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Clinical Commissioning Policy Proposition: Rituximab in Connective Tissue Disease associated Interstitial Lung Disease (adults)

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Clinical Commissioning Policy Proposition: Rituximab for Connective Tissue Disease associated Interstitial Lung Disease

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Equality Statement

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Plain Language Summary

The policy proposition aims to confirm NHS England's commissioning approach to Rituximab for Connective Tissue Disease with Interstitial Lung Disease (CTD-ILD).

Interstitial lung disease (scarring or inflammation around the alveoli, which are the air sacs in the lung) is a potentially fatal complication that develops in 10 – 35% of patients with specific connective tissue diseases (a group of conditions caused by over activity of the immune system).

Description of Intervention: Rituximab is a type of drug called a monoclonal antibody which works by damping down the body's immune system. It is available as a treatment for immune-mediated lung disease (that is interstitial lung disease occurring in individuals with an underlying connective tissue disease). However, evidence to support the use of rituximab in connective tissue associated interstitial lung disease is limited.

NHS England has concluded that there is not sufficient evidence to support a proposal for the routine commissioning of Rituximab for Connective Tissue Disease with Interstitial Lung Disease.

1. Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to not routinely commission Rituximab for Connective Tissue Disease with Interstitial Lung Disease.

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 Rituximab for Connective Tissue Disease with Interstitial Lung Disease will be routinely commissioned is planned to be made by NHS England by May 2016 following a recommendation from the Clinical Priorities Advisory Group.

2. The proposed intervention and clinical indication

Rituximab is a type of drug called a monoclonal antibody which works by damping down the body's immune system. It is available as a treatment for immune-mediated lung disease (that is interstitial lung disease occurring in individuals with an underlying connective tissue disease). However, evidence to support the use of rituximab in connective tissue associated interstitial lung disease is limited.

Patients treated at Specialist ILD centres (see NHS England website for further detail) with interstitial lung disease secondary to scleroderma, idiopathic inflammatory myositis, mixed connective tissue disease or lung-predominant undifferentiated connective tissue disease would, in specific circumstances, be treated with Rituximab.

All patients treated at specialist ILD centres would be monitored for indicators of lung function (forced vital capacity and total lung diffusion for carbon monoxide), quality of life (with specific questionnaires) and overall disease activity (with clinical examination and blood tests).

3. Definitions

Rituximab is a chimeric monoclonal anti CD-20 antibody.

Connective tissue disease associated interstitial lung disease is inflammation and/or fibrosis of the lung occurring in the context of immune-mediated systemic disease. For the purposes of this policy proposition CTD-ILD patients being considered are

those with ILD secondary to;

1) Systemic sclerosis OR
2) Idiopathic inflammatory myositis (dermatomyositis or polymyositis) OR
3) Mixed or overlap connective tissue disease OR
4) Lung-dominant undifferentiated connective tissue disease

4. Aim and objectives

This policy proposition aims to ensure equitable and cost-effective use of rituximab as a treatment for patients with connective tissue disease associated interstitial lung disease.

5. Epidemiology and needs assessment

The precise numbers of individuals with CTD-ILD has not been well defined. Of the conditions covered by this policy document the best researched is scleroderma. Scleroderma has an estimated annual incidence of 19 per 1 000 000 population. Only 25 – 30% of patients with scleroderma develop clinically significant ILD. It can be estimated that in England there will be 250 new cases of Scleroderma related ILD per year. The majority of these cases will be controlled with conventional oral immunosuppressant therapy. Less than one in five (approximately 50 patients per year) will have ILD resistant to conventional treatment thus requiring rituximab therapy. The remaining CTD-ILDs have a combined incidence that is approximately equal to that of scleroderma associated ILD. (the estimated incidence of idiopathic inflammatory myositis is 2 – 8 per million population with up to a third having ILD; the incidence of MCTD is 2 – 5 per million with between 10 – 35% having ILD. Lung dominant undifferentiated connective tissue disease is a very rare condition for which an incidence has not previously been calculated).

Based on available epidemiological evidence, existing specialist centre experience and previous individual funding requests it can be estimated that rituximab will be required to treat between 80 – 120 patients in England per year.

6. Evidence base

Rituximab is licensed for the treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia. Rheumatoid arthritis and granulomatous vasculitis. It is not licensed for CTD-ILD but has been shown to have efficacy as a treatment for this condition. The evidence base for rituximab in CTD-ILD is limited to small case series

and retrospective cohort studies. In most of these studies rituximab has been described as rescue therapy for individuals with disease progressing despite conventional treatment. These are low quality sources of evidence. To address this issue of low quality evidence the Efficacy and Mechanism Evaluation (EME) Programme, funded and managed by the National Institute for Health Research (NIHR) on behalf of the MRC-NIHR partnership, has recently provided funding for a UK-based randomized controlled trial of rituximab compared to cyclophosphamide in CTD-ILD (the RECITAL study NCT01862926).

The evidence for existing standard therapy in CTD-ILD is also limited. To date there have been two randomized controlled trials of cyclophosphamide compared to placebo in scleroderma-related ILD. The first of these showed a marginal benefit in terms of change of the primary end-point (forced vital capacity) over 12 months.

There are no published analyses of cost effectiveness or impact on health care utilization.

In summary the evidence, as it exists, suggests that;

a) In patients with scleroderma refractory to other treatments, including cyclophosphamide, rituximab is associated with a small but clinically meaningful improvement in lung function 6 and 12 months following therapy.
b) The safety of rituximab has been established across a broad range of disease indications. Frequent side effects include, infusion reactions and increased frequency of infections
c) Impact on quality of life has not been assessed (but is being measured as a key secondary outcome in the RECITAL study)

Cost effectiveness has not been assessed (but is being evaluated as part of the RECITAL study).

12. Documents which have informed this policy

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2. Hoyles RK, Ellis RW, Wellsbury J, et al. A multicenter, prospective, randomized, double-blind, placebo-controlled trial of corticosteroids and intravenous cyclophosphamide followed by oral azathioprine for the treatment of pulmonary fibrosis in scleroderma. Arthritis and rheumatism 2006;54:3962-70.
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in scleroderma lung disease. N Engl J Med 2006;354:2655-66.
4. Perosa F, Prete M, Racanelli V, Dammacco F. CD20-depleting therapy in autoimmune diseases: from basic research to the clinic. J Intern Med 2010;267:260-77
5. Sem M, Molberg O, Lund MB, Gran JT. Rituximab treatment of the anti-synthetase syndrome: a retrospective case series. Rheumatology (Oxford) 2009;48:968-71.
6. Daoussis D, Liossis SN, Tsamandas AC, et al. Is there a role for B-cell depletion as therapy for scleroderma? A case report and review of the literature. Semin Arthritis Rheum 2010;40:127-36.
7. Daoussis D, Liossis SN, Tsamandas AC, et al. Experience with rituximab in scleroderma: results from a 1-year, proof-of-principle study. Rheumatology (Oxford) 2010;49:271-80.
8. Keir GJ, Maher TM, Hansell DM, et al. Severe interstitial lung disease in connective tissue disease: Rituximab as rescue therapy. Eur Respir J 2012; 40:641-8.
9. Maher TM, Denton C et al A randomized, double blind controlled trial comparing Rituximab against intravenous Cyclophosphamide in Connective Tissue Disease (CTD) associated Interstitial Lung Disease (ILD) – study protocol. Available at http://clinicaltrials.gov/show/NCT018629266
10. Keir G, Maher TM, Ming D, Abdullah R, de Lauretis A, Hansell D, Nicholson A, Wells AU, Renzoni E. Rituximab in severe treatment refractory interstitial lung disease. Respirology 2013 (in Press)

13. 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 May 2016).