The Royal College of Pathologists
Pathology: the science behind the cure

18th September 2015

Dr Margaret Helliwell
Vice chair
National Institute for Health and Care Excellence
10 Spring Gardens
London
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Dear Margaret

Re: Final Appraisal Determination – Tolvaptan for treating autosomal dominant polycystic kidney disease [ID652]

The Royal College of Pathologist would like to appeal against the Final Appraisal Determination for the above mentioned technology appraisal on the following grounds, which come under the category of Ground 2: A large number of question marks are raised in the appraisal document and there are a number of inaccuracies/inappropriate assumptions, some of which have been acknowledged by the Evidence Review Group (ERG), which have been highlighted by the Company. These inaccuracies/inappropriate assumptions have been used in the modelling process and may have a bearing on the outcome.

Ground 2: The recommendation is unreasonable in the light of the evidence submitted to NICE

2.1 The Appraisal Committee has continued to assume that there is equal kidney pain in both groups on the basis that kidney pain is a symptom of chronic kidney disease, despite acknowledging that clinical experts indicate that kidney pain is not necessarily a reflection of chronic kidney disease. The ERG use a reference by Pham PC et al Clin Nephrol 2010: (reference 9 in the ERGs critique of the companies additional evidence) to support this, however this reference is an assessment of all types of pain, not just kidney pain. The predominant type of pain is musculoskeletal, with kidney pain relatively uncommon, so this reference is not supportive. Kidney pain related to ADPKD can be severe enough to require surgical removal of the kidney(s).

2.2 The worst case scenario used by the ERG for drug induced liver failure requiring transplantation, with 0% survival is unrealistic based on liver transplant survival rates. The company has provided evidence of a more likely lower percentage of cases developing drug induced liver injury and has provided the European survival data indicating that there is a 79% 1 year and 72% 5 year survival. The UK data is even better than this: NHSBT data shows that for super-urgent liver transplants (in which acute liver failure due to drugs will fall), the 90 day patient and graft survival rates are 91.5% and 88.7 respectively and the 1 year and 5 year patient survival rates are 85.1% and 81.2% respectively, this data is based on 2004-14, the numbers are further improved for more recent years eg 2011-14 with a 1year survival of 89.8%. (http://odt.nhs.uk/pdf/organ_specific_report_liver_2014.pdf).

2.3 From the patients comments it is apparent that the thirst / requirement to drink large amounts of water, which has been taken to be a negative side effect by the ERG, is seen by patients as a positive thing. This is not reflected in the modelling.

The points outlined in 2.1-2.3 suggest that the guidance cannot be reasonably justified and that further modelling is required to take these points into account.

Conclusion
The Royal College of Pathologists wished to appeal the decision on the above grounds and is happy to proceed with a written appeal.