NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Odevixibat for progressive familial intrahepatic cholestasis

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of Odevixibat within its marketing authorisation for treating progressive familial intrahepatic cholestasis for national commissioning by NHS England.

Background

Progressive familial intrahepatic cholestasis (PFIC) is the name given to a group of genetic disorders that affect the liver and result in the flow of bile from the liver to the gut being reduced or stopping completely (cholestasis).

Bile is produced by the liver, stored in the gall bladder and then released during digestion. It is used to help the body absorb fats and nutrients and get rid of toxins. Bile acids are then re-absorbed and returned to the liver via the small intestine. When bile flow is reduced or stops completely it can lead to poor weight gain and slower growth, and an excess of toxins in the body.

Initial symptoms of PFIC include greasy stools or watery diarrhoea, jaundice and itching (pruritus). Untreated it leads to complications including portal hypertension, liver scarring (cirrhosis) and failure, and hepatocellular carcinoma, a type of liver cancer. It can also cause problems outside the liver such as diarrhoea, deafness and pancreatitis[1,2].

PFIC is inherited in an autosomal recessive pattern[3], meaning that two copies of the mutated gene (one from each parent) must be present for it to develop. It has been reported that the three main subtypes of the disorder, PFIC1, PFIC2, and PFIC3 are mainly caused by mutations and variations in ATP8B1, ABCB11, and ABCB4 genes respectively[4]. PFIC1 and PFIC2 onset usually occurs in the first months of life, whereas PFIC3 can also appear later in infancy, in childhood or even during young adulthood[2].

The exact prevalence of PFIC remains unknown. Estimated prevalence at birth has been reported as varying between 1 per 50,000 and 1 per 100,000; this is likely to be a worldwide estimate but the data on which these rate are based is unclear[2, 5, 6]. Approximately 32 children per year may require genetic testing for PFIC in the UK according to estimates from the UK Genetic Testing Network (closed 2018)[3].

PFIC usually progresses to cirrhosis within the first decade of life and is ultimately fatal if untreated[3]. A 2010 multi-centre retrospective study of 145 patients with PIFC with mutations in either ATP8B1 or ABCB11 found that 50% of patients not undergoing surgical diversion or liver transplant survived to the age of 10 but almost none were alive at the age of 20 years[7]. Itching

can have a significant impact on the quality of life of babies and children with PFIC and their carers, often interrupting sleep and contributing to fatigue.

There are currently no licensed therapies for PFIC. Current clinical management focusses on relieving symptoms and slowing liver damage. It often includes initial off-label drug treatment with ursodeoxycholic acid. Common surgical interventions include partial external biliary diversion and internal ileal exclusion. Liver transplant remains the only definitive treatment for some patients with PFIC and requires lifelong medical follow-up and use of anti-rejection medications. In addition, patients may require additional nutritional support, for example nasogastric feeding[2,3].

The technology

Odevixibat (brand name unknown, Abireo) is a selective inhibitor of ileal bile acid transporters (IBATs). IBATs help the reabsorption of bile acids through the small intestine. Odevixibat aims to stop the recycling of bile acids to prevent toxic levels accumulating in the liver. Odevixibat is administered orally as a capsule.

Odevixibat does not currently have a marketing authorisation in the UK for PFIC. It is being studied in a double-blind, randomised, placebo-controlled trial of children with PFIC types 1 and 2.

Intervention(s)	Odevixibat
Population(s)	People with progressive familial intrahepatic cholestasis
Comparators	Established clinical management without Odevixibat which may include: • off-label drug treatments such as ursodeoxycholic acid • surgical interventions such as partial external biliary diversion or internal ileal exclusion
Outcomes	The outcome measures to be considered include: • change in serum bile acid level • change in symptoms of PFIC including reduction pruritus • measures of faltering growth • overall survival • measures of disease progression • number of patients requiring surgical interventions • adverse effects of treatment • health-related quality of life (for patients and carers)

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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
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.
Related NICE recommendations and NICE Pathways	Related Guidelines: 'Faltering growth: recognition and management of faltering growth in children' (2017). NICE guideline 75 Review date to be confirmed. Related NICE Pathways: Faltering growth (2018) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 69 Liver transplantation service (adults and children), Chapter 110 Specialist gastroenterology, hepatology and nutritional support services for children, Chapter 111. Clinical genomic services (adults and children) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 4 & 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

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