NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Tolvaptan for treating autosomal dominant polycystic kidney disease

Final scope

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. However, the actual prevalence of both diagnosed and undiagnosed population remains unclear.

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 1 or 2) have normal or slightly reduced kidney function, however as the disease progresses they may develop moderate (stage 3) to severe renal impairment (stage 4), or established renal failure (stage 5). 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 aneurysms, 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 182) 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 pain, cyst infections, urinary tract infections and high blood pressure. If kidney failure occurs, treatment options include dialysis and transplantation.

The technology

Tolvaptan (Jinarc, 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 marketing authorisation in the UK for the treatment of ADPKD. It has been studied in clinical trials compared with placebo in adults with ADPKD.

Intervention(s)	Standard care in combination with tolvaptan
Population(s)	People with autosomal dominant polycystic kidney disease
Comparators	Standard care including routine surveillance without tolvaptan
Outcomes	The outcome measures to be considered include: • rate of decline of renal function • 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. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. If evidence allows, subgroups stratified by the rate of decline of renal function and by baseline total kidney volume should be considered in the manufacturer's submission. If evidence allows the use of different stopping rules based on treatment response will also be considered
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. 182, July 2014, 'Early identification and management of chronic kidney disease in adults in primary and secondary care'. Clinical Guideline No. 125, July 2011, 'Peritoneal dialysis in the treatment of stage 5 chronic kidney disease'. Review decision date June 2015. 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/
Related National Policy	Chapter 15. Adult specialist renal services http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf