NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

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

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Thomas Powles

Name of your organisation [redacted]

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?

Yes

- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?

Yes

- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?

I am a member of the [redacted] **(but not an employee).**

- other? (please specify)

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What is the expected place of the technology in current practice?

Q: How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

A: Sunitinib is standard therapy for first line metastatic or advanced renal cancer. It has NICE approval. Other previous treatments such as interferon have been superseded by sunitinib. Other targeted therapies in the first line setting have been rejected by NICE. After progression on sunitinib everolimus is of benefit. Everolimus in undergoing appraisal with NICE at present (after initial rejection).

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

A: The studies include clear cell renal cancer patients. There is less data on the non clear cell population. Attempts do identify subgroups who benefit have not been successful.

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

A: Targeted therapy is administered cancer centres or cancer units by people with experience in this field. Monitoring is required during therapy with CT and blood tests.

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

A: Pazopanib is licensed, but is not widely given as it does not have NICE approval. Due to the pricing structure and efficacy data some areas are planning to give pazopanib instead of sunitinib in selected patients after local agreement with funders. Business cases have been prepared.

Please tell us about any relevant clinical guidelines and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

A: The current UK guidelines have not been updated since the EMA approval of pazopanib, therefore it does not appear in these. The UK guidelines were written and approved by a wide spectrum of experts in the field and were

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based on the results of randomized phase III studies. In view of these criteria pazopanib would be recommended in the first line setting.

UK guidelines for the systemic treatment of renal cell carcinoma. Nathan P, Wagstaff J, Porfiri E, Powles T, Eisen T. Br J Hosp Med. 2009 May;70(5):284-6. Review.

In the US pazopanib appears in the NCCN guidelines in the first line setting.

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

Pazopanib is used in the first line metastatic and advanced RCC setting. It would be a direct alternative to sunitinib, which is the current standard in the UK has NICE approval. The drugs have more similarities than differences, however the toxicity profiles of the drug appear different and this is important.

A trial (COMPARZ), which directly compared the 2 agents (sunitinib and pazopanib), is due to report in 2011-12. Indirect comparison is not statistically valid, however the progression free survival data is remarkably similar in the 2 pivotal randomized phase III studies (11 months for both). Of particular note is the difference in toxicity profile for the 2 drugs. Oral VEGFTKI therapy is associated with significant toxicity, these toxicities overlap between drugs . They are important as they affect patient's day to day life (particularly mucositis, lethargy and hand and foot syndrome). Indeed 50% of patients in the pivotal sunitinib study required a dose reduction. Pazopanib's toxicity appears different. For example the hand and foot syndrome may be lower while abnormalities in liver function occur more frequently.
This toxicity profile of pazopanib may be attractive to patients, particular those who we know are likely to develop sunitinib related toxicity (female, increased age, low body surface area). It is not clear if this same population develops pazopanib related toxicity. In view of the fact that pazopanib is an alternative to sunitinib and the 2 drugs appear equally efficacious, adding a 2nd drug to the first line setting as an alternative appears attractive to patients, without having a major impact on resources.

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If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

The NICE guidelines the use of sunitinib are extensive. Pazopanib directly competes with sunitinib in this setting and the same rules should apply. However there is a paucity of pazopanib data in the non-clear cell population.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

We have treated 17 patients with pazopanib. Our experience reflects the clinical trial data in terms of response, progression free survival and toxicity. The feeling from our multi-disciplinary group is that the drug is well tolerated and has a role in the 1st line setting in renal cancer.

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

The side effects of this class of drugs are extensive and well documented. Sunitinib and pazopanib appear to have slightly different toxicity profiles making the option of using alternative agents to sunitinib attractive. For example patients with manual jobs may prefer pazopanib in view of the reduced reported palmer planter syndrome. Nevertheless a direct comparison of the 2 agents will not be available until COMPARZ reports. On the other hand patients with known liver abnormalities may be wise to avoid pazopanib as it appears to have increased LFT derangement.

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

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No, the randomised data should drive this appraisal.

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

As this directly competed with sunitinib and the 2 drugs are similar no extra facilities or equipment will be required.