Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nintedanib for treating progressive fibrosing interstitial lung disease excluding idiopathic pulmonary fibrosis

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nintedanib within its marketing authorisation for treating progressive fibrosing interstitial lung disease excluding idiopathic pulmonary fibrosis.

Background

Interstitial lung disease (ILD) is an overarching term used to describe a large group of many different and often rare disorders that cause inflammation or scarring (fibrosis) of the functional (parenchymal) lung tissue. Prognosis varies depending on the type of ILD.

In some other cases ILD is known to be caused by a specific condition or exposure, for example rheumatoid arthritis-ILD is caused by rheumatoid arthritis and hypersensitivity pneumonitis is caused by the repeated inhalation of a toxin or foreign substance that causes an immune response. In other cases, for example, idiopathic pulmonary fibrosis the underlying cause of the ILD is unknown.

A key feature of idiopathic pulmonary fibrosis is the presence of progressive fibrosis and a specific radiological pattern called 'usual interstitial pneumonia'[1]. Recently, any ILDs that appear to share common characteristics with or progress in a similar way to idiopathic pulmonary fibrosis, despite treatment for any known underlying cause, have been described as having a progressive-fibrosing phenotype. Some examples of types of ILD most likely to have a progressive-fibrosing phenotype are:

- idiopathic pulmonary fibrosis, idiopathic non-specific interstitial pneumonia and unclassifiable idiopathic interstitial pneumonias (all types of idiopathic interstitial pneumonia)
- interstitial pneumonia with autoimmune features and rheumatoid arthritis-ILD (both are types of autoimmune ILD)
- hypersensitivity pneumonitis
- sarcoidosis

The most common symptom of ILD is shortness of breath during physical activity. Other symptoms include non-productive cough, fatigue and chest

pain, anxiety and depression. 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 ILD is difficult to estimate as data are usually for specific underlying conditions. The most common types of ILD are idiopathic pulmonary fibrosis and sarcoidosis. Estimates based on general practice records suggest that there were 107,824 people living with in sarcoidosis the UK in 2013[2]. Up to 20% of patients diagnosed with sarcoidosis develop fibrotic lung disease[2,3].

Treatment for ILD may depend on the underlying cause. NICE recommends pirfenidone and nintedanib as options for treating idiopathic pulmonary fibrosis in people with a forced vital capacity between 50% and 80% predicted (NICE Technology Appraisal 379 and NICE Technology Appraisal 504). Current treatment for progressive fibrosing ILD that is not idiopathic is focused on relieving symptoms, preventing the disease getting worse, and detecting and treating any complications. Treatment options used in clinical practice may include corticosteroids 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 (NICE evidence summary 2).

The technology

Nintedanib (OFEV), 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), systemic sclerosis associated interstitial lung disease, and for other chronic fibrosing interstitial lung disease with a progressive phenotype.

Intervention(s)	Nintedanib
Population(s)	People with fibrosing interstitial lung disease that has progressed despite treatment (excluding idiopathic progressive fibrosis)

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Comparators	Established clinical management without nintedanib (may depend on underlying cause of ILD) 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:
	• measures of disease progression such as:
	  ○ lung function
	  ○ physical function
	  ○ exacerbation rate
	  ○ lung transplantation
	• 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	If the evidence allows subgroup analyses by ILD type will be considered. 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. Review date 2021. Pirfenidone for treating idiopathic pulmonary fibrosis (2018). NICE Technology Appraisal 504. Review date 2021. Proposed technology appraisals: Nintedanib for treating systemic sclerosis associated with interstitial lung disease. Proposed NICE technology appraisal [ID1420]. Appraisal suspended. 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.
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)

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	Service Specification The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS 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

References

1. Cottin V, Hirani NA, Hotchkin DL, et al. Presentation, diagnosis and clinical course of the spectrum of progressive-fibrosing interstitial lung diseases. Eur Respir Rev 2018; 27: 180076 [https://doi.org/10.1183/16000617.0076-2018].

2. Lung disease in the UK – big picture statistics. British Lung Foundation Accessed November 2019

3. Olson AL, Gifford AH, Inase N, et al. The epidemiology of idiopathic pulmonary fibrosis and interstitial lung diseases at risk of a progressive-fibrosing phenotype. Eur Respir Rev 2018; 27: 180077 [https://doi.org/10.1183/16000617.0077-2018].