NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Obeticholic acid for treating primary biliary cirrhosis

Draft scope (pre-referral)

Draft 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) 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 leads to scarring of the liver (cirrhosis). PBC increases a person's risk of developing other autoimmune diseases, such as thyroid disease, and is associated with an increased cardiovascular morbidity and mortality. Liver failure is the usual cause of death in people with PBC, however other causes include a bleed from the oesophagus or stomach (variceal haemorrhage), infection, or cancer of the liver (hepatocellular carcinoma). 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. People who are asymptomatic or whose only symptom is pruritus can be expected to live more than 20 years after first presentation. In the later stage of the disease, people can also experience jaundice and abdominal pain. People presenting with jaundice usually survive less than 5 years.

The estimated prevalence of PBC in England is approximately 13,400 people[1]. In 2013 there were 131 deaths from PBC in England and Wales[2]. 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 can be used alone or in combination with immunosuppressive therapies such as methotrexate, and corticosteroids to delay end-stage liver disease. The estimated proportion of people whose disease have an inadequate response to ursodeoxycholic acid ranges between 15 and 40%[3,1]. Symptomatic treatment of pruritus related to PBC includes the use of cholestrymine, and antihistamines. Liver transplantation is the only treatment that can improve prognosis for people with PBC, however, the disease can recur following transplantation.

The technology

Obeticholic acid (brand name unknown, Intercept Pharmaceuticals) is a bile analogue derived from the 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 compared with placebo in adults who had had ursodeoxycholic acid for at least 12 months or who were unable to tolerate ursodeoxycholic acid. It has also been studied in combination with ursodeoxycholic acid compared with placebo in combination with ursodeoxycholic acid in people who had been on a stable dose of ursodeoxycholic acid for at least 6 months.

Intervention(s)	Obeticholic acid alone or in combination with ursodeoxycholic acid
Population(s)	People with primary biliary cirrhosis who have had, or who are unable to tolerate, ursodeoxycholic acid.
Comparators	Established clinical practice without obeticholic acid including, but not limited to, immunosuppressive therapy, and: • Ursodeoxycholic acid • No additional treatment
Outcomes	The outcome measures to be considered include: • mortality • liver function/damage • symptoms, including pruritus, jaundice and abdominal pain • time to liver transplantation • high-density lipoprotein metabolism • 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

Questions for consultation

Have all relevant comparators for obeticholic acid alone or in combination with ursodeoxycholic acid been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for primary biliary cirrhosis?

Are there any subgroups of people in whom obeticholic acid alone or in combination with ursodeoxycholic acid is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider obeticholic acid will fit into the existing NICE pathway, Liver conditions?

- 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 obeticholic acid will be 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 obeticholic acid 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 obeticholic acid 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.

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/article/pmg19/chapter/1-Introduction)

References

1. Horizon Scanning Centre (2013) Obeticholic acid for primary biliary cirrhosis – second line

2. Office for National Statistics (2013) Mortality Statistics: Deaths Registered in England and Wales. Accessed February 2015

3. PBC Foundation http://www.pbcfoundation.org.uk/Home/CMSPageView/531. Accessed April 2015