

**Clinical
Commissioning
Policy: Rituximab for
the treatment of
idiopathic
membranous
nephropathy in adults**

Reference: NHS England: 16047/P



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Medical	Operations and Information	Specialised Commissioning
Nursing	Trans. & Corp. Ops.	Commissioning Strategy
Finance		

Publications Gateway Reference: 05527s

Document Purpose	Policy
Document Name	Clinical Commissioning Policy 16047/P
Author	Specialised Commissioning Team
Publication Date	22 August 2016
Target Audience	CCG Clinical Leaders, Care Trust CEs, Foundation Trust CEs , Medical Directors, Directors of PH, Directors of Nursing, NHS England Regional Directors, NHS England Directors of Commissioning Operations, Directors of Finance, NHS Trust CEs

Additional Circulation List

Description Not for Routine Commissioning - NHS England will not routinely commission this specialised treatment in accordance with the criteria described in this policy.

Cross Reference This document is part of a suite of policies with Gateway Reference 05527s.

Superseded Docs
(if applicable) N/A

Action Required N/A

Timing / Deadlines
(if applicable) N/A

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Document Status

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Clinical Commissioning Policy: Rituximab for the treatment of idiopathic membranous nephropathy in adults

First published: August 2016

**Prepared by NHS England Specialised Services Clinical Reference Group for
Renal Dialysis**

Published by NHS England, in electronic format only.

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Policy Statement

NHS England will not routinely commission rituximab for the treatment of idiopathic membranous nephropathy in adults in accordance with the criteria outlined in this document. In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources. This policy document outlines the arrangements for funding of this treatment for the population in England.

Equality Statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

Plain Language Summary

About membranous nephropathy

Kidneys help filter waste products from the blood. Membranous nephropathy (MN) is a rare kidney disease where the immune system attacks certain cells in the kidney. It causes distressing symptoms including severe swelling of the legs and sometimes kidney failure. The worst affected patients eventually need kidney dialysis or a kidney transplant.

About the current treatment

There are established treatments for membranous nephropathy. However, none are 100% effective and all have side-effects. These treatments work by suppressing the

body's natural immune system. Their side-effects can be serious - such as severe infections where patients need to go into hospital.

About the new treatment

Rituximab is a medicine that doctors believe may work for some types of kidney disease - those that do not respond to the usual treatments. The NHS needs more information about how well rituximab works - compared to current treatments. It needs to know how safe it is and how cost-effective it is.

What we have decided

NHS England has carefully reviewed the evidence to treat membranous nephropathy with rituximab. We have concluded that there is not enough evidence to make the treatment available at this time.

1 Introduction

The aim of treatment of Membranous Nephropathy (MN) is both supportive and immunomodulatory. Supportive treatment is largely based on medications that block the renin angiotensin aldosterone system (RAAS blockade), using angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB). Diuretics are used to address oedema and statins to treat secondary dyslipidaemia. In contemporary observational cohort studies, where patients have received these supportive treatments, up to 70% of patients achieve partial or complete remission at 5 years. Because of this natural history, most UK physicians will adopt a supportive approach for 6-12 months after diagnosis. Clinical features that predict progressive Chronic Kidney Disease (CKD) include very heavy proteinuria (>8g/day, especially where this is prolonged), impaired kidney function at diagnosis or early in the course of the disease.

Where supportive therapy has failed to induce partial or complete remission of nephrotic syndrome (NS), immunomodulatory treatment is considered. There is evidence from randomized controlled trials (RCT) to support regimes based on alkylating agents (cyclophosphamide or chlorambucil) or calcineurin inhibitors (CNI - cyclosporine or tacrolimus), in combination with corticosteroids. Where there is impairment of kidney function, either at diagnosis or during supportive therapy, alkylating agents are the preferred therapy. 88-92% of patients with moderate disease will be dialysis free at 10 years if treated by an alkylating agent, compared to 32-47% of controls. Use of alkylating agents is associated with significant complication including leucopenia, infection, secondary infertility and a late malignancy risk. CNIs are also associated with significant complication including hypertension, progressive CKD, dyslipidaemia and a spectrum of metabolic abnormalities. Corticosteroids add to the morbidity associated with these regimes.

2 Definitions

MN is a rare disease with an incidence of 6-10 per million population per year. 25% of MN cases are secondary to malignancy, infection, medications or systemic

autoimmune disease (usually Systemic Lupus Erythematosus). In 75% of cases, no underlying associated pathology can be identified and the disease is termed idiopathic. This policy refers only to idiopathic cases of MN.

MN is the most common biopsy proven cause of NS in Caucasian adults. This policy refers only to idiopathic cases of MN. Membranous Nephropathy results in:

1. Debilitating symptoms and complications of NS, the latter of which include hospitalization with infection and venous thromboembolism.
2. There is a risk of progressive CKD, including established renal failure (ERF)

Rituximab is a chimeric monoclonal antibody that depletes human B Cells and is given by intravenous infusion in specialist centres. After therapy, peripheral B Cells are depleted for 6-12 months. It is licensed for the treatment of certain lymphomas / leukaemias, rheumatoid arthritis and antineutrophil cytoplasmic autoantibodies (ANCA) associated vasculitis. Rituximab is not licensed for the treatment of MN.

3 Aims and Objectives

Rituximab is a potentially promising, unlicensed therapy for a serious disease that is difficult to treat, but at the current time there is an insufficient quality and quantity of evidence to support routine commissioning by NHS England. Rituximab has been used off-license to treat MN but at the present time there are no published RCTs

The evidence considered the use of rituximab in membranous nephropathy in adults, particularly in patients with relapsing disease, with primary treatment failure or with adverse reactions or contra-indications to cyclophosphamide or calcineurin inhibitors.

4 Epidemiology and Needs Assessment

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5 Evidence Base

Rituximab has been used as immunomodulatory treatment in MN. The evidence for the use of MN is presented in a recent evidence review published by NHS England. There are no RCTs assessing the efficacy, safety and cost-effectiveness of Rituximab in MN. At the time of writing, there were 12 publications describing experience with Rituximab in MN, 10 case series (Scottish Intercollegiate Guidelines Network [SIGN] level 3 evidence) and 2 cohort studies (SIGN level 2 evidence). The majority of the studies are small (7-28 plus one case series of 100) and there is probably some overlap of included patients. The majority assessed Rituximab as a secondary therapy for MN. Most assessed a treatment regime of Rituximab 375mg/m², four doses at weekly intervals, but some used the alternative regime of two doses of 1000mg on day 1 and 15. The results can be summarised:

1. Efficacy
 - a. Reduction in proteinuria at 12 months 48-66%
 - b. Remission at 12 months 45-75%
 - c. Insufficient data to report on progression to ERF

6 Documents which have informed this Policy

None

7 Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

References

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