NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Nintedanib for treating interstitial lung disease caused by systemic sclerosis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nintedanib within its marketing authorisation for treating interstitial lung disease caused by systemic sclerosis.

Background

Systemic sclerosis (SSc) is a complex condition in which the immune system attacks the connective tissue resulting in the body overproducing connective tissue. This causes scarring and thickening of tissue which interferes with the normal functioning of many organs, most notably the skin but also the lungs, blood vessels, heart, kidneys, gastrointestinal tract and the musculoskeletal system.

When SSc affects the lungs, people can develop inflammation and scarring of the lung tissue which is referred to as interstitial lung disease (ILD). In some people ILD develops very early and very rapidly but stabilises for several years whereas in others it may continue to progress. 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 systemic sclerosis is estimated at around 31 to 88 per million in the UK [1,2] , implying that there are between 1700 and 4800 people with SSc in England. ILD develops in up to 80% of people with SSc and ILD will be clinically significant in about a third of people.[1]

The aim of treatment for SSc is to relieve symptoms, prevent the disease getting worse, detect and treat any complications, and minimise the impact of disability through occupational therapy and physiotherapy. SSc-ILD is treated in a number of settings in the UK, including by rheumatologists and by lung specialists. There are currently no licensed therapies for SSc-ILD and few drugs have been assessed in clinical trials for this disease; treatment options used in clinical practice include immunosuppressive agents such as mycophenolate and cyclophosphamide, and corticosteroids.[1,3]

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 does not currently have marketing authorisation for SSc-ILD. It has been studied in a clinical trial compared with placebo in adults with SSc-ILD.

Intervention(s)	Nintedanib
Population(s)	People with interstitial lung disease caused by systemic sclerosis
Comparators	Established clinical management without nintedanib including, but not limited to, immunosuppressants (such as 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) and best supportive care.
Outcomes	The outcome measures to be considered include: • lung function • breathlessness • 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.
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: Tocilizumab for treating systemic sclerosis. Proposed NICE technology appraisal [ID1396]. 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: Scleroderma: oral mycophenolate (2014). NICE

	evidence summary for unlicensed or off-label medicine 32. 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 NHS England (2017) Manual for Prescribed Specialised Services 2017/18. https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf 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? Will it be considered for all patients with SSc-ILD or only those with clinically significant disease?

Have all relevant comparators for nintedanib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for SSc-ILD?

- Should any other treatments for systemic sclerosis be included?
- Is rituximab used in the NHS to treat SSc-ILD?
- Is autologous stem cell transplant used in the NHS to treat SSc-ILD?
- Are other immunosuppressants (for example, azathioprine) considered for this condition?
- How should best supportive care be defined?

Are the outcomes listed appropriate?

- Are there any other outcomes that should be included?
- Are skin-related outcomes relevant?

Is pulmonary arterial hypertension relevant in this appraisal?

- Would nintedenib be expected to affect the development or severity of pulmonary hypertension?
- Additionally, would people who have SSc-ILD and pulmonary hypertension be expected to have different costs or health outcomes to

others with SSc-ILD (that is, should this be considered as a separate subgroup)?

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?

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. BSR and BHPR guideline for the treatment of systemic sclerosis, Rheumatology (2016). Accessed: October 2018

2. Systemic sclerosis, Patient Info. Accessed: October 2018

3. Kowal-Bielecka O, Landewé R, Avouac J, et al. (2009) EULAR recommendations for the treatment of systemic sclerosis: a report from the EULAR Scleroderma Trials and Research group (EUSTAR). Annals of the Rheumatic Diseases 68:620–628.