estimation. Log-cumulative hazard plot shows assumption of proportional hazard is violated.	Survival curves for Nexavar should be modelled independently rather than estimated curve via the hazard ratio.	The Weibull parameters for fitting independent Nexavar curves are estimated to be (shape,scale) - 0.0592 and 1.4090 for PFS, 0.0122 and 1.3862 for OS. Estimated ICER using these parameters is £61,745.

Issue 2

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
Use of a 42 day Markov cycle length. This cycle is inappropriate for usual treatment with Nexavar, whereby patients are treated based on a 4 week pack cycle, and care decisions based on multiples of this timeframe.	No amendments have been made in regard to this issue.	The 42 day cycle is expected to overestimate the ICER compared to a more clinically and economically relevant 28 day cycle.