NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Obeticholic acid for treating primary biliary cirrhosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of obeticholic acid within its marketing authorisation for treating primary biliary cirrhosis.

Background

Primary biliary cirrhosis (PBC), sometimes known as primary biliary cholangitis, is a progressive autoimmune disease that affects the liver and biliary system and destroys the small interlobular bile ducts. This prevents bile flowing from the liver to the small intestine (cholestasis) and leads to a build-up of bile in the liver cells, which damages the liver. PBC causes the formation of excess fibrous connective tissue (fibrosis) and eventually may lead to scarring of the liver (cirrhosis). The exact cause of PBC is not known, although it is thought a combination of environmental and genetic factors may play a part. The most common symptoms of PBC are itchy skin (pruritus) and fatigue, however, up to half of people with PBC do not have any symptoms until extensive liver damage occurs.

The estimated prevalence of PBC in England is approximately 18,900 people based on 35 people per 100,000 being diagnosed with PBC[1, 2]. In 2013 there were 131 deaths from PBC in England and Wales[3]. Most people with PBC are aged between 30 and 65 years, and around 90% of people with the condition are women.

Treatment for PBC aims to alleviate symptoms and slow disease progression. Ursodeoxycholic acid is the only current treatment available for primary biliary cirrhosis. The estimated proportion of people whose disease have an inadequate response to ursodeoxycholic acid ranges between 20% and 70%[1,4]. Fibrates have been used in clinical practice alone and in combination with ursodeoxycholic acid for people whose disease has an inadequate response to, or are unable to tolerate ursodeoxycholic acid. Symptomatic treatment of pruritus related to PBC includes the use of cholestyramine, rifampicin or naltrexone. Liver transplantation is the only treatment that can improve prognosis for people with PBC who have end-stage liver disease, however, the disease can recur following transplantation.

The technology

Obeticholic acid (brand name unknown, Intercept Pharmaceuticals) is a farnesoid-X receptor agonist and modified bile acid derived from the endogenous human bile acid chenodeoxycholic acid. It is administered orally.

Obeticholic acid does not currently have a marketing authorisation in the UK for primary biliary cirrhosis. It is being studied in clinical trials alone and in combination with ursodeoxycholic acid compared with placebo alone or in combination with ursodeoxycholic acid in adults whose disease had an inadequate response to ursodeoxycholic acid or who were unable to tolerate ursodeoxycholic acid.

Intervention(s)	Obeticholic acid alone or in combination with ursodeoxycholic acid
Population(s)	People with primary biliary cirrhosis whose disease has an inadequate response to, or who are unable to tolerate, ursodeoxycholic acid.
Comparators	For people whose disease has an inadequate response to ursodeoxycholic acid: • Ursodeoxycholic acid alone or in combination with fibrates For people who are unable to tolerate ursodeoxycholic acid: • Fibrates • No additional treatment
Outcomes	The outcome measures to be considered include: • mortality • liver function based on markers of liver biochemistry • symptoms, including pruritus, fatigue and abdominal pain • time to liver transplantation • primary biliary cirrhosis related events, including ascites, varices, encephalopathy and hepatic cell carcinoma • 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.
Related NICE recommendations and NICE Pathways	Related Guidelines: Clinical Guideline in Preparation, 'Assessment and management of cirrhosis'. Earliest anticipated date of publication May 2016. Related NICE Pathways: NICE Pathway: Liver conditions, Pathway created: Mar 2014. http://pathways.nice.org.uk/pathways/liver-conditions
Related National Policy	NHS England commissions specialist services for Primary Biliary Cirrhosis under its policy for Liver transplantation services in adults and children. Source: Manual for prescribed specialised services Page 161 Department of Health (2013) NHS Outcomes Framework 2014-2015, Domains 1, 2, 4 and 5

References

1. UK-PBC http://www.uk-pbc.com/about/aboutpbc/. Accessed July 2015
2. Office for National statistics (2013) Population Estimates for UK, England and Wales, Scotland and Northern Ireland, Mid-2013. Accessed July 2015
3. Office for National Statistics (2013) Mortality Statistics: Deaths Registered in England and Wales. Accessed February 2015
4. Expert opinion at the scoping workshop