Rituximab (Truxima) in Renal Patients - Full Clinical Guideline

Reference no.: CG-REN/2019/002

Protocol for the Administration of Intravenous Rituximab in renal patients

1. Purpose

To ensure that patients are receiving Rituximab (Truxima) in a safe and effective manner.

Rituximab is a monoclonal antibody directed against the CD20 antigen on B cells.

2. Guidelines

Indications for treatment

Rituximab is indicated for the treatment of adult patients with ANCA-associated vasculitis. The commissioning criteria for the use of Rituximab in induction and maintenance therapy for adult patients with vasculitis is set out in this policy document: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/a13-ritux-anca-vascul.pdf

Rituximab has also been used, off license and uncommissioned, for a variety of glomerular diseases, including lupus nephritis, membranous nephropathy, minimal change disease and focal segmental glomerulosclerosis (FSGS). The use of Rituximab in these circumstances will need to be approved by the associate clinical director, service manager and the Drug and Therapeutic committee.

Prior to treatment

- Counselling of the patient regarding possible side effects of Rituximab therapy and provision of information sheet to take place before first treatment.
-

Contraindications

- Active severe infection
- Women who are breast feeding or pregnant (discontinue for 12 months in males and females before conception)
- History of hypersensitivity to the drug or any other components of the infusion or to murine proteins
- NYHA grade 4 congestive cardiac failure (CCF) or severe, uncontrolled cardiac disease

Treatment Schedule
Initiation of therapy should be by Consultant Nephrologist only.

Induction therapy is administered as two intravenous infusions of 1000mg at an interval of 2 weeks.

Maintenance Therapy
If indicated by disease activity, treatment can be repeated as maintenance therapy at a dose of 1000mg at a minimum of 6 monthly intervals providing immunoglobulin levels are satisfactory.

Rituximab should only be administered in an environment with immediately available full resuscitation facilities. A bed is required for all infusions. A doctor should be readily available in case of reaction.

Patients should be given 125mg IV methylprednisolone in 100mls normal saline infused over 30 minutes, 1 hour before being given Rituximab. Patients should also be pre-treated 1 hour before with paracetamol 1g orally and chlorphenamine (piriton) 10mg intravenously.

Patient should be started on pneumocystis pneumonia prophylaxis for at least 6 months after receiving Rituximab induction therapy.

For patients who are receiving maintenance therapy pneumocystis pneumonia prophylaxis should continue until at least 6 months after cessation of therapy.

Prior to initiating therapy please check the following has been done:

- Full blood count, ESR
- Initial profile and Liver function tests
- CRP
- urinalysis
- Chest x-ray within the past 6 months and TB screening as per guidelines
- Baseline immunoglobulins
- Hepatitis screen
- Pneumovax status (need to have at least 4 weeks before treatment if not had unless it is emergency)

Preparation
Rituximab 1000mg (in 350ml of sodium chloride 0.9%) is available as a ready-made bag which is supplied from the pharmacy department. Pre-infusion medications are given one hour before the rituximab which allows an hour for the infusion to be ordered and supplied. Other strengths are made in the pharmacy department and the infusion may be prepared in advance if the patient is able to be assessed the day before the infusion.

A Peripheral Catheter needs to be inserted on the day of the infusion. A 500ml bag of normal saline should be hanging by the patient's bed in case of hypotension.

Do not give other IV fluids or drugs through the same line. A filter is not required.

Before each administration

Measure and record: weight,
pulse,
blood pressure
temperature,
urinalysis

Collect*:* Full blood count, ESR
IP and LFT CRP

NB. If these have not been done within a week of the infusion these should be done as urgent samples and the results checked prior to prescribing treatment.

Paracetamol, chlorpheniramine 10 mg IV and Adrenaline 0.5ml 1 in 1000 IM should be readily available (as per anaphylaxis protocol).

During infusion

NB This infusion must be given via a Volumetric Infusion pump (i.e. Baxter Colleague) and an infusion Pump Checklist completed. A rituximab infusion chart will be provided from the pharmacy department describing the administration rate below.

Infusion schedule:

First infusion	50mg/hr for first 30 minutes Then increase by 50mg/hr every 30 minutes to maximum of 400mg/hr (ie. over 4hrs 15 minutes in total)
Second infusion (if first infusion tolerated)	100mg/hr for first 30 minutes Then increase by 100mg/hr every 30 minutes to maximum of 400mg/hr (ie. over 3 hrs 15 minutes in total)

If the first two cycles of treatment are uneventful, subsequent courses of rituximab may be infused at a faster rate:

250mg/hr for first 30 minutes
Then increase to 600mg/hr for the remainder of the infusion
(ie. over 2 hours in total)

This faster rate should not be used in patients who have had previous serious infusions reactions to any previous biologic or in patients with clinically significant cardiovascular disease including arrhythmias.

A doctor should be readily available for the entire infusion

Check BP, pulse and temperature every 30 minutes during the infusion and for 1 hour post infusion.

.

If **minor infusion reactions** occur slow the infusion, stop if necessary and restart at a slower rate (50%)

If **severe reactions** occur **(bronchospasm, severe breathlessness, hypoxia).** Treat with adrenaline, chlorphenamine and intravenous steroids in accordance with the current anaphylaxis guidelines.

Side Effects

Infusion reactions occur in 15% of patients following the first infusion and in 2% in the second infusion. Infusion reactions may include pruritis, fever, urticaria/rash, chills, pyrexia, rigors, sneezing, angioneurotic oedema, throat irritation, cough and brochospasm, with or without hypotension or hypertension. Premedication with IV steroids significantly reduces the incidence and severity of these events

Patients are at increased risk of infection (approx 1% per patient per year) particularly upper respiratory tract infections and urinary tract infections.

Other side effects include indigestion or abdominal pain (2-4%), arthralgia/musculoskeletal pain or muscle spasms, worsening angina, migraines, tingling or numbness.

Rare (<1/1000) side effects reported include late neutropenia (more than 4 weeks after last infusion, severe cardiac events (associated with infusion reaction and mainly with prior heart condition)
Very rare (<1/10,000) side effects reported include pancytopenia, aplastic anaemia, cranial or peripheral neuropathy, renal failure, pneumonitis, severe bullous skin reactions and cutaneous vasculitis, tumour lysis syndrome (associated with infusion reaction) and reactivation of hepatitis B.
There have also been reports of progressive focal leukoencephalopathy in patients treated with Rituximab.
It is unknown if there is a long term increased risk of some malignancies.

After infusion

Giving set is disconnected after a saline flush, but the cannula is left in situ until after observation period is complete.
Patient can go home 1 hour after infusion (see infusion schedule section for details) if they are well and observations have been satisfactory.
Inform patient of date of next infusion.
Monitoring of blood tests as for monitoring of the underlying disease
It is for the physician to report severe adverse reactions to the manufacturers

Subsequent Assessment of Disease

Blood tests (FBC, ESR, U+E, LFT, immunoglobulins) should be performed before each infusion and results checked.

Health and Safety

Rituximab is not cytotoxic and requires no special precautions or procedures in case of spillage

Withdrawal from Treatment

Failure to respond at 6 months will lead to withdrawal of treatment

3. References

1. Truxima summary of product characteristics November 2018
2. Clinical Commissionong Policy: Rituximab for the treatment of ANCA-associated vasculitis in adults.

4. Documentation Controls

Development of Guideline:	Dr Sheila O'Reilly, Consultant Rheumatologist Dr Janson Leung, Consultant Nephrologist Dr Zoe Pittman, Consultant Nephrologist Dr Sue Shaw, Renal Services Pharmacist
Consultation with:	Rheumatology
Approved By:	Renal - 14/12/18 Medical Division - 13/03/2019
Implementation Date:	14/03/2019
Review Date:	March 2022
Key Contact:	Dr Janson Leung, Consultant Nephrologist