NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Nintedanib for treating progressive fibrosing interstitial lung disease

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nintedanib within its marketing authorisation for treating progressive fibrosing interstitial lung disease (PF-ILD).

Background

Interstitial lung disease (ILD) refers to inflammation and scarring of the lung tissue. ILD is associated with over 200 rare and heterogeneous conditions, including most commonly idiopathic pulmonary fibrosis (IPF), sarcoidosis, and extrinsic allergic alveolitis (EAA). Progressive fibrosing interstitial lung disease (PF-ILD) is a subtype of ILD with a similar natural history to IPF that includes worsening of respiratory symptoms, lung function, health-related quality of life and functional status; limited response to immunomodulatory therapies; and may lead to organ failure and early mortality.

The most common symptom of ILD is shortness of breath during physical activity. Other symptoms include non-productive cough, fatigue and chest pain. Some people with ILD may have no symptoms. As the disease progresses, lung function declines leading to reduced quality of life and shortened life expectancy.

The prevalence of PF-ILD is difficult to estimate as estimates are usually for specific conditions and/or grouped together. It is estimated that between 2,000 and 4,000 new patients are diagnosed with ILD in England each year with the majority having either sarcoidosis or IPF; it is not clear how many of these have PF-ILD[1]. The most common 3 ILDs (IFP, sarcoidosis, EAA) affect between 1,500 and 3,000 individuals in England each year[1].

Treatment for PF-ILD may depend on the underlying cause, where known. Currently, it is focused on relieving symptoms, preventing the disease getting worse, and detecting and treating any complications. NICE recommends pirfenidone and nintedanib as options for treating IPF in people with a forced vital capacity between 50% and 80% predicted (NICE Technology Appraisal 379 and NICE Technology Appraisal 504). While there are licensed therapies for IPF, there are currently no licensed therapies for other forms of PF-ILD. Some treatment options used in practice may include corticosteroids or methotrexate for sarcoidosis, as well as immunosuppressive agents such as azathioprine, mycophenolate and cyclophosphamide, or rituximab. NICE has produced an evidence summary on infliximab for sarcoidosis and rituximab for scleroderma (NICE evidence summary 2 and 7).

The technology

Nintedanib (brand name unknown, Boehringer Ingelheim) targets 3 growth factor receptors involved in pulmonary fibrosis. The mechanism of nintedanib is not fully understood but it is thought that by blocking the signalling pathways involved in fibrotic processes, nintedanib may reduce disease progression by slowing the decline of lung function. It is administered orally.

Nintedanib (Ofev) has a marketing authorisation for the treatment of idiopathic pulmonary fibrosis (IPF) but does not currently have marketing authorisation for PF-ILD. It has been studied in a clinical trial compared with placebo in adults with PF-ILD (people with idiopathic pulmonary fibrosis were excluded from the trial).

Intervention(s)	Nintedanib
Population(s)	People with progressive fibrosing interstitial lung disease (excluding idiopathic progressive fibrosis)
Comparators	Established clinical management without nintedanib including, but not limited to: • immunosuppressants (such as azathioprine, cyclophosphamide, mycophenolate; do not currently have a marketing authorisation in the UK for this indication) • corticosteroids (do not have currently have a marketing authorisation in the UK for this indication) • infliximab (does not have currently have a marketing authorisation in the UK for this indication) • rituximab (does not have currently have a marketing authorisation in the UK for this indication) • best supportive care.
Outcomes	The outcome measures to be considered include: • lung function • physical function • exacerbation rate • progression-free survival • mortality • 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 commercial arrangements for the intervention, comparator and subsequent treatment 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. The availability and cost of biosimilar products should be taken into account.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Nintedanib for treating idiopathic pulmonary fibrosis (2016). NICE Technology Appraisal 379. Pirfenidone for treating idiopathic pulmonary fibrosis (2018). NICE Technology Appraisal 504. Review date February 2021. Proposed technology appraisals: Nintedanib for treating systemic sclerosis associated with interstitial lung disease. Proposed NICE technology appraisal [ID1420]. Publication date to be confirmed. Related Guidelines: Idiopathic pulmonary fibrosis in adults: diagnosis and management (2013). NICE guideline 163. Updated May 2017. Related Quality Standards: Idiopathic pulmonary fibrosis (2015). NICE quality standard 79. Related NICE Pathways: Idiopathic pulmonary fibrosis (2018) NICE pathway. Other related NICE products:

	Pulmonary sarcoidosis: infliximab (2016) NICE evidence summary 2. Skin involvement in systemic sclerosis: Rituximab (2017). NICE evidence summary 7.
Related National Policy	NHS England (2017) Clinical Commissioning Policy: Rituximab for connective tissues disease associated with interstitial lung disease NHS England (2017) Interstitial Lung Disease (Adults) Service Specification The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) Manual for Prescribed Specialised services 2018/19. See Chapter 4, p. 27. Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4, 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

At what point in the treatment pathway will nintedanib be used in people with PF-ILD? Will it be considered for all people with PF-ILD or only some (i.e. those with clinically significant disease)?

What is the estimated prevalence of people with PF-ILD? What proportion of people with IPF and SSc-ILD will have PF-ILD?

Have all relevant comparators for nintedanib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for PF-ILD? Does the choice of treatment differ depending on the underlying cause of PF-ILD? If so, how does this differ for each underlying condition?

- Are infliximab and rituximab used in the NHS to treat PF-ILD?
- How should best supportive care be defined?

Are the outcomes listed appropriate? Are there any other outcomes that should be included?

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

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. NHS England (2018) Manual for Prescribed Specialised services 2018/19. Chapter 4, p. 27.

