NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Nanoliposomal irinotecan for treating pancreatic cancer after prior treatment with gemcitabine

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nanoliposomal irinotecan within its marketing authorisation for treating pancreatic cancer after prior treatment with gemcitabine.

Background

The pancreas is a large gland located behind the stomach that is part of the digestive system. Pancreatic cancer does not usually cause any symptoms in its early stages, which can make it difficult to diagnose. The first symptoms may include pain in the back or stomach area, unexpected weight loss or jaundice (yellowing of the skin and whites of the eyes). The most common type of pancreatic cancer is pancreatic ductal adenocarcinoma.[1]

In 2012, 7371 people were diagnosed with pancreatic cancer in England.[2] Pancreatic cancer affects men and women equally and about 75% of people diagnosed with pancreatic cancer are aged 65 years or over.[2] There were around 7200 deaths because of pancreatic cancer in 2013 in England.[3] The prognosis depends on how advanced the disease is when it is diagnosed. On average, about 21% of people with pancreatic cancer survive beyond 12 months.[4]

Surgery is usually the only way pancreatic cancer can be cured, but it is only suitable for the 15-20% of people who have 'early stage' disease. At the time of diagnosis, about 35–40% of people have locally advanced disease (meaning the cancer has grown into the tissues surrounding the pancreas) and about 45–55% have metastatic disease (meaning the cancer has spread to other parts of the body).[1]

People with locally advanced or metastatic disease may be offered chemotherapy, radiotherapy or palliative surgery to help control tumour growth and symptoms. These treatments may be given alone or in combination with each other. NICE technology appraisal guidance 25 recommends gemcitabine for untreated advanced or metastatic adenocarcinoma of the pancreas, only if the person has a Karnofsky performance score of 50 or more and potentially curative surgery is not a suitable treatment. NICE technology appraisal guidance 25 states that there is insufficient evidence to support the use of gemcitabine as a second-line treatment in patients with pancreatic adenocarcinoma.

There is no consensus about the preferred treatment for patients with pancreatic cancer that has previously been treated with gemcitabine. Options used in clinical practice include gemcitabine in combination with capecitabine, oxaliplatin in combination with fluorouracil, and fluorouracil in combination with folinic acid, oxaliplatin and irinotecan (FOLFIRINOX). Capecitabine, oxaliplatin and irinotecan do not have marketing authorisations in the UK for treating pancreatic cancer.

The technology

Nanoliposomal irinotecan (brand name unknown, Baxalta) consists of the anti-cancer medicine irinotecan contained within tiny fat particles called nanoliposomes. The nanoliposomes are expected to accumulate within the tumour and release the irinotecan slowly over time. Irinotecan blocks an enzyme called topoisomerase I, which causes DNA strands to break. This prevents the cancer cells from dividing and they eventually die. Nanoliposomal irinotecan is administered intravenously.

Nanoliposomal irinotecan does not currently have a marketing authorisation in the UK. It has been studied in a clinical trial that compared a regimen of nanoliposomal irinotecan, fluorouracil and folinic acid with a regimen of fluorouracil and folinic acid. The trial recruited patients with metastatic adenocarcinoma of the pancreas that had previously been treated with gemcitabine.

Intervention(s)	Nanoliposomal irinotecan in combination with fluorouracil and folinic acid
Population(s)	People with pancreatic cancer that has previously been treated with gemcitabine
Comparators	• Gemcitabine in combination with capecitabine • Oxaliplatin in combination with fluorouracil • Fluorouracil in combination with folinic acid, oxaliplatin and irinotecan (FOLFIRINOX)
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 Appraisal: Guidance on the use of gemcitabine for the treatment of pancreatic cancer (2001). NICE Technology Appraisal 25. Moved to static list in March 2006. Guideline in development: Pancreatic cancer. Publication expected January 2018. Related Interventional Procedure: Irreversible electroporation for treating pancreatic cancer (2013). NICE interventional procedures guidance 442. Related NICE Pathway: Gastrointestinal cancers (2015) NICE pathway http://pathways.nice.org.uk/
Related National Policy	NHS England Manual for Prescribed Specialised Services 2013/14. Chapter 105: Specialist cancer services (adults) http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf NHS England Standard Contract For Cancer: Pancreatic (Adult) 2013/14. Section B Part 1 - Service Specifications http://www.england.nhs.uk/wp-content/uploads/2013/06/a02-cncr-panc.pdf Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 4 and 5.

	https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

Questions for consultation

Have all relevant comparators for nanoliposomal irinotecan been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for treating pancreatic cancer after prior treatment with gemcitabine?
- Should any additional treatments be considered as comparators? In particular:
    - Is irinotecan in combination with fluorouracil and folinic established practice for people who have had prior treatment with gemcitabine for their pancreatic cancer?
    - Is irinotecan monotherapy established practice for people who have had prior treatment with gemcitabine for their pancreatic cancer?

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

Where do you consider nanoliposomal irinotecan will fit into the existing NICE pathway on gastrointestinal cancers?

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 nanoliposomal irinotecan 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 nanoliposomal irinotecan 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 pancreatic cancer)?

Do you consider that the use of nanoliposomal irinotecan 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 intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

References

1. Pancreatic cancer UK (2015) Facts about pancreatic cancer. Accessed May 2015.
2. Office for National Statistics (2012) Cancer Registration Statistics, England.
3. Cancer Research UK (2015) Pancreatic cancer mortality statistics. Accessed May 2015.
4. Cancer Research UK (2015) Pancreatic cancer survival statistics. Accessed May 2015.