# Clinical Commissioning Policy
# Rituximab for idiopathic membranous nephropathy (Adults) (2012) [201005P]

## Publication date: October 2022 version number: V1.0

## Commissioning position

### Summary

Rituximab is recommended to be available as a routine commissioning treatment option for idiopathic membranous nephropathy within the criteria set out in this document.

### 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.

## Executive summary

## Plain language summary

### About Idiopathic Membranous Nephropathy (IMN)

Idiopathic membranous nephropathy (IMN) is a rare kidney disease where the immune system attacks certain cells in the kidneys. No cause can be found. One role of the kidneys is to filter waste products and excess fluids from the blood into the urine. In IMN the filtering membrane of the kidney has become damaged and cannot function properly. This results in protein from the bloodstream leaking into the urine and the body retaining excess fluids. The condition causes distressing symptoms including severe swelling of the legs and kidney failure. The worst affected patients eventually need kidney dialysis or a kidney transplant.

### About current treatment

There are established treatments for membranous nephropathy including alkylating agents and calcineurin inhibitors. However, none of these treatments are100% 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 drug that tries to stop the immune system attack on kidney cells, in order to preserve kidney function. It was originally used to treat lymphoma but is increasingly used for the treatment of diseases that affect the immune system such as IMN. It is given as an intravenous infusion.

## What we have decided

NHS England has carefully reviewed the evidence to treat idiopathic membranous nephropathy with rituximab. We have concluded that there is enough evidence to make the treatment available at this time.

## Committee discussion

The Clinical Priorities Advisory Group are asked to consider the evidence and the policy. See the committee papers (link) for full details of the evidence.

### The condition

Membranous nephropathy is a leading cause of nephrotic syndrome in adults. If an underlying aetiology is not identified, the disorder is termed IMN. IMN is characterized by an accumulation of immune deposits on the outer aspect of the glomerular basement membrane of the kidneys, causing a membrane-like thickening. Patients may present with symptoms of nephrotic syndrome. Diagnosis is made by a combination of antibody tests (anti-PLA2R or anti-THSD7A antibodies) and kidney biopsy which is carried out as a day case procedure or requires overnight stay.

### Current treatments

The current standard treatment for people with less severe IMN is a period of monitored supportive care. This includes treatment with renin-angiotensin system (RAS) blockade, blood pressure control and diuretics to control oedema as necessary. If partial or complete remission is not achieved within 6 months (or if high risk features such as declining function or significant complication of the nephrotic syndrome are seen), immunosuppressive therapy is then started alongside continuation of supportive care.

Patients presenting with severe disease (life-threatening fluid overload, rapidly declining kidney function, or thromboembolic disease) receive supportive care and immediate immunosuppression. The two leading immunosuppression therapies used are alkylating agents and calcineurin inhibitors (CNIs). Alkylating agents (cyclophosphamide or chlorambucil) are typically given alongside oral or intravenous corticosteroids, and CNIs (ciclosporin or tacrolimus) can be given as monotherapy or in combination with corticosteroids. The choice of immunosuppressive therapy is individualised to the patient and takes into consideration pre-existing co-morbidities.

Calcineurin inhibitors have a high relapse rate of 40% to 50% and are not effective for people with progressive kidney disease. Alkylating agents are effective with dialysis free survival at 10 years being over 90%. However, alkylating agents are associated with significant treatment toxicity with 60% of patients experiencing serious adverse events including hospitalisation for infection, cancer, infertility, leucopenia, osteoporosis and diabetes. If the person is intolerant or has contraindications to both calcineurin inhibitors and alkylating agents, they are offered continued treatment with supportive care.

### Proposed treatments

Rituximab is a chimeric monoclonal antibody that depletes human B Cells and is given as an intravenous infusion. B cells are central in the production of antibodies and therefore rituximab has been widely used for the treatment of autoimmune conditions, where antibodies play a key role in the development of disease. Rituximab is currently licensed for the treatment of certain

lymphomas and leukaemias, and autoimmune conditions such as rheumatoid arthritis and vasculitis.

In recent years, rituximab has surfaced as a potential treatment option and may be superior to CNI therapy in inducing a complete or partial remission of IMN. This policy proposal therefore suggests that Rituximab should be offered as the primary immunosuppressive therapy to patients with IMN who are intolerant or have contraindications to cytotoxic therapy.

## Epidemiology and needs assessment

Published data indicates an incidence of MN between 6-10 per million population per year (pmp/year). Recent audit data from two centres in England (Sheffield and Manchester) suggests the current incidence may be lower at 6.5-7 pmp/year. Of the patients with MN, 80% will have IMN and published data indicates that 50% of these patients will require immunosuppression.

## Evidence summary

An independent evidence review was conducted for the use of rituximab for idiopathic membranous nephropathy. NHS England has concluded that there is sufficient evidence to support a policy for the routine commissioning of this treatment for the indication. The evidence review which informs this commissioning position can be accessed here.

## Implementation Criteria

### Inclusion criteria

Primary immunosuppressive therapy with rituximab can be considered for patients who meet **All** of the following inclusion criteria:

1) Diagnosis of IMN. Diagnosis is made by a combination of antibody tests (anti-PLA2R or anti-THSD7A antibodies) and kidney biopsy.
2) Contraindications or intolerances to cytotoxic or steroid therapy OR inability to comply with the monitoring requirements for cytotoxic therapy.
3) eGFR >20mls/min/1.73m2.
4) Multi-disciplinary team (MDT) agreement, that rituximab at the specified frequency and dose is the most appropriate treatment option.

### Exclusion criteria

The Summary of Product Characteristics (SmPC) should be referred to when considering treating patients with rituximab, and patients should be excluded as appropriate according to this guidance. In particular the sections outlining contraindications, cautions, special warnings, precautions for use, and fertility, pregnancy, and lactation should be consulted.

### Starting criteria

Patients who meet all of the inclusion criteria and none of the exclusion criteria can start treatment with rituximab. The decision to commence treatment with rituximab must be made in conjunction with the patient and by a MDT. Individual providers will have policies for the prescription and administration of rituximab prescription, which should be followed.

### Stopping criteria

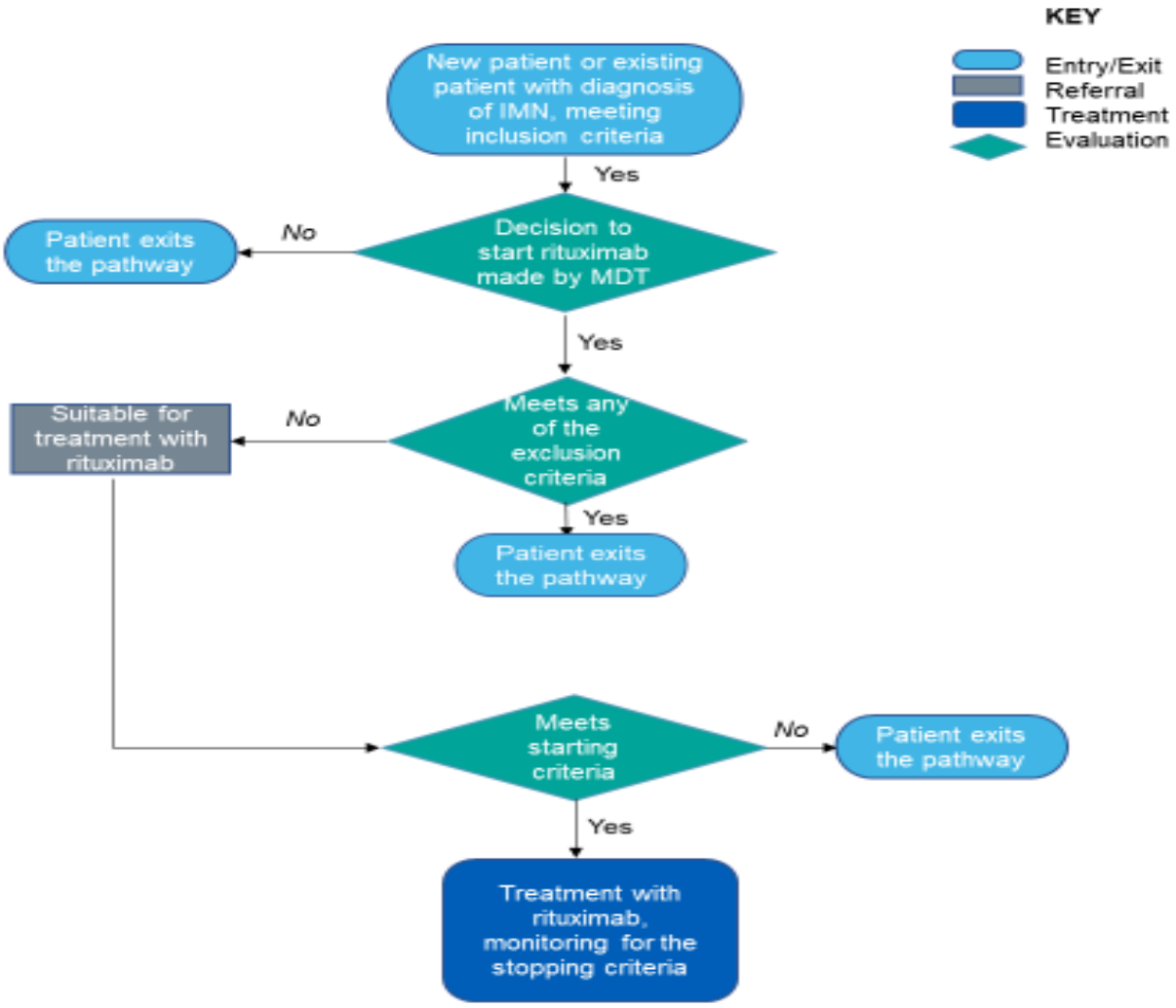
Treatment with rituximab should be stopped in any of the following circumstances:

- Adverse events (particularly infusion associated reactions) where harm exceeds the benefit at any time during treatment.
- The patient is unable to tolerate the side effects of treatment. Reference should be made to the SmPC, especially the criteria for permanent discontinuation of treatment with rituximab.
- Re-dosing will not be given to those patients who have no evidence of treatment response,

**Dose**

Two doses of 1000mg of intravenous rituximab at baseline, with further re-dosing after 4-6 months. Re-dosing will not be given to those patients who have no evidence of treatment response, specifically a reduction in proteinuria. The decision to re-dose should be made by the MDT. Rituximab will be given as a day case infusion.

## Patient pathway



### Governance arrangements

The use of rituximab in the treatment of IMN is off label, any provider organisation treating patients with this intervention will be required to assure themselves that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics committee (or similar) and NHS England may ask for assurance of this process.

Provider organisations will be expected to follow Trust policies for the safe prescribing and monitoring of off-label licensed medications including compliance with the Medicines and Healthcare products Regulatory Agency (MHRA) safety alerts.

Each provider organisation treating children with a medicine approved under this policy will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics Committee (or similar) and NHS England can ask for documented evidence that these processes are in place.

### Mechanism for funding

Rituximab is no longer listed on the NHS Payment Scheme Annex A (high-cost drugs), so use of this drug is in-tariff.

## Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

## Definitions

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| Antibody | A type of protein produced by the body's immune system, which combines with foreign material in the body (such as bacteria or viruses) to act against it. |
| Autoimmune | The body's immune system mistakes its own healthy tissues as foreign and attacks them. |
| Multidisciplinary team (MDT) | A group of health care workers who are members of different disciplines (this may include pharmacists, nurses, renal physicians, radiologists, histopathologists, physiotherapists, occupational therapists) each providing specific services to the patient. |
| IMN | Idiopathic membranous nephropathy (IMN) is a rare kidney disease where the immune system attacks certain cells in the kidneys. |

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| Rituximab | A monoclonal antibody that targets CD-20, which is a cell surface marker that is widely expressed on B-cells, leading to B cell depletion. |

## References

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