N-acetylcysteine (NAC)
Shared care guidelines

Introduction

Idiopathic pulmonary fibrosis (IPF) is associated with a median survival of approximately three years from the time of diagnosis. The disease is characterised by increasing breathlessness and cough, with progressive decline in lung function. Most patients with IPF die in respiratory failure.

Pharmacological treatment of IPF is limited by the lack of trials demonstrating clinical effectiveness in terms of mortality or morbidity. However N-acetylcysteine (NAC) was rigorously scrutinised in a double blind, randomised, placebo controlled, multicentre trial (n=182) (Demedts et al, New England Journal of Medicine 2006, 353, 2229-42). Patients with IPF receiving prednisolone and azathioprine (as 'standard' treatment for IPF) were randomised to receive NAC (600mg three times a day) or placebo.

NAC was found to result in a significant reduction in the rate of decline of lung function at 12 months. NAC was not associated with any increase in adverse effects over those described in patients receiving placebo – the only significant difference observed was a lower rate of bone marrow toxicity in patients taking NAC than in patients receiving placebo.

More recently a randomised trial of acetylcysteine in Idiopathic Pulmonary Fibrosis was conducted by the Idiopathic Pulmonary Fibrosis Clinical Research Network (New England Journal of Medicine 2014; 370: 2093-2101). The trial (n=264) compared acetylcysteine with placebo in IPF patients with mild to moderate disease. Results concluded that acetylcysteine offered no significant benefit with respect to the preservation of FVC in patients with idiopathic pulmonary fibrosis with mild-to-moderate impairment in lung function. The trial excluded patients with more advanced disease.

NAC is significantly better tolerated than prednisolone or azathioprine.

NICE CG163 (June 2013) Idiopathic pulmonary fibrosis in adults: diagnosis and management says advise the patient that oral N-acetylcysteine is used for managing idiopathic pulmonary fibrosis, but its benefits are uncertain.

N-acetylcysteine is currently unlicensed for use in pulmonary fibrosis.

Indication:

Idiopathic Pulmonary Fibrosis (Cryprogenic Fibrosing Alveolitis)

Form:

Tablets, capsules, effervescent tablets.

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AUTHOR: Dr T Howes, Consultant Chest Physician, CHUFT & Dr M Sidhu, Consultant Chest Physician, CHUFT

Dosage and administration:

600mg three times a day orally.

Hospital Specialist Responsibilities:

- Diagnosis of IPF based on a timely and comprehensive assessment
- Initiation of prescription of N-acetylcysteine 600mg. Supplying the initial 28 days treatment
- Monitoring for response.
- Report adverse events to the Medicines and Healthcare Products Regulatory Agency (MHRA) https://yellowcard.mhra.gov.uk/
- Liaison with the general practitioner (GP) to establish that they are willing to share the patient's care when proven benefit has been established
- Outlining to GP when therapy may be stopped assuming no improvement is recognised in the patient's condition
- Evaluating ADRs raised by the GP and evaluating any concerns arising from physical checks and reviews undertaken by GP
- Advising GP on related issues such as drug interactions etc
- Refer to the formulary regarding choice of N-acetylcysteine for prescribing.
- Act promptly on any communication from GP colleagues requesting advice and support.

GP responsibilities:

- Submit letter of reply confirming acceptance.
- Monitoring the patient's overall health and well being
- Observing patient for evidence of ADRs or any abnormalities and discussing with secondary care clinician if necessary
- Prescription of N-acetylcysteine after achievement of a stable dose regime by secondary care
- Refer to the formulary regarding choice of N-acetylcysteine for prescribing
- Ensuring advice is sought from the secondary care clinician if there is any significant change in the patient's physical health status
- Reducing and stopping treatment in line with secondary care clinicians original request

Patient (and if appropriate, the carer) responsibilities:

- Report to the Secondary Care Specialist or GP if he or she does not have a clear understanding of the prescribed treatment.
- Take the N-acetylcysteine therapy in accordance with the prescribed instructions.
- Attend GP surgery/hospital for all required follow-up appointments.
- Share any concerns in relation to treatment with N-acetylcysteine.
- Report any adverse effects to the Secondary Care Specialist or GP whilst taking N-acetylcysteine therapy.

Adverse Effects, Precautions and Contra-Indications:

Hypersensitivity to N-acetylcysteine is described but is rare. Adverse effects are considered rare.

None of the adverse effects described in the clinical trial were significantly more common than found in the placebo group (Demedts et al, NEJM 2005, 353, 2229-42), and bone marrow toxicity was significantly less common in the NAC group.

Abdominal pain was more common in the NAC than in the placebo group (15% v 9%, ns) as was a rise in alkaline phosphatase (8% v 1%, ns).

Caution is advised in patients with asthma, liver cirrhosis and peptic ulcer disease. Patients should be advised to drink at least six - eight glasses of water per day in order to prevent cysteine renal stones which are rare but can occur.

Common Drug Interactions:

No known significant interactions.

Communication:

For any queries relating to this patient's treatment with NAC, please contact the patient's named specialist.

Contact Numbers for Advice and Support:

Consultants:

Colchester Hospital University NHS Foundation Trust (01206) 747474 (Switchboard)

- Dr Timothy Howes
- Dr Peter Hawkins
- Dr Samantha Cooper
- Dr Rekha Badiger
- Dr Misha Sidhu

CHUFT Pharmacy Department (01206) 742355

CHUFT Medicines Information Help Line: (01206) 742161

Section A (to be completed by Secondary Care Specialist):

Hospital Number:	
NHS No:	
Date:	
GP Courier No:	
GP Name:	

Name of patient:	
Date of Birth:	
Address:	

Dear GP

See attached clinic letter. Please can you sign and return (using the fax number on the clinic letter) to indicate you are in agreement with the Shared Care Guidelines.

Yours sincerely,

Section B (to be completed by General Practitioner):

The above patient has been accepted and I will continue prescribing N-acetylcysteine.

Accepting GP Name:	
Accepting GP Signature:	
Date:	

Practice Stamp:

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