Appendix G - professional organisation submission template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Tolvaptan for treating autosomnal dominant polycystic kidney disease

Thank you for agreeing to make a submission 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 submission, 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: [redacted]

Name of your organisation: Royal College of Pathologists
Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- 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)?
- other? (please specify) **A specialist involved in diagnosis/ histological assessment of biopsies and resection specimens (kidneys and liver predominantly) from patients with ADPKD and polycystic liver disease (explanted kidneys for infection and/or pain and/or haematuria and/or to make room for a renal transplant and livers if require a liver transplant). In kidneys have to exclude malignancy. Also assess post transplant biopsies.**

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

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?

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?

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)?

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?

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.

There is no specific approved treatment currently. Current alternatives are to manage as CKD with control of blood pressure etc, decrease in size of kidney (or liver) by aspiration, surgical procedures or embolization (don't think this is done in the UK), removal of kidney for infection, pain, bleeding or malignancy. Dialysis or transplantation when end stage renal failure reached.

Subgroups: PKD 1 and 2 and 3 undefined mutation(s). PKD 2 has a later onset and slower progression – so may be worth a subgroup analysis.

Mixture of primary and secondary care: blood checks by GP (LFT rise a side effect which may require stopping drug) with less frequent follow up in secondary care to manage by nephrologists as part of usual renal follow-up. Unlikely to require significant staffing change/increase.

Tolvaptan is licensed for use in hyponatraemia due to SIADH.

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?

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.

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?

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 advantages are that it is for prevention of disease progression and will prevent or significantly delay the requirement for current management of these problems. There are currently no other disease modifying treatments available.

Requirement for regular monitoring of liver function tests as an elevation may require discontinuation of Tolvaptan. Most common side effect relate to increased thirst, dry mouth and increase frequency of urination, this includes waking at night to urinate so could adversely affect quality of life.

Most important outcome – slowing of deterioration in renal function with delay in requirement for renal replacement therapy. Slowing of cyst growth (size of kidneys) also important, but there are microscopic cysts which significantly outnumber the cysts measured by imaging studies to produce total kidney volume, which potentially influence long term outcome.

Grantham JJ, Mulamalla S, Grantham CJ, et al. Detected renal cysts are tips of the iceberg in adults with ADPKD. Clin J Am Soc Nephrol 2012; 7:1087–1093.

Any additional sources of evidence

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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.

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)?

Delivery of Care: oral drug – so no NHS staff training required. Need monitioring of LFTs as this was a reason for patient withdrawal in the TEMPO study. As this treatment slows progression of disease would minimise requirement for more specialised renal replacement therapy options

Equality
NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could lead to recommendations that have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Discussed in scoping exercise – nothing further to add