National Institute for Health and Clinical Excellence

Single (STA)

Pazopanib for the first-line treatment of advanced and/or metastatic renal cell carcinoma

Response to consultee and commentator comments on the final remit and draft scope

Comment 1: the draft scope

Section	Consultees	Comments	Action
Background information	GlaxoSmithKline	Whilst we recognise that incidence data will vary depending on the source, it is worth noting that GSK has used a different assumption based on an estimated 32% of patients with RCC presenting with advanced/metastatic disease (Decision Resources, Onkos Study #7, Renal Cell Carcinoma, June 2008.)	Comment noted, no action required.
	Royal College of Physicians (comments submitted by DR. Patrick Cadigan) on behalf of NCRI/RCP/RCR/ACP/JCCO – comments coordinated by Dr. Paul Nathan)	Reasonable	Comment noted, no action required.
	Royal College of Nursing-1	Should be TNM not (TMN)	Comment noted, the scope has been amended accordingly.
	Royal College of Nursing-2	There is also a first line trial recruiting at present. It is comparing sutent with pazopanib in metastatic renal cell cancer.	Comment noted, the scope has been amended accordingly.

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The technology/ intervention	GlaxoSmithKline	Under this section the draft scope states that "Pazopanib is currently being studied in clinical trials compared with placebo" . GSK would like to clarify that the pazopanib phase III pivotal study (VEG105192) will be the key source of evidence for this appraisal. Hence, we believe the suggested wording below may be more accurate. "Pazopanib has been studied in a randomised, double-blind, placebo-controlled, multi-centre phase III study of which the objective was to evaluate the efficacy and safety of pazopanib compared to placebo in patients with locally advanced and/or metastatic renal cell carcinoma (RCC).The trial included patients who had either received no prior systemic therapy; received only one prior systemic cytokine-based treatment; or whose disease was refractory to cytokine based treatment".	Comment noted, the scope is a brief document, intending to summarise the key points of the condition and the technology.
	Royal College of Physicians (comments submitted by DR. Patrick Cadigan) on behalf of NCRI/RCP/RCR/ACP/JCCO – comments coordinated by Dr. Paul Nathan)	Yes	Comment noted, no action required.
	Royal College of Nursing-2	Yes	Comment noted, no action required.
Population	GlaxoSmithKline	Yes, the population has been defined appropriately in the scope. No groups within this population should be considered separately.	Comment noted, no action required.
	Royal College of Physicians (comments submitted by DR. Patrick Cadigan) on behalf of NCRI/RCP/RCR/ACP/JCCO – comments coordinated by Dr. Paul Nathan)	Yes	Comment noted, no action required.

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	Pfizer	The population is appropriately defined.	Comment noted, no action required.
	Royal College of Nursing-2	Yes. Non-clear cell cancers could be considered separately.	Comment noted. The scope has been amended accordingly.
Comparators	GlaxoSmithKline	We do not have additional comments as best supportive care reflects the comparator in the pazopanib pivotal trial and sunitinib the current standard of care in the NHS.	Comment noted, no action required.
	Royal College of Physicians (comments submitted by DR. Patrick Cadigan) on behalf of NCRI/RCP/RCR/ACP/JCCO – comments coordinated by Dr. Paul Nathan)	Yes	Comment noted, no action required.
	Pfizer	Sutent is an appropriate comparator. However it is unclear how evidence from the placebo controlled trial will support this comparison. Best supportive care is not an appropriate treatment in the first line setting in the UK unless performance status is poor or patient co-morbid state renders them unfit for active treatment. Best supportive care may be used in second or further treatment lines. We believe that high dose interferon alpha and high dose interleukin-2 should also be included as comparators within this appraisal. They are given in the first line metastatic setting as potentially curative treatments.	Comment noted. Comment noted. Comment noted.
	Royal College of Nursing-1	Should include immunotherapy , but not as 'best alternative care'	Comment noted.
	Royal College of Nursing-2	Yes	Comment noted, no action required.

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Outcomes	GlaxoSmithKline	Yes, these clinical outcomes capture the most important health related benefits/harms of the technology	Comment noted, no action required.
	Royal College of Physicians (comments submitted by DR. Patrick Cadigan) on behalf of NCRI/RCP/RCR/ACP/JCCO – comments coordinated by Dr. Paul Nathan)	Yes	Comment noted, no action required.
	Royal College of Nursing-2	Yes	Comment noted, no action required.
Economic analysis	GlaxoSmithKline	As stated in the reference case the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. The time horizong in our economic analysis would be 10 years.	Comment noted, no action required.
	Royal College of Physicians (comments submitted by DR. Patrick Cadigan) on behalf of NCRI/RCP/RCR/ACP/JCCO – comments coordinated by Dr. Paul Nathan)	None	Comment noted, no action required.
Equality and Diversity	GlaxoSmithKline	No comments	Comment noted, no action required.
	Royal College of Physicians (comments submitted by DR. Patrick Cadigan) on behalf of NCRI/RCP/RCR/ACP/JCCO – comments coordinated by Dr. Paul Nathan)	None	Comment noted, no action required.

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Other considerations	Royal College of Physicians (comments submitted by DR. Patrick Cadigan) on behalf of NCRI/RCP/RCR/ACP/JCCO – comments coordinated by Dr. Paul Nathan)	Suggestion of resected vs unresected tumour probably not possible to answer given available data	Comment noted, no action required.
Questions for consultation	GlaxoSmithKline	Should immunotherapy be considered as an appropriate comparator? It is felt that immunotherapy (IFN alpha/IL-2) should not be considered as a relevant comparator as it no longer constitutes a standard treatment in the NHS. Indeed, UK oncologist estimated that currently only around 5% of patients in the UK are receiving immunotherapy as the first line treatment of advanced/metastatic RCC and this population is diminishing rapidly. In addition, data presented in 2005 by Negrier showed that the benefit of immunotherapy was restricted to a very limited group of patients and for the rest was a toxic and ineffective treatment. It is worth noting that since no head to head data for pazopanib versus sunitinib are currently available a indirect comparison via IFN will be necessary for the puspose of our submission. Furthermore, a randomised head to head trial comparing pazopanib with sunitinib is currently being conducted. Preliminary results from this study are expected to be available in Q2 2011. How should best supportive care be defined? (Zafar 2008). In the pazopanib pivotal study best supportive care included transfusion of blood and blood products, treatment with antibiotics, anti-emetics, anti-diarrhoeal agents, anti-hypertensive agents, erythropoietin, or bisphosphonates, when appropriate.	Comment noted. It was agreed that sunitinib is the standard f care for most people. However, for people who are unsuitable immunotherapy and best supportive care are currently the only available treatment options. Comment noted.

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	GlaxoSmithKline	Best supportive care can be defined as "Treatment administered with the intent to maximise quality of life without a specific antineoplastic regimen" (Zafar 2008). In the pazopanib pivotal study best supportive care included transfusion of blood and blood products, treatment with antibiotics, anti-emetics, anti-diarrhoeal agents, anti-hypertensive agents, erythropoietin, or bisphosphonates, when appropriate.	Comment noted.
	Royal College of Physicians (comments submitted by DR. Patrick Cadigan) on behalf of NCRI/RCP/RCR/ACP/JCCO – comments coordinated by Dr. Paul Nathan)	Immunotherapy is no longer standard of care for the vast majority of patients and would therefore be an inappropriate comparator.	Comment noted. It was agreed that sunitinib is the standard f care for most people. However, for people who are unsuitable immunotherapy and best supportive care are currently the only available treatment options.
		Resected subgroup inappropriate as appropriate data not available	Comment noted, no action required.
		Definition of "clear cell carcinoma" difficult. "RCC with a clear cell component" less ambiguous.	Comment noted, no action required.
	Pfizer	If the evidence allows the analysis of subgroups based upon performance status (ECOG status) this should be considered. Current guidance for Sutent in this patient population only covers ECOG PS 0 or 1 patients, ECOG PS 2 patients could be considered to have an unmet clinical need.	Comment noted, the scope has been amended accordingly.

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	Royal College of Nursing-1	Yes immunotherapy should be considered as a comparator. Best supportive care should be 'best active care'- to prevent, control or relieve complications and side effects to improve patient's comfort and quality of life.	Comment noted. It was agreed that sunitinib is the standard f care for most people. However, for people who are unsuitable immunotherapy and best supportive care are currently the only available treatment options.
Additional comments on the draft scope.	GlaxoSmithKline	Are the subgroups suggested in 'other considerations' appropriate? Whilst it may be appropriate to consider unresected versus resected subpopulations, it should be noted that most patients (89%) in the pazopanib pivotal trial had had a nephrectomy. Are there any other subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately? GSK is considering conducting a number of subgroup analyses (including baseline assesment by site and number of metastases)	Comment noted. Comment noted

The following consultees/commentators indicated that they had no comments on the final remit and/or the draft scope

- Department of Health
- Macmillan Cancer Support
- Marie Curie Cancer Care
- Medicines and Healthcare products Regulatory Agency
- National Public Health Service for Wales (now Public HealthWales NHS Trust)
- NHS Quality Improvement Scotland
- Welsh Assembly Government