NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Ivosidenib for treating advanced cholangiocarcinoma with an IDH1 mutation after at least 1 therapy

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of ivosidenib within its marketing authorisation for treating cholangiocarcinoma.

Background

Cholangiocarcinoma is cancer of the bile duct. It mainly affects people aged over 65. Most people already have advanced cholangiocarcinoma when they are diagnosed because early disease is often asymptomatic. When symptoms occur, they include jaundice, weight loss, pain, sickness and fever.

Cholangiocarcinoma can be classified into 3 subtypes, depending on which part of the bile duct the cancer starts in. Intrahepatic cholangiocarcinoma (between 10-20% of cases) starts in the bile ducts inside the liver, peri-hilar cholangiocarcinoma starts just outside the liver (where the left and right hepatic ducts meet) and distal cholangiocarcinoma starts in the bile ducts near the bowel.[1,2] The overall incidence of cholangiocarcinoma is increasing with currently around 2,800 people diagnosed each year in England.[1] Mutations in the metabolic enzyme isocitrate dehydrogenase-1 (IDH1) are detected in approximately 13% of intrahepatic and 1% of extrahepatic cholangiocarcinomas.[3] These enzymes play a role in cholangiocarcinoma pathogenesis. In 2017 there were 2,187 people diagnosed with cholangiocarcinoma in England, 1,069 were males and 1,118 were female. Of people diagnosed in England in 2012, 28.5% of men and 24.6% of women survived for 1 year or more. Of people diagnosed in England in 2008, 6.6% of men and 4.4% of women survived for 5 years or more.[4]

Surgery is currently the only curative treatment for cholangiocarcinoma.[5] When surgery is not an option people can be offered gemcitabine and cisplatin. After systemic chemotherapy, people may be offered modified folinic acid, fluorouracil and oxaliplatin (mFOLFOX). NICE technology appraisal 722 recommends pemigatinib for treating advanced cholangiocarcinoma with FGFR2 fusion or rearrangement after systemic therapy in adults.

The technology

Ivosidenib (Tibsovo, Servier laboratories) is a small molecule inhibitor of IDH1. Blocking IDH1 activity is expected to reduce the growth and spread of the cancer. It is administered orally.

Ivosidenib does not currently have a marketing authorisation in the UK for cholangiocarcinoma. It has been studied in clinical trials in people with advanced or metastatic cholangiocarcinoma with an IDH1 mutation, who received at least 1 and no more than 2 prior regimens of systemic therapy.

Intervention(s)	Ivosidenib
Population(s)	People with locally advanced or metastatic cholangiocarcinoma with an IDH1 mutation, who were previously treated by at least one prior line of systemic therapy
Comparators	• Chemotherapy (including fluorouracil and oxaliplatin) • Folinic acid • Best supportive care (active symptom control, including stent insertion)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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 use of ivosidenib is conditional on the presence of IDH1 gene mutation. The economic modelling should include the costs associated with diagnostic testing for IDH1 gene mutation in people with advanced cholangiocarcinoma who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).

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:** Pemigatinib for treating relapsed or refractory advanced cholangiocarcinoma with FGFR2 fusion or rearrangement (2021) NICE technology appraisal guidance 722 **Related Interventional Procedures:** Selective internal radiation therapy for unresectable primary intrahepatic cholangiocarcinoma (2018) Interventional procedures guidance IPG630 Photodynamic therapy for bile duct cancer (2005) Interventional procedures guidance IPG134 Endoscopic bipolar radiofrequency ablation for treating biliary obstruction caused by cholangiocarcinoma or pancreatic adenocarcinoma Interventional procedures guidance in development.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)

Questions for consultation

Have all relevant comparators for ivosidenib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for locally advanced or metastatic cholangiocarcinoma with an IDH1 mutation, who were previously treated by at least one prior line of systemic therapy?

How should best supportive care be defined?

Where do you consider ivosidenib will fit into the existing care pathway for cholangiocarcinoma?

Is genetic testing conducted in clinical practice?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom ivosidenib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Would ivosidenib be a candidate for managed access?

Do you consider that the use of ivosidenib 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 ivosidenib 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 intends to evaluate this technology through its Single Technology Appraisal process. We welcome 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).

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

- Would it be appropriate to use the cost-comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Khan, SA, Tavolari, S, Brandi, G. Cholangiocarcinoma: Epidemiology and risk factors. Liver Int. 2019; 39(Suppl. 1): 19– 31. https://doi.org/10.1111/liv.14095

2. Cancer Research UK (2022) What is bile duct cancer? [Accessed 15 October 2022]

3. Zhu AX, Macarulla T, Javle MM, Kelley RK, Lubner SJ, Adeva J, et al. Final Overall Survival Efficacy Results of Ivosidenib for Patients With Advanced Cholangiocarcinoma With IDH1 Mutation: The Phase 3 Randomized Clinical ClarIDHy Trial. JAMA Oncology. 2021;7(11):1669-77. Available from: https://doi.org/10.1001/jamaoncol.2021.3836.

4. Public Health England Age-standardised incidence rates, one- and five-year survival, all patients diagnosed with upper gastrointestinal cancers, England [accessed October 2022]

5. BMJ Best Practice (Accessed 15 September 2022)