NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Lenvatinib for advanced, unresectable, untreated hepatocellular carcinoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of lenvatinib within its marketing authorisation for advanced hepatocellular carcinoma not previously treated with systemic therapy.

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 2,456 people diagnosed with HCC in England in 2015[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 potentially curative surgery (hepatic resection), or percutaneous radiofrequency/thermal ablation in patients with well-preserved liver function, or liver transplantation for those with impaired liver function.

However, treatment is palliative rather than curative for people with more advanced disease. Treatment options include interventional procedures such as transarterial chemoembolisation (using doxorubicin or cisplatin) or selective internal radiation therapy, and external beam radiotherapy. People for whom these treatments are not suitable, or those with metastatic disease, are treated with sorafenib (a multi-kinase inhibitor). Some people with HCC are treated with best supportive care. NICE Guidance TA474 (Cancer Drugs Fund reconsideration of TA189) recommends sorafenib as an option for treating advanced HCC only for people with Child-Pugh grade A liver impairment. Sorafenib was available for people with both Child-Pugh grade A and B advanced HCC via the Cancer Drugs Fund. The indication for people with Child-Pugh grade B liver function was removed from the Cancer Drugs Fund on 5th November 2017.[4]

The technology

Lenvatinib (Lenvima, Eisai) is a multi-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.

Lenvatinib does not currently have marketing authorisation in the UK for treating hepatocellular carcinoma. It has been studied in clinical trials in comparison with sorafenib in adults with unresectable hepatocellular carcinoma who have not previously received systemic treatment.

Intervention	Lenvatinib
Population	Adults with unresectable hepatocellular carcinoma who have not previously received systemic treatment
Comparators	• sorafenib • best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • time to progression • 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 availability of any patient access scheme and commercial access agreement for the intervention or comparator technologies 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 and NICE Pathways	**Related Technology Appraisals:** Sorafenib for the treatment of advanced hepatocellular carcinoma (2017) NICE technology appraisal 474 (update of NICE technology appraisal 189). Next review August 2020. **Appraisals in development:** Regorafenib for previously treated unresectable hepatocellular carcinoma' NICE technology appraisals guidance [ID991]. Publication expected March 2018. **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.

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 (2015) Cancer registration statistics. Accessed September 2017.
4. Cancer Drug Fund (2017) National Cancer Drug Fund List ver1.41. Accessed September 2017.