Clinical Commissioning Policy Proposition:

Dornase alfa inhaled therapy for primary ciliary dyskinesia (all ages)

Reference: NHS England E03X05/01

DRAFT FOR CONSULTATION

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Plain Language Summary

The policy proposition aims to confirm NHS England's commissioning approach to dornase alfa in the treatment of patients with primary ciliary dyskinesia.

Primary ciliary dyskinesia (PCD) is an inherited and relatively rare condition that affects tiny, hair-like structures that line the airways called cilia.

If the cilium are not functioning properly, bacteria accumulates in the airways which can cause breathing problems, infections and other disorders that mainly affect the sinuses, ears, and lungs. If left untreated, primary ciliary dyskinesia can lead to irreversible lung damage. Significant medical input is required with regular out-patient review and hospitalisations for antibiotics and intense physiotherapy, including nebulised antibiotics and mucolytics. Occasionally, ventilatory support is necessary and in severe cases, surgical intervention such as lobectomy or transplantation may be required

Inhaled therapies are used to relieve tightness in airways and inflammation in the lungs, reduce the stickiness of mucus in the airways or treat serious infections in the lungs. Currently individual funding requests are received for the use of dornase alfa for primary ciliary dyskinesia particularly for patients who have not responded to conventional treatments, although it is off-label for this indication. There is clinical evidence that dornase alfa can be effective in preventing progressive lung function decline, further lung damage and respiratory failure in cystic fibrosis (CF). There is therefore clinical interest as to whether dornase alfa may be clinically effective in the treatment of primary ciliary dyskinesia as the symptoms also relate to a defect of mucociliary clearance in a similar way to CF. Dornase alfa is being requested for short term use (three to six months) to rescue and recover lung function decline in some patients or for use as part of a permanent therapy approach in others.

NHS England has concluded that there is not sufficient evidence to support a proposal for the routine commissioning of dornase alfa in the treatment of patients with primary ciliary dyskinesia.

1. Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to not routinely commission dornase alfa as second line treatment for selected patients with primary ciliary dyskinesia who have not responded to conventional treatments.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether dornase alfa will be routinely commissioned in the treatment of primary ciliary dyskinesia is planned to be made by NHS England by June 2016 following a recommendation from the Clinical Priorities Advisory Group.

2. The proposed intervention and clinical indication

Primary ciliary dyskinesia (PCD) is a relatively rare hereditary disorder characterised by chronic infection of the upper and lower airway. Approximately half of patients with PCD will have situs inverses, a congenital condition in which the major visceral organs are reversed. Male infertility is common.

The airway symptoms are caused by impaired mucociliary clearance which results in the accumulation of airway secretions, often containing bacteria and allergens, leading to inflammation and chronic infection. The impaired mucociliary clearance is a consequence of abnormal ciliary beat function. Without appropriate early treatment, progressive chronic lung disease and bronchiectasis develop, and mismanagement of hearing impairment is common. Bronchiectasis can occur in infancy demonstrating the need for early instigation of appropriate treatments. Once irreversible lung damage is established, significant medical input is required with regular hospitalisation for antibiotics, ventilator support with some cases requiring surgical intervention including lobectomy and lung transplantation.

Dornase alfa is a highly purified solution of recombinant human deoxyribonuclease (rhDNase), it reduces viscosity in the lungs and promotes improved clearance of secretions, and is an established inhaled therapy in cystic fibrosis (CF). Individual funding requests are being received for the use of dornase alfa for PCD although its use is off-label for this indication. It is being requested for use in patients who have not responded to conventional treatments with the aim of preventing progressive lung function decline, further lung damage and respiratory failure. Dornase alfa is being requested for short term use (three to six months) to rescue and recover lung function decline in some patients or for use as part of a permanent therapy approach in others.

3. Definitions

Primary ciliary dyskinesia (PCD) is a genetic disorder characterised by ultra-structural defects of the cilia. This leads to abnormal function of the cilia in different organs, including the lungs. PCD is an autosomal-recessive disease. The main presentation of PCD includes chronic airway infection, inflammation, recurrent pneumonia, bronchiectasis and sinusitis. If untreated, it can lead to irreversible damage of the lung.

Dornase alfa is a highly purified solution of recombinant human deoxyribonuclease (rhDNase), it reduces viscosity in the lungs and promotes improved clearance of secretions. The recommended dose for use in most people with CF is 2.5 mg (in one single-use ampoule) inhaled once daily using a recommended nebulizer; however, some individuals may benefit from twice-daily inhalation. Dornase alfa is an established therapy in CF and is used in conjunction with other standard CF therapies.

4. Aim and objectives

This policy proposition aims to define whether there is sufficient evidence to support the routine commissioning of dornase alfa as part of the treatment pathway for patients with primary ciliary dyskinesia (PCD).

The objective is to ensure evidence based commissioning with the aim of improving outcomes for adults and children with PCD.

5. Epidemiology and needs assessment

Primary ciliary dyskinesia (PCD) is inherited as an autosomal recessive condition. The prevalence is unknown but is probably between 1:26,000 and 1:40,000 in the Caucasian population, with higher incidence in the Asian population. There are estimated to be 700 cases of primary ciliary dyskinesia in England, 350 adults and 350 children.

6. Evidence base

NHS England has concluded that there is not sufficient evidence to support a proposal for the routine commissioning of Dornase Alfa in the treatment of Primary Ciliary Dyskinesia.

There is only low level evidence (Grade 3 studies) on the use of dornase alfa (DNase) in primary ciliary dyskinesia. Three case reports (1995-2007) were identified in the literature search. These three case reports reported improvement in respiratory symptoms (respiratory rate, cough, sputum production), suggestive of improvement in quality of life. No studies used a quality of life index. No studies reported incidence of lung infections.

Two case studies measured pulmonary function at both baseline and post dornase alfa (one reported improvement 11 days post intervention, second study measured lung function 4 weeks post intervention).

No side effects were reported in the cases reports. No data was provided on cost effectiveness.

7. Documents which have informed this policy

NHS Clinical Commissioning Policy: Inhaled Therapy for Adults and Children with Cystic Fibrosis. Ref: NHS England A01/P/b
Primary Ciliary Dyskinesia (PCD) Diagnosis and Management Service (Children). Ref: NHS England E13/S(HSS)/g

8. Date of review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it is routinely or non-routinely commissioned (expected by June 2016)