NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Lenvatinib for advanced, unresectable, untreated hepatocellular carcinoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lenvatinib within its marketing authorisation for advanced, unresectable, untreated hepatocellular carcinoma.

Background

Hepatocellular carcinoma (HCC) is the most common form of liver cancer in England, accounting for 55% of primary liver cancer diagnoses in men and 28% of diagnoses in women[1]. It is commonly associated with cirrhosis (scarring of the liver), which can be caused by excessive alcohol intake, viral infections such as hepatitis B or C, or other conditions that result in chronic inflammation of the liver[2]. There were 2,374 people diagnosed with HCC in England in 2014[3]. The risk of developing HCC increases with age, with the average age at diagnosis being 66 years[2].

Treatment for HCC depends on the location and stage of the cancer, and how well the liver function is preserved. Early stage hepatocellular carcinoma may be treated with surgery (hepatic resection or liver transplantation), or percutaneous radiofrequency or thermal ablation to cure the disease. However, treatment is palliative rather than curative for many people. Other treatment options include interventional procedures such as transarterial chemoembolisation (using doxorubicin or cisplatin) and selective internal radiation therapy, external beam radiotherapy, systemic chemotherapy (such as doxorubicin or cisplatin) and targeted therapies such as sorafenib. Some people with HCC are treated with best supportive care. Sorafenib is not recommended as an option for treating advanced hepatocellular carcinoma in NICE's technology appraisal guidance on sorafenib for the treatment of advanced hepatocellular carcinoma (TA189). It is currently going through the Cancer Drugs Fund (CDF) rapid re-consideration process at NICE.

The technology

Lenvatinib (Lenvima, Eisai) is a multi-targeted tyrosine kinase inhibitor. This selectively inhibits the kinase activities of all vascular endothelial growth factor receptors, in addition to other proangiogenic and oncogenic pathways, including fibroblast growth factor receptors, the platelet derived growth factor receptor alpha KIT and RET. Lenvatinib is given orally.

Levatinib does not currently have marketing authorisation in the UK for hepatocellular carcinoma. It has been studied in clinical trials versus sofafenib in adults with unresectable hepatocellular carcinoma who have not been previously received systemic treatment.

Intervention(s)	Lenvatinib
Population(s)	Adults with unresectable hepatocellular carcinoma who have not been previously received systemic treatment
Comparators	• sorafenib • best supportive care
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. 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 Technology Appraisals:** 'Sorafenib for the treatment of advanced hepatocellular carcinoma' ' (2010). NICE Technology Appraisal 189. Review date February 2013: Static list Appraisals in development

	Hepatocellular carcinoma (advanced and metastatic) sorafenib (first line) (review of TA189) NICE Technology Appraisal 1012. Publication date to be confirmed. **Related NICE Pathways:** Liver cancers (2015) NICE pathway.
Related National Policy	**NHS England:** NHS England (May 2016) Manual for prescribed specialised services 2016/17, chapter 131 (page 300): Specialist services for complex liver, biliary and pancreatic diseases in adults. NHS England 2013/14 NHS standard contract for hepatobiliary and pancreas (ADULT) A02/S/a **Department of Health:** Department of Health (2011) Improving Outcomes: A Strategy for Cancer Department of Health (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.

Questions for consultation

Have all relevant comparators for lenvatinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for advanced, unresectable, untreated, hepatocellular carcinoma?

How should best supportive care be defined?

Are the outcomes listed appropriate?

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

Where do you consider lenvatinib will fit into the existing NICE pathway?

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 levatinib 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 lenvatinib 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 lenvatinib 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 has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made. We welcome comments on the appropriateness and suitability of the cost comparison methodology to 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 technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. National Cancer Registration and Analysis Service (2010) Trends in incidences in primary liver cancer subtypes. Accessed July 2017

2. Patient (2015) Hepatocellular carcinoma. Accessed July 2017

3. Office for National Statistics (2016) Cancer registration statistics. Accessed July y 2017.

4. Dufour J-F, Bargellini I, De Maria N et al. (2013) Intermediate hepatocellular carcinoma: current treatments and future perspectives. Annals of Oncology 24: ii24-ii29

5. Zhang Z-M, Guo J-Z, Zhang Z-C et al. (2011) Therapeutic options for intermediate-advanced hepatocellular carcinoma. World Journal of Gastroenterology 17: 1685-9