**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

# Elafibranor for treating primary biliary cholangitis

**Draft scope**

## Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of elafibranor within its marketing authorisation for treating 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 cells. 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 do not respond completely to it or cannot tolerate it. NICE technology appraisal (TA443) 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

Elafibranor (brand name unknown, Ipsen Limited) does not currently have a marketing authorisation in the UK for primary biliary cholangitis. It is being studied in clinical trials compared with placebo in adults aged between 18 to 75 years who had been taking ursodeoxycholic acid for at least 12 months prior to screening visit or who were unable to tolerate ursodeoxycholic acid.

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| **Intervention(s)** | Elafibranor alone or in combination with ursodeoxycholic acid |
| **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:<br>• Ursodeoxycholic acid<br>• Obeticholic acid in combination with ursodeoxycholic acid<br>For people who are unable to tolerate ursodeoxycholic acid:<br>• Obeticholic acid |
| **Outcomes** | The outcome measures to be considered include:<br>• mortality<br>• liver function based on markers of liver biochemistry<br>• symptoms including pruritus, fatigue and abdominal pain<br>• time to liver transplantation<br>• primary biliary cholangitis related events, including ascites, varices, encephalopathy and hepatic cell carcinoma<br>• adverse effects of treatment<br>• 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.<br>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.<br>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.<br>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. |

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| **Related NICE recommendations** | **Related Technology Appraisals:**<br><br>'Obeticholic acid for treating primary biliary cholangitis' (2017) NICE technology appraisal guidance 443<br><br>**Related NICE guidelines:**<br><br>Cirrhosis in over 16s: assessment and management. (2016) NICE guideline NG50 |
| **Related National Policy** | NHS England commissions specialist services for Primary Biliary Cirrhosis (PBC) under its policy for liver transplantation services in adults and children Source: Prescribed Specialised Services Manual Page 200 NHS England (2023)<br><br>NHS Outcomes Framework Indicators – March 2022<br><br>Domains 1<br><br>The NHS Long Term Plan (2019) The NHS long term plan<br><br>NHS England (2013) 2013/14NHS STANDARD CONTRACT FOR HEPATOBILIARY AND PANCREAS (ADULT<br><br>Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017<br><br>NHS Digital (2022) NHS Outcomes Framework England, March 2022 Annual Publication |

**Questions for consultation**

Where do you consider elafibranor will fit into the existing care pathway for PBC?

Are ursodeoxycholic acid and obeticholic acid the only relevant comparators?

Is best supportive care a relevant comparator? If so, how should it be defined?

Would elafibranor be a candidate for managed access?

Do you consider elafibranor 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 elafibranor 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 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 elafibranor 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.

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 the technology 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 the intervention 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 the intervention be used to treat the same population as the comparator(s)?

- Overall is the technology 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 [online; accessed; 27 October 2023]
2. NORD Primary Biliary Cholangitis [online; accessed 27 October 2023]
3. NHS Primary Biliary Cholangitis [online; accessed 27 October 2023]