NICE National Institute for Health and Care Excellence

NICE guidance

Pirfenidone for treating idiopathic pulmonary fibrosis

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guidance replaces TA282.

1 Recommendations

1.1 Pirfenidone is recommended as an option for treating idiopathic pulmonary fibrosis in adults only if:

- the person has a forced vital capacity (FVC) between 50% and 80% predicted
- the company provides pirfenidone with the discount agreed in the patient access scheme and
- treatment is stopped if there is evidence of disease progression (an absolute decline of 10% or more in predicted FVC within any 12-month period).

1.2 This recommendation is not intended to affect treatment with pirfenidone that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

2 Information about pirfenidone

Description of the technology

2.1 Pirfenidone (Esbriet, Roche) is an oral immunosuppressant with anti-inflammatory and antifibrotic effects.

Marketing authorisation

2.2 Pirfenidone has a marketing authorisation in the UK for treating mild to moderate idiopathic pulmonary fibrosis in adults.

Adverse reactions

2.3 The summary of product characteristics states that the very common adverse reactions (affecting 1 in 10 or more people) associated with using pirfenidone are nausea, rash, diarrhoea, fatigue, dyspepsia, anorexia, headache and photosensitivity reactions. For full details of adverse reactions and contraindications, see the summary of product characteristics.

Recommended dose and schedule

2.4 The recommended dosage of pirfenidone is three 267-mg capsules 3 times daily (that is, a total of 2,403 mg per day).

Price

2.5 The list price of pirfenidone is £501.92 for 63 capsules (excluding VAT; British national formulary online, accessed May 2016). This equates to a daily cost of

£71.70. The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of pirfenidone, with the discount applied at the point of purchase or invoice. The level of discount is commercial in confidence. The Department of Health considered that the patient access scheme does not constitute an excessive administrative burden on the NHS.

3 Committee discussion

The appraisal committee considered evidence submitted by Roche Products and a review of this submission by the evidence review group. See the committee papers for full details of the evidence.

Review objectives

3.1 The appraisal committee reviewed existing and new data on the clinical and cost effectiveness of pirfenidone, having considered evidence on the nature of idiopathic pulmonary fibrosis and the value placed on the benefits of pirfenidone by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources. The committee recognised that this appraisal reviewed NICE's previous technology appraisal guidance on pirfenidone to take into account new evidence relating to people with a forced vital capacity (FVC) above 80% predicted and to consider removing the stopping rule, that is, to no longer stop pirfenidone after an absolute decline of 10% or more in predicted FVC within any 12-month period. The review considered the whole of pirfenidone's marketing authorisation.

Current practice

3.2 The committee discussed the treatments for idiopathic pulmonary fibrosis in current NHS practice. The committee heard the clinical experts explain that they offer treatment with pirfenidone or nintedanib to people with an FVC between 50% and 80% predicted; this reflects NICE's previous technology appraisal guidance on pirfenidone and nintedanib for treating idiopathic pulmonary fibrosis. The clinical experts noted that they would offer best supportive care to people with an FVC above 80% predicted because NICE does not recommend pirfenidone or nintedanib in this population. The committee noted comments received during consultation that clinicians would like to offer active treatments to people with an FVC above 80% predicted. The committee concluded that the current treatment options are nintedanib and pirfenidone for people with an FVC between 50% and 80% predicted, and best supportive care for those with an FVC

above 80% predicted.

3.3 The committee discussed the stopping rule included in NICE's previous technology appraisal guidance on pirfenidone and nintedanib, and how this is implemented in clinical practice. It heard from clinical experts that they follow this stopping rule, that is, stopping treatment if there is an absolute decline of 10% or more in predicted FVC within any 12-month period, and that they often confirm the drop in percent predicted FVC with repeat testing. The committee heard from the clinical experts during the committee meeting and from the comments received during consultation about the limitations of using percent predicted FVC to assess lung function in people with idiopathic pulmonary fibrosis. It heard that the disease course varies, both between patients and over time. It heard that there were periods of relative stability interspersed with acute exacerbations, and that acute exacerbations are associated with permanently reduced lung function and an increased risk of dying. The committee noted that the clinical experts could not suggest a better way of objectively defining treatment success or failure than using percent predicted FVC. It noted the limitations of FVC but understood that, in clinical practice, the wider patient characteristics would be taken into account in interpreting percent predicted FVC.

Comparators

3.4 The committee recalled that current NICE recommendations for treatment depend on percent predicted FVC, and discussed whether best supportive care or nintedanib were relevant comparators for pirfenidone. The committee was aware that nintedanib is recommended for a subgroup of the population, but recognised that the recommendation for nintedanib was based on the comparison of nintedanib with pirfenidone, rather than nintedanib with best supportive care. The committee therefore agreed it was more appropriate to compare pirfenidone with best supportive care and it did not consider the comparison with nintedanib further.

Clinical effectiveness

3.5 The committee considered the clinical evidence presented by the company. It noted that the evidence came from 4 randomised double-blind placebo-controlled phase III trials (CAPACITY 1, CAPACITY 2, ASCEND and SP3) and other observational data:

- The committee was aware that the results of SP3 and the CAPACITY trials were considered during NICE's previous technology appraisal of pirfenidone. It recognised that the new data presented by the company came from ASCEND, RECAP (an open label extension follow-up study of the CAPACITY trials) and observational data for best supportive care (the 'INOVA' registry).The committee noted that the primary end point in both ASCEND and the CAPACITY trials was the change in percent predicted FVC from baseline, and that this was after 52 weeks in ASCEND and after 72 weeks in CAPACITY 1 and 2.
- The committee was aware that the company and the evidence review group (ERG) included data from ASCEND in their network meta-analyses with data from CAPACITY 1, CAPACITY 2 and SP3. It concluded that the trials included in the ERG's meta-analysis were appropriate.

3.6 The committee noted that the inclusion criteria of the trials differed with respect to percent predicted FVC: the CAPACITY trials recruited patients with an FVC above 50% predicted and without an upper limit. ASCEND recruited patients with an FVC between 50% and 90% predicted, and the SP3 trial did not specify the range, but reported an average baseline FVC of 77% predicted. The committee understood that most of the data presented by the company (92% of patients in ASCEND and the CAPACITY trials) came from patients with an FVC up to 90% predicted. The committee concluded that the trial evidence was most generalisable to people with an FVC of up to 90% predicted.

3.7 The committee discussed whether the populations in the pirfenidone trials reflected people with idiopathic pulmonary fibrosis in current NHS practice. It understood that only 25% of patients across ASCEND and the CAPACITY trials had an FVC above 80% predicted, compared with 36% to 41% in UK practice (as a proportion of people with an FVC above 50% predicted; estimates are based on data from the British Thoracic Society idiopathic pulmonary fibrosis registry and

comments from the company at the committee meeting). The committee concluded that people with an FVC above 80% predicted were under-represented in the clinical trials.

3.8 The committee discussed the clinical effectiveness of pirfenidone. It was aware that in NICE's previous technology appraisal for pirfenidone the committee concluded that 'pirfenidone seemed to have a modest but measurable effect on slowing the decline in lung function'. The committee acknowledged that the company had provided new long-term and mature data in this appraisal, mainly relating to mortality, for patients with an FVC up to 90% predicted. The committee considered the results of the ERG's meta-analyses. It agreed that pirfenidone reduced disease progression compared with placebo. It also agreed that there was evidence that it may reduce mortality. It concluded that it had not seen anything to contradict the conclusion in NICE's previous technology appraisal. The committee concluded that pirfenidone is effective in people with an FVC between 50% and 90% predicted.

3.9 The committee discussed whether the effect of pirfenidone on slowing the decline in lung function may differ according to a person's baseline percent predicted FVC. It considered the evidence for people with an FVC above or below 80% predicted, noting that:

- There was a smaller estimate of treatment effect at week 52 in the FVC above 80% predicted subgroup than in the FVC 80% predicted or less subgroup in each trial (between subgroups, these difference were not statistically significant).
- In the CAPACITY 1 trial, the treatment effect at week 52 was no longer statistically significant when considering the FVC above 80% predicted group alone.
- The results of the treatment-by-subgroup interaction tests from the company's analysis of covariance (ANCOVA) showed that there was no statistically significant difference in results between people with an FVC above 80% predicted at baseline and people with an FVC of 80% predicted or less (the p value varied between 0.20 and 0.78 depending on the clinical trial).
- In an analysis using FVC data from only the CAPACITY trials (measured at

week 72), the company's treatment-by-subgroup interaction test showed that there was no statistically significant difference in results between the 3 pre-defined subgroups in CAPACITY: predicted FVC at baseline of more than 80%; between 70% and 80%; and lower than 70% (p=0.35). The committee was aware of the company's opinion that the analysis with 3 subgroups was not as robust as the ANCOVA method.

The committee observed that none of the studies were designed to determine the effectiveness of pirfenidone in people with FVC above 80% predicted, or to compare this group with those with an FVC between 50% and 80% predicted. The committee acknowledged the practical difficulties in designing studies to detect differences in outcomes between subgroups. The committee agreed to accept that pirfenidone has the same relative effectiveness in people with an FVC above 80% predicted and in people with an FVC of 80% predicted or less.

Evidence on the stopping rule

3.10 The committee discussed whether or not to keep the stopping rule (stopping pirfenidone after disease progression, defined by an absolute decline of 10% or more in predicted FVC within any 12-month period). It recalled that clinicians follow the rule in clinical practice (see section 3.3), however, it noted the consultation comments from professional groups that clinicians would like to continue treating people after disease progression because it may still be beneficial. The committee agreed that not all treatments are universally effective, and that stopping rules can improve the cost effectiveness of a technology by stopping treatment when it is no longer considered clinically effective.

3.11 The committee considered the company's post-hoc subgroup analyses of patients who continued pirfenidone after a decline in predicted FVC of 10% or more within any 12-month period. These data showed that fewer people in the pirfenidone group (1 patient out of 24) experienced a further 10% decline in predicted FVC compared with those in the placebo group (15 patients out of 60; p=0.032). The committee was concerned with the results of this analysis because:

- the sample size of 84 patients was small, meaning that decisions based on this subgroup are uncertain
- the analysis broke the randomisation of the clinical trials
- to test the hypothesis that people benefit from continuing pirfenidone treatment after disease progression, it would be more informative to compare people who do not stop pirfenidone after disease progression with people who do stop it after disease progression, rather than to compare people continuing pirfenidone after disease progression with people who had been randomised to placebo at baseline.

  The committee concluded that the company's evidence did not conclusively show that people continue to benefit from pirfenidone after disease progression. However, the committee recognised the comments from clinical experts that some patients may benefit after disease progression. It concluded it was appropriate to consider cost-effectiveness analyses with and without the stopping rule.

Cost effectiveness

3.12 The committee considered the company's partitioned survival model, which had 3 mutually exclusive health states: progression-free, progressed and dead. The company's model assumed that the effectiveness of pirfenidone relative to best supportive care was the same regardless of a person's baseline percent predicted FVC. The committee considered this to be appropriate based on the data currently available (see section 3.9). The committee heard from the ERG that the company's model did not capture the progressive nature of idiopathic pulmonary fibrosis. The committee noted that the company, in choosing the model structure, made several clinically implausible assumptions. For example:

- No relationship between time on treatment, time to disease progression (defined as a 10% decline in predicted FVC, a decline in 6-minute walking distance of 50 metres or more, or death) and mortality. The committee agreed that these were likely to be linked, so it was not appropriate to model them independently.

- Acute exacerbations were not explicitly connected to disease progression and mortality. Clinical experts advised that exacerbations had a substantial effect on quality of life and mortality. The committee agreed that the model may not fully represent the impact of idiopathic pulmonary fibrosis on patients.

  The committee had serious concerns about the company's model and understood that the ERG could address only some of the issues in its exploratory analyses. The committee noted that, in its response to the appraisal consultation document, the company did not provide new clinical evidence but did provide revised analyses with:

- New parametric survival curves for mortality (see section 3.13 for discussion about the survival curves).

- New assumptions around how long the benefits of treatment last (see section 3.14 for discussion about the time the benefits of treatment last).

- A new subgroup with an FVC between 50% and 90% predicted.

  In its response to consultation, the company suggested that it based its model on mortality because of the data available and, in its view, increasing complexity would not improve the fit to available data on costs and utilities. The committee acknowledged the limitations in the data and concluded that the model could be used for its decision-making.

3.13 The committee discussed how the company estimated the potential long-term mortality benefit with pirfenidone over a patient's lifetime by extrapolating from relatively short trials. It noted that the choice of mortality parametric curve was a key driver of the cost-effectiveness results, and that the company estimated long-term mortality based on data from ASCEND, CAPACITY 1 CAPACITY 2 and RECAP. The committee agreed that this was appropriate. It noted that the company had modelled mortality using the Weibull distribution, and that the ERG had used the Gompertz distribution.

- It heard from the ERG that, although the Weibull distribution fitted the observed data well, it predicted a lower probability of death for older people than in the general UK population; the ERG did not consider this to be

clinically plausible.

- The ERG considered that the Gompertz distribution also fitted the data well but provided more clinically plausible long-term estimates for mortality beyond the observed data.
- In its response to the appraisal consultation document, the company adjusted the annual probability of death by age distribution in the UK population to show that the Weibull distribution did not predict a lower probability of death until the age of around 90 years. The company suggested that registry data (that is, the INOVA registry of people with idiopathic pulmonary fibrosis on best supportive care in the United States) supported the estimates of mortality using the Weibull rather than Gompertz distribution.
- The ERG accepted that the adjustment addressed one of their concerns, but remained concerned that INOVA had a high proportion of censoring after 10 years (that is, people for whom there were no additional data).
- The ERG acknowledged that there was uncertainty associated with the Gompertz distribution because it did not fit the data as well as the Weibull distribution, and advised the committee that both curves were plausible.
- The committee agreed that the risk of death in people with idiopathic pulmonary fibrosis was likely to increase with length of time with the disease relative to the general population. With both the Gompertz and Weibull distributions, the risk of death increased with disease duration. The committee observed that, with the Weibull distribution, the risk of death for people with idiopathic pulmonary fibrosis increased more slowly than the risk of death over time in the general population. With the Gompertz distribution, the risk of death increased more rapidly with disease duration, above the risk of death over time in the general population. The committee agreed that the true risk of death of people with idiopathic pulmonary fibrosis might lie between the Weibull and Gompertz distributions, but closer to the Gompertz distribution.
- The committee also considered the company's new analysis that used a weighted parametric survival curve based on a statistical test of model fit (that is, the Akaike information criterion). The committee agreed with the ERG that it did not consider the approach credible because it included curves

(such as a log-logistic distribution) with limited clinical plausibility, and agreed that it was not appropriate.

On balance, the committee acknowledged the company's different opinion on the choice of parametric survival curve and agreed to take the Weibull and Gompertz curves into account in its decision-making. However, the committee concluded that it was more plausible to use the Gompertz distribution to estimate mortality.

3.14 The committee discussed the company's modelling assumption that the mortality benefit of pirfenidone compared with best supportive care remains constant over a person's lifetime. It appreciated that the randomised trials were too short (that is, either 52 or 72 weeks) to provide evidence to support this assumption. The committee also noted that, although follow-up data for pirfenidone were collected for over 8 years in RECAP, there was no best supportive care group in the study and so no long-term relative effectiveness could be estimated from the study. The committee was also aware that the model was very sensitive to the assumptions around duration of treatment benefit. It heard from 1 clinical expert that the treatment benefit of pirfenidone was likely to be constant over a person's lifetime. The committee did not agree that this was plausible, based on advice from the ERG that the trials showed a reduction in treatment effect over time for mortality. In its response to the appraisal consultation document, the company used data from INOVA to support its argument that the treatment effect lasts for at least 8 years. The company provided a Kaplan–Meier plot and log-cumulative hazard plot for mortality based on data from the trials and INOVA. The committee noted that the log-cumulative hazard plots for pirfenidone and best supportive care were not parallel after 5 years. It determined that, although there was some maintained treatment effect, it was not constant. The committee concluded that the evidence did not justify assuming a constant mortality benefit for 8 years. It further concluded that it was reasonable to assume a constant benefit up to 5 years.

3.15 The committee discussed the population in the model. It recognised that the model was based on the pirfenidone clinical trials and therefore included fewer people with an FVC above 80% predicted than are seen in NHS clinical practice (see section 3.7). The committee considered whether the incremental cost-effectiveness ratios (ICERs) would be affected if the modelled population

included a higher proportion of people with an FVC above 80% predicted, to better reflect NHS practice. It understood from the analyses presented that there was a consistent trend for higher ICERs in the population with an FVC above 80% predicted than in the population with an FVC between 50% and 80% predicted. For example, when assuming a 5-year treatment effect and including the stopping rule, the ICER for pirfenidone compared with best supportive care was between:

- £24,933 (Weibull) and £27,780 (Gompertz) per quality-adjusted life year (QALY) gained for people with an FVC between 50% and 80% predicted
- £32,643 (Weibull) and £38,687 (Gompertz) per QALY gained for people with an FVC above 80% predicted.

Therefore, the committee expected that the ICERs for the full population (specified in the marketing authorisation for pirfenidone) would be higher if the model included a higher proportion of people with an FVC above 80% predicted. The committee concluded that the current cost-effectiveness estimates for the full population are likely to be underestimated.

3.16 The committee discussed whether the company's model appropriately incorporated the treatment stopping rule. The ERG explained that ICERs including the stopping rule for pirfenidone would likely be biased in favour of pirfenidone when compared with best supportive care. This was because, in the model, the stopping rule reduced pirfenidone costs without affecting treatment outcomes. The committee had concluded that analyses including a stopping rule for pirfenidone would underestimate the ICER because of the model structure. However, at its third meeting, the committee heard from the company that analyses including a stopping rule would overestimate the ICERs in scenarios where the mortality benefit of pirfenidone is not constant over a person's lifetime. The company had not submitted any evidence to support its statement and therefore the committee could not draw a firm conclusion about whether reducing the duration of treatment benefit under- or overestimated the ICERs with a stopping rule. The committee concluded that all ICERs including the stopping rule for pirfenidone were associated with uncertainty.

Cost-effectiveness results and conclusions

3.17 The committee considered the cost effectiveness of pirfenidone compared with best supportive care. The committee noted that, for the population specified in the marketing authorisation (people with 'mild to moderate' idiopathic pulmonary fibrosis, that is, people with an FVC above 50% predicted), the ICER (including the stopping rule) that most closely matched the committee's preferred assumptions was between £25,706 (Weibull) and £28,870 (Gompertz) per QALY gained when assuming a 5-year treatment effect. The committee agreed that the estimate using the Gompertz survival curve was more plausible (see section 3.13). The committee then discussed the cost-effectiveness estimates for the group with an FVC between 50% and 90% predicted, because most of the data presented by the company was from this group (see section 3.6), noting that the ICERs were similar to those for the full population.

3.18 The committee recognised that, when above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources must take account of the degree of certainty around the ICER, the innovative nature of the technology and whether its benefits have been adequately captured in the model. The committee recalled that all of the ICERs were uncertain, noting that:

- The modelled population did not include as many people with an FVC above 80% predicted as expected in NHS practice (see section 3.7 and section 3.15), and accounting for this may increase the ICER.
- The impact of the stopping rule on the ICER was uncertain (see section 3.16).
- There was still uncertainty about how long the survival benefit of pirfenidone would last; it could be less than 5 years (see section 3.14). The committee understood that the model was sensitive to this assumption, noting that the ICERs increased substantially, to around £58,000 per QALY gained, when assuming a 2-year treatment effect (including the stopping rule).

  The committee noted the company's suggestion that pirfenidone is associated with health-related benefits that cannot be adequately captured in the QALY calculation. These benefits include: a reduction in breathlessness; improved patient choice based on a different adverse event

profile; improved NHS capacity by reducing inpatient stays attributed to acute exacerbations; and the effect on people of working age. The committee acknowledged that, although these aspects were important to people with idiopathic pulmonary fibrosis, it did not consider that any sizeable health-related benefits had been excluded from the economic model. Because of this, and the uncertainties in the ICERs, the committee concluded that pirfenidone could not be considered a cost-effective use of NHS resources for adults with mild to moderate idiopathic pulmonary fibrosis. It was aware that removing the stopping rule increased the ICERs and therefore did not consider estimates without the stopping rule for this population.

3.19 The committee then discussed whether there was a subgroup for whom pirfenidone could be recommended. The committee was aware that pirfenidone was associated with a lower ICER in populations with a lower FVC (see section 3.15). It recalled that treatment decisions based on percent predicted FVC are currently implemented in clinical practice (see section 3.2). The committee was aware that, in NICE's previous technology appraisal guidance, pirfenidone was regarded as cost effective for people with an FVC between 50% and 80% predicted if the company provided pirfenidone with the discount agreed in the patient access scheme. It noted that the company had presented analyses for this group. The ICER (including the stopping rule) that most closely matched the committee's preferred assumptions for pirfenidone compared with best supportive care was between £24,933 (Weibull) and £27,780 (Gompertz) per QALY gained when assuming a 5-year treatment effect. The committee agreed that these ICERs were also subject to uncertainty relating to the stopping rule and duration of survival benefit, and recalled its conclusion that no sizeable health-related benefits had been excluded from the economic model (see section 3.18). However, the committee understood that pirfenidone was considered a reasonably innovative treatment at the time of the previous appraisal because it was the first drug to improve outcomes in idiopathic pulmonary fibrosis without the long-term side effects of immunosuppressants. It agreed that it had not seen any clinical evidence contradictory to that considered in NICE's previous technology appraisal on pirfenidone (see section 3.8), and therefore it was not minded to change this recommendation and withdraw an existing treatment option for people with moderate disease, despite the relatively high ICERs. The committee concluded that the recommendations in NICE's

previous technology appraisal guidance on pirfenidone remained appropriate for people with idiopathic pulmonary fibrosis with an FVC between 50% and 80% predicted.

3.20 The committee considered the cost effectiveness of removing the requirement to stop treatment if a person's predicted FVC drops by an absolute value of 10% in the population with an FVC between 50% and 80% predicted. The committee was aware that removing the stopping rule increased the ICERs. Having concluded that the ICER for pirfenidone in this group was high, and associated with uncertainty, when a stopping rule is included (see section 3.19), the committee concluded that pirfenidone could not be considered cost effective without the stopping rule.

Potential equality issues

3.21 The committee noted the potential equality issue raised by consultees that restricting treatment based on percent predicted FVC could discriminate against:

- minority ethnic groups, particularly people of south Asian family origin
- disabled people who have difficulty standing straight because FVC is expressed as a percentage of the predicted normal value for a person of the same height
- older people because the reference tables are derived from populations under the age of 70 years, but the average age of people with idiopathic pulmonary fibrosis is 72 years.

The committee discussed these issues with the clinical experts, noting that:

- The Global Lung Initiative has introduced equations to predict FVC values in minority ethnic groups and, when these equations were used, FVC values for these groups were comparable to the FVC values of people in clinical trials. Thus, when using the newer equations, people would not be denied treatment because of their ethnicity.
- For people who cannot stand straight, their armspan (which estimates their

height) can be used to calculate percent predicted FVC. Thus, when using this measure people would not be denied treatment because of their disability.

- According to clinical experts, it is difficult to compare the predicted FVC values of older people with the FVC values of people in clinical trials because older people show a wide range of predicted FVC.

  The committee recognised the limitations of FVC but understood that, in clinical practice, wider patient characteristics would be taken into account when interpreting percent predicted FVC. It concluded that its recommendations did not discriminate against any groups of people protected by the Equality Act.

The Pharmaceutical Price Regulation Scheme

3.22 The committee was aware of NICE's position statement on the Pharmaceutical Price Regulation Scheme (PPRS) 2014 and, in particular, the PPRS payment mechanism. It accepted the conclusion 'that the 2014 PPRS payment mechanism should not, as a matter of course, be regarded as a relevant consideration in its assessment of the cost effectiveness of branded medicines'. The committee heard nothing to suggest that there is any basis for taking a different view about the relevance of the PPRS to this appraisal. It therefore concluded that the PPRS payment mechanism was not relevant in considering the cost effectiveness of the technology in this appraisal.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has idiopathic pulmonary fibrosis and the healthcare professional responsible for their care thinks that pirfenidone is the right treatment, it should be available for use, in line with NICE's recommendations.

4.4 The Department of Health and Roche Products have agreed that pirfenidone will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to global.pas@roche.com.

5 Appraisal committee members, guideline representatives and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee B.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Sophie Cooper
Technical Lead

Rosie Lovett, Jasdeep Hayre
Technical Advisers

Jeremy Powell
Project Manager

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