NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Tolvaptan for treating autosomal dominant polycystic kidney disease

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of tolvaptan within its licensed indication for treating autosomal dominant polycystic kidney disease.

Background

Polycystic kidney disease (PKD) is a genetic disorder that causes the growth of multiple cysts on the kidneys. PKD occurs in two forms - autosomal recessive polycystic kidney disease (ARPKD) and autosomal dominant polycystic kidney disease (ADPKD). ADPKD is the most common inherited disorder of the kidneys and the fourth leading cause of end-stage kidney disease in adults worldwide. It is estimated that between 1 to 2 in 1000 people are born with ADPKD indicating that at least 60,000 people may have the disease in the UK.

ADPKD is characterised by a progressive increase in the number and size of bilateral renal cysts, resulting in enlargement of the kidneys to 3 to 4 times their normal size. This may result in renal impairment and in some cases people with ADPKD will lose all their kidney function (referred to as kidney failure or end-stage chronic kidney disease). There are 5 stages of chronic kidney disease, classified according to kidney function. People with mild disease (stages I or II) have normal or slightly reduced kidney function, however as the disease progresses they may develop moderate (stage III) to severe renal impairment (stage IV), or established renal failure (stage V). Severe renal impairment may be fatal unless treated with dialysis or a kidney transplant.

Disease progression in ADPKD is highly variable and symptoms usually appear between the ages of 30 and 60 years. People with ADPKD may experience complications such as hypertension, haematuria (blood in the urine), liver and pancreatic cysts, intracranial aneurisms, kidney stones and urinary tract infections. Approximately 50% of people with ADPKD have established renal failure by 60 years of age, but one third will reach 70 years of age with some preservation of renal function.

People with or suspected of having ADPKD should be referred for specialist assessment (NICE Clinical guideline 73) and monitored to identify evidence of progressive chronic kidney disease. There are no pharmacological treatments available that reduce progression or growth of renal cysts in ADPKD. Therapies currently used aim to control symptoms and associated

complications of kidney disease, such as controlling high blood pressure. If kidney failure occurs, treatment options include dialysis and transplantation.

The technology

Tolvaptan (Samsca, Otsuka Pharmaceuticals) is a treatment that aims to delay the progression of kidney disease by reducing cyst fluid accumulation and epithelial cell growth. It is administered orally.

Tolvaptan does not have a UK marketing authorisation for the treatment of ADPKD. It has been studied in clinical trials compared with placebo in adults with ADPKD.

Intervention(s)	Tolvaptan
Population(s)	People with autosomal dominant polycystic kidney disease
Comparators	Standard care without tolvaptan
Outcomes	The outcome measures to be considered include: • time to established renal failure • symptoms of chronic kidney disease (including pain) • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that 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. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. *Subject to referral by the Department of Health, the invite for participation in this technology appraisal is anticipated for after January 2014, when new arrangements for the pricing of pharmaceuticals are expected to be in place. Consequences for this appraisal will be explored through further consultation on the scope pre invitation.*
Related NICE recommendations	Related Technology Appraisals: Technology appraisal No. 48, September 2002, 'Guidance on home compared with hospital haemodialysis for patients with end-stage renal failure'. This guidance is on the static list (October 2005). Related Guidelines: Clinical Guideline No. 73, September 2008, 'Early identification and management of chronic kidney disease in adults in primary and secondary care'. Currently being updated. Earliest anticipated date of publication Jul 2014 Clinical Guideline No. 125, July 2011, 'Peritoneal dialysis in the treatment of stage 5 chronic kidney disease'. Review date July 2014. Related Quality Standards: Quality Standard No.5, Mar 2011. 'Chronic kidney disease'. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways Chronic kidney disease. Pathway created: May 2011. http://pathways.nice.org.uk/

Questions for consultation

Has the most appropriate comparator for tolvaptan for the treatment of ADPKD been included in the scope?

How should 'standard care without tolvaptan' be defined? What stage of chronic kidney disease would treatment with tolvaptan be started?

Have the most appropriate outcomes for tolvaptan for the treatment of ADPKD been included in the scope?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which tolvaptan will 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 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.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits

Where do you consider tolvaptan will fit into the existing NICE pathway; Chronic kidney disease (http://pathways.nice.org.uk/)?

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)