NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nintedanib for untreated malignant pleural mesothelioma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nintedanib with pemetrexed and cisplatin followed by nintedanib monotherapy within its marketing authorisation for untreated unresectable malignant pleural mesothelioma.

Background

Malignant pleural mesothelioma is a cancer affecting the membranes lining the outer surface of the lungs and the inside of the chest wall (the pleura). It is a highly aggressive tumour; the majority of people with this condition present and are diagnosed in the advanced stages of the disease and most have a poor prognosis.

In 2016 approximately 2281 people were diagnosed with mesothelioma in England. Mesothelioma is more common in men than women with 82% of diagnoses in England in 2016 in men.[1] Pleural mesothelioma accounts for approximately 90% of diagnoses and is linked to exposure to asbestos.[2] People typically present with the condition 20 to 50 years after exposure, therefore the incidence rate is higher in older people, with around half of all diagnoses in the UK between 2013 and 2015 in people aged 75 and older.[2]

Mesothelioma can be divided into 3 histologic subtypes, epithelioid (about 60% of cases), sarcomatoid (10 to 20%) and a combination of epithelioid and sarcomatoid known as biphasic (about 30%).[3] The survival of patients with malignant pleural mesothelioma is typically around one year, with improved outcomes for people who have the epithelioid subtype or are surgically treated.[4]

The aim of treatment is to reduce tumour size and improve symptoms. Standard care includes chemotherapy and radiotherapy. NICE technology appraisal guidance 135 recommends pemetrexed with cisplatin as a treatment option for people with untreated malignant pleural mesothelioma for whom surgical resection is inappropriate. British Thoracic society guidelines recommend carboplatin in combination with pemetrexed where cisplatin is contraindicated or has adverse risk. The guidelines also indicate that raltitrexed is an alternative to pemetrexed.[5]

The technology

Nintedanib (Vargatef, Boehringer Ingelheim) is a tyrosine kinase inhibitor which targets multiple growth factor receptors that are involved in tumour growth and spread. It is administered orally.

Nintedanib does not currently have a marketing authorisation in the UK for the treatment of malignant pleural mesothelioma. It has been studied in clinical trials in combination with pemetrexed and cisplatin, followed by nintedanib monotherapy, in

adults with untreated unresectable malignant pleural mesothelioma of epithelioid histology.

Intervention(s)	Nintedanib with pemetrexed and cisplatin followed by nintedanib maintenance monotherapy
Population(s)	Adults with untreated unresectable malignant pleural mesothelioma
Comparators	**Induction** • Pemetrexed with cisplatin • Raltitrexed with cisplatin • Pemetrexed with carboplatin (for people for whom treatment with cisplatin is unsuitable) **Maintenance** • 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. The availability of any patient access schemes for the intervention or comparator technologies will 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: Pemetrexed for the treatment of malignant pleural

	mesothelioma (2008) NICE Technology Appraisal Guidance 135. On static list, last reviewed: July 2017 Terminated appraisals Bevacizumab for untreated malignant pleural mesothelioma (terminated appraisal) (2017) NICE Technology Appraisal Guidance [ID1183] Related NICE Pathways: Respiratory conditions (2018) NICE Pathway
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Chapter 105: Specialist cancer services (adults). Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2013) 2013/14 NHS Standard contract for cancer: malignant mesothelioma (adult) Ref: B10/S/a Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report

Questions for consultation

Have all relevant comparators for nintedanib been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for malignant pleural mesothelioma?

- Is raltitrexed used in NHS clinical practice?
- Is carboplatin used in the NHS in people for whom cisplatin is contraindicated?
- Is pemetrexed with cisplatin used as maintenance therapy in NHS clinical practice?
    - What constitutes best supportive care for patients who do not receive pemetrexed with cisplatin as maintenance therapy?

Does identification of histologic subtype require testing in addition to that carried out in routine clinical practice?

Are the outcomes listed appropriate?

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

Where do you consider nintedanib will fit into the existing NICE pathway, Respiratory conditions (2018)?

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 nintedanib 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 nintedanib 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 nintedanib 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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. Office for National Statistics Cancer registration statistics, England (2016). Accessed May 2018. Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/cancerregistrationstatisticsengland/2016
2. Cancer Research UK (2017) Mesothelioma incidence statistics. Accessed May 2018. Available at: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/mesothelioma/incidence

3. van Zandwijk N, Clarke C, Henderson D, et al. (2013) Guidelines for the diagnosis and treatment of malignant pleural mesothelioma. Journal of Thoracic Disease 5(6), E254–E307.
4. Meyerhoff RR, Yang CJ, Speicher PJ et al. (2015) Impact of mesothelioma histologic subtype on outcomes in the Surveillance, Epidemiology, and End Results database. Journal of Surgical Research 196(1), 23–32.
5. Woolhouse I, Bishop L, Darlison L et al. (2018) British Thoracic Society guideline for the investigation and management of malignant pleural mesothelioma. Thorax 73, Suppl. 1.