Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Seladelpar for previously treated primary biliary cholangitis ID6429

Draft scope

Draft 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), also 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

Appendix B

Population(s)	Adults with primary biliary cholangitis 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:
	  ○ Obeticholic acid in combination with ursodeoxycholic acid
	  ○ Ursodeoxycholic acid monotherapy
	  ○ Fibrates in combination with ursodeoxycholic acid
	  ○ Elafibranor in combination with ursodeoxycholic acid (subject to NICE evaluation)
	• Where ursodeoxycholic acid cannot be tolerated:
	  ○ Obeticholic acid monotherapy
	  ○ Best supportive care
	  ○ Fibrates
	  ○ Elafibranor (subject to NICE evaluation)

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

Questions for consultation

Where do you consider seladelpar will fit into the existing care pathway for primary biliary cholangitis?

Please select from the following, will seladelpar be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would seladelpar be a candidate for managed access?

Are fibrates (such as bezafibrate and fenofibrate) relevant comparators for seladelpar?

Do you consider that the use of seladelpar can result in any potential 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 committee to take account of these benefits.

NICE is considering evaluating this technology through its cost comparison evaluation process.

Please provide comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will

route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is seladelpar likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?
- Will seladelpar be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.
- Will seladelpar be used to treat the same population as the comparator(s)?
- Overall is seladelpar likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

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.