NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Pirfenidone for treating idiopathic pulmonary fibrosis (review of TA282)

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pirfenidone within its marketing authorisation for treating idiopathic pulmonary fibrosis.

Background

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive lung disease in which scarring (fibrosis) occurs. The cause of IPF is unknown although it is thought to be related to an abnormal immune response. It is a difficult disease to diagnose and requires a multidisciplinary team. Most people with IPF experience symptoms of breathlessness, which may initially be only on exertion. Cough, with or without sputum, is a common symptom. Over time, these symptoms are associated with a decline in lung function, reduced quality of life and death.

The median survival for people with IPF in the UK is approximately 3 years from the time of diagnosis. About 20% of people with IPF survive for more than 5 years. The rate of disease progression can vary greatly. Prognosis is difficult to estimate at the time of diagnosis and may only become apparent after a period of careful follow-up.

The incidence of IPF is approximately 8 to 9 per 100,000 person-years, which equates to more than 5000 new diagnoses each year in the UK. The incidence is higher in men than women, and increases with age (median age of presentation is 70 years). IPF co-exists with chronic obstructive pulmonary disease in around 8-15% of people.

The aim of treatment is to manage the symptoms and slow progression. NICE clinical guideline 163 on the diagnosis and management of suspected idiopathic pulmonary fibrosis recommends that best supportive care (including symptom relief, management of co-morbidities, withdrawal of therapies suspected to be ineffective or causing harm and end of life care) should be offered to people from diagnosis and be tailored according to disease severity, rate of progression and the person's preference. If pharmacological treatment is considered appropriate, the guideline recommends use of pirfenidone if a person's forced vital capacity (FVC) is between 50% and 80% of their expected value in line with recommendations in NICE technology appraisal guidance 282. Treatment with pirfenidone should be discontinued if there is evidence of disease progression (a decline in per cent predicted FVC of 10% or more within any 12 month period). Lung transplantation is an option if there are no contraindications.

In NICE technology appraisal guidance on pirfenidone, the Committee discussed the definition of 'mild-to-moderate' idiopathic pulmonary fibrosis (which is the indication covered by pirfenidone's UK marketing authorisation). It was unclear how the population covered by the marketing authorisation related to the patient population in the clinical trials. The Committee heard from the clinical specialists that although there are no recognised criteria for defining these disease stages, it is widely accepted that severe idiopathic pulmonary fibrosis is defined as FVC less than 50% predicted and a diffusing capacity for carbon monoxide less than 35% predicted. Therefore mild-to-moderate idiopathic pulmonary fibrosis could be defined as FVC greater than or equal to 50% predicted, although the Committee had some reservations about the lack of an upper limit of per cent predicted FVC.

NICE technology appraisal guidance 282 was considered for review within 6 months of publication of the ASCEND study, which showed that people with a predicted FVC greater than 80% could potentially benefit from treatment with pirfenidone.

The technology

Pirfenidone (Esbriet, Roche) is an immunosuppressant that is thought to have anti-inflammatory and antifibrotic effects. Its mechanism of action is not fully understood but it is thought that pirfenidone exerts its effects by suppressing fibroblast proliferation, reducing the production of fibrosis-associated proteins and cytokines and attenuating the response to growth factors such as transforming growth factor-beta (TGF-β) and platelet-derived growth factor (PDGF).

Pirfenidone has a marketing authorisation in the UK for treating mild to moderate IPF in adults.

Intervention(s)	Pirfenidone
Population(s)	Adults with mild to moderate idiopathic pulmonary fibrosis
Comparators	• Best supportive care

Outcomes	The outcome measures to be considered include: • pulmonary function parameters • 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 patient access schemes for the intervention or comparator technologies should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 282, April 2013, 'Pirfenidone for treating idiopathic pulmonary fibrosis'. Technology Appraisal in preparation, 'Nintedanib for treating idiopathic pulmonary fibrosis [ID752]', Anticipated publication date: January 2016. Related Guidelines: Clinical Guideline No.163, July 2013, 'Idiopathic pulmonary fibrosis: The diagnosis and management of suspected idiopathic pulmonary fibrosis'. Review Proposal Date June 2015. Related Quality Standards: Quality Standard No. 79, January 2015, 'Idiopathic pulmonary fibrosis'. http://www.nice.org.uk/guidance/qs79

	Related NICE Pathways: NICE pathway: Idiopathic pulmonary fibrosis, Pathway created June 2013. http://pathways.nice.org.uk/pathways/idiopathic-pulmonary-fibrosis
Related National Policy	National Service Frameworks: Older People Department of Health, November 2013, 'NHS Outcomes Framework 2014-2015'.

Questions for consultation

Have all relevant comparators for pirfenidone been included in the scope? Which treatments are considered to be established clinical practice in the NHS for idiopathic pulmonary fibrosis? Should nintedanib (subject to NICE approval) be included as a comparator?'

Are there any subgroups of people in whom pirfenidone 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 pirfenidone is 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 pirfenidone 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 pirfenidone 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.