NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Seladelpar for previously treated primary biliary cholangitis [ID6429]

Final scope (updated July 2025)

Final remit/evaluation objective

To appraise the clinical and cost effectiveness of seladelpar within its marketing authorisation for previously treated primary biliary cholangitis.

Background

Primary biliary cholangitis (PBC), previously known as primary biliary cirrhosis, is a chronic and progressive autoimmune disease. PBC leads to a build-up of bile in the liver. It causes damage to the liver and to the small interlobular bile ducts, leading to impairment of bile flow from the liver to the small intestine (cholestasis). PBC can cause the formation of excess fibrous connective tissue (fibrosis) and can lead to scarring of the liver (cirrhosis). The cause of PBC is unknown but is thought to be a mix of environmental and genetic triggers. Not all people with PBC experience symptoms, and many do not have any symptoms until significant liver damage has occurred. The most common symptoms are fatigue and itchy skin (pruritus).

There are around 20,000 people living with PBC in the UK.[1] It has a prevalence of around 35 per 100,000 people and an annual incidence of 2 to 3 per 100,000 people.[1] Approximately 90% of the people who have PBC are women, with 25% of these being under 40 years of age.[2]

Treatment for PBC aims to alleviate symptoms and slow disease progression. Treatments for PBC in the UK include ursodeoxycholic acid and obeticholic acid. Ursodeoxycholic acid is the preferred first-line treatment, however some people's disease does not respond completely to it, or they cannot tolerate it. NICE technology appraisal (TA443) also recommends obeticholic acid in combination with ursodeoxycholic acid for people whose disease has responded inadequately to ursodeoxycholic acid or as monotherapy for people who cannot tolerate ursodeoxycholic acid. Treatments are also available for some symptoms associated with PBC. Itching can be treated with colestyramine (previously cholestyramine) and rifampicin. There are currently no known treatments for fatigue related to PBC. A liver transplant is the only treatment when significant liver damage endangerers life. A transplant will cure itching and other symptoms, but fatigue may persist.[3]

The technology

Seladelpar (brand name unknown, Gilead Sciences) does not currently have a marketing authorisation in the UK for PBC. It has been studied in a clinical trial compared with placebo in adults with PBC whose disease has an inadequate response to, or who are unable to tolerate, ursodeoxycholic acid.

Intervention(s)	Seladelpar
Population(s)	Adults with primary biliary cholangitis whose disease has an inadequate response to, or who are unable to tolerate, ursodeoxycholic acid
Subgroup(s)	If the evidence allows the following subgroups will be considered: • Early-moderate stage PBC (minimal / moderate fibrosis) with isolated elevated ALP values above the upper limit of normal • Individuals with pruritus • Those who have inadequately responded to ursodeoxycholic acid and/or obeticholic acid.

Comparators	• For people, whose disease has an inadequate response to ursodeoxycholic acid:
	  ○ Obeticholic acid in combination with ursodeoxycholic acid
	  ○ Ursodeoxycholic acid monotherapy
	  ○ Elafibranor in combination with ursodeoxycholic acid (subject to NICE evaluation)
	  ○ Fibrates in combination with ursodeoxycholic acid [a]
	• Where ursodeoxycholic acid cannot be tolerated:
	  ○ Obeticholic acid monotherapy
	  ○ Best supportive care
	  ○ Elafibranor (subject to NICE evaluation)
	  ○ Fibrates [a]

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 cholangitis related consequences, 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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 and cost of biosimilar and generic products should 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	**Related technology appraisals:** Obeticholic acid for treating primary biliary cholangitis (2017) NICE technology appraisal guidance 443. **Related technology appraisals in development:** Elafibranor for treating primary biliary cholangitis. NICE technology appraisal guidance [ID6331] Publication date to be confirmed. **Related NICE guidelines:** Cirrhosis in over 16s: assessment and management (2023) NICE guideline NG50. **Related interventional procedures:** Living-donor liver transplantation (2015) NICE interventional procedures guidance IPG535.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Prescribed specialised services manual (version 6) Chapter 69, Liver transplantation service (adults and children) NHS England (2023) Prescribed specialised services manual (version 6) Chapter 131, Specialist services for complex liver, biliary and pancreatic diseases in adults Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017 NHS Digital (2022) NHS Outcomes Framework England, March 2022 Annual Publication

[a]At the committee meeting to discuss seladelpar for previously treated primary biliary cholangitis, the committee heard from clinical experts that fibrates are used in clinical practice to treat PBC and associated pruritus. The committee thought for people in clinical practice with PBC with pruritus, fibrates were a potential comparator so the scope has been re-issued listing fibrates as a potential comparator.

References

1. UK-PBC: Epidemiology of PBC. Available from: https://www.uk-pbc.com/about/aboutpbc/epidemiology-of-pbc/ Accessed August 2024.

2. NORD: Primary Biliary Cholangitis. Available from: https://rarediseases.org/rare-diseases/primary-biliary-cholangitis/ Accessed August 2024.

3. NHS: Primary biliary cirrhosis treatment. Available from: https://www.nhs.uk/conditions/primary-biliary-cholangitis-pbc/treatment/ Accessed August 2024.