ACETYLCYSTEINE in idiopathic pulmonary fibrosis

The Pan Mersey Area Prescribing Committee does not recommend the prescribing of oral acetylcysteine in idiopathic pulmonary fibrosis.

One randomised-controlled study\(^\text{(1)}\) of the combination of N-acetylcysteine (oral acetylcysteine), prednisolone and azathioprine compared to prednisone and azathioprine, found the addition of acetylcysteine delayed the deterioration of laboratory measures of lung function in idiopathic pulmonary fibrosis (IPF) but the difference between the two groups was modest and probably of little clinical significance and was not translated into improved breathlessness or survival. An interim analysis of a second randomised trial\(^\text{(2)}\) of this combination revealed that patients in the combination-therapy group, as compared with the placebo group, had an increased rate of death and hospitalization and as a result this combination is no longer recommended. The acetylcysteine versus placebo arm was continued but found no significant benefit on the primary outcome of Forced Vital Capacity or on death rate\(^\text{(6)}\).

There is no conclusive evidence supporting the use of any medication to increase the survival of people with IPF and treatment consists of best supportive care\(^\text{(3)}\). Pirfenidone is recommended by [NICE TA504 Idiopathic pulmonary fibrosis - pirfenidone](https://www.nice.org.uk/guidance/ta504) in patients fitting defined criteria as it has been shown to have beneficial effects on measures of lung function\(^\text{(5)}\). [NICE CG163 Idiopathic pulmonary fibrosis](https://www.nice.org.uk/guidance/cg163) states that patients should be advised that oral acetylcysteine is used for managing idiopathic pulmonary fibrosis, but its benefits are uncertain\(^\text{(3)}\).

Findings from the PANORAMA study\(^\text{(6)}\) suggest that the addition of acetylcysteine to pirfenidone does not substantially alter the tolerability profile of pirfenidone and is unlikely to be beneficial in patients with IPF.

Existing patients should be reviewed by the specialist responsible for care of their IPF and where appropriate therapy discontinued. In individual cases, patients currently receiving therapy with acetylcysteine that is not recommended according to this prescribing policy statement should be able to continue their treatment, with prescribing of acetylcysteine retained by the specialist, until they and their clinician consider it appropriate to stop.

Oral acetylcysteine is now licensed in the UK as a respiratory mucolytic and not for IPF specifically.

**Note:** Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.
# ACETYLCYSTEINE in idiopathic pulmonary fibrosis

## EFFECTIVENESS

In a randomised, double-blind trial, acetylcysteine was administered in combination with prednisone and azathioprine\(^1\). Compared to prednisone and azathioprine alone, acetylcysteine delayed the deterioration of laboratory measures of lung function, such as forced vital capacity (FVC). The difference between the two groups was modest and probably of little clinical significance and was not translated into improved breathlessness or survival. In another randomised, double-blind, placebo-controlled trial\(^3\), the acetylcysteine-prednisolone-azathioprine combination led to an increased rate of death and hospitalization. The acetylcysteine-alone versus placebo arm of the study found no significant benefit on the primary outcome of Forced Vital Capacity or on death rates\(^4\).

## SAFETY

In a randomised, double-blind trial\(^1\), there was no difference in the number of patients reporting adverse events (90% with acetylcysteine and 89% with standard therapy). Most adverse events involved the respiratory tract and were seen in similar numbers of patients in both groups. Only bone marrow toxicity showed a statistically significant difference: 4% with acetylcysteine and 13% on standard therapy (P=0.03) suggesting a possible protective effect of acetylcysteine to the myelotoxicity of azathioprine. Only 70% of patients who took study medication completed the study, so the results have to be interpreted with caution. Although there was little difference in adverse events between the two groups, long-term or rare adverse events are unknown. In a second randomized, trial\(^2\), acetylcysteine-prednisolone-azathioprine combination therapy led to an increased rate of death and hospitalization compared to placebo.

## COST

The Drug Tariff price for acetylcysteine effervescent 600mg tablets is £89.50 per month at a dose of 600mg daily. (Doses of 600mg three times daily have been used in studies in patients with IPF). Annual expenditure on acetylcysteine across the Pan-Mersey area is £13,000. This may include other indications.

## PATIENT FACTORS

No patient groups require dose adjustment or monitoring.

## PRESCRIBING INFORMATION

Prescribing acetylcysteine for IPF is not recommended due to evidence of a lack of benefit. Acetylcysteine is licensed in the UK as a respiratory mucolytic at a maximum dose of 600mg daily and there is a Pan Mersey Grey statement for this indication.

## IMPLEMENTATION NOTES

Existing patients should be reviewed by the specialist responsible for care of their IPF and therapy discontinued where appropriate.

## REFERENCES

5. NICE TA504 Idiopathic pulmonary fibrosis - pirfenidone: guidance February 2018