University Hospitals Birmingham NHS
NHS Foundation Trust

CONTROLLED DOCUMENT

Guidance on the administration of Rituximab Infusions for immune-mediated systemic and renal inflammatory disease such as Vasculitis, Systemic Lupus Erythematosus and Primary Glomerular Disease

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AFFIX PATIENT LABEL
NAME

DOB

HOSPITAL NUMBER

RITUXIMAB INFUSION RECORD AND PATHWAY

FOR RENAL PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY RENAL AND SYSTEMIC DISEASE

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Guidance on the administration of Rituximab Infusions for immune-mediated systemic and renal inflammatory disease such as Vasculitis, Systemic Lupus Erythematosus and Primary Glomerular Disease

To be used in conjunction with Trust Medicines Policy and associated procedures, Procedure for Safe Prescription, Handling and Administration of Cytotoxic and other Chemotherapeutic Agents and Expanded Practice Protocol for the Administration of Intravenous Drugs and Infusions by Registered Practitioners

Intravenous Rituximab infusion is licensed to treat patients with severe life or organ threatening Vasculitis and used off licence for Systemic Lupus Erythematosus in conjunction with corticosteroids and primary glomerular disease such as Minimal Change and Membranous Nephropathy. Rituximab should be given on days 0 and 14. After the second dose, B cell depletion usually lasts for a period of months. Repeat dosing may be undertaken either pre-emptively or in response to further disease activity. The interval to repeat dosing is usually at least 6 months. Some patients will receive 1g of Rituximab every 6 months as maintenance therapy for their immune mediated disease.

Rituximab prescribing:

Prescribing is restricted to Renal Consultants and designated Rheumatology Consultants working within combined Renal/Rheumatology Clinics.

Patients attending as a day case must have a day case admission on the Prescribing, Information & Communication System (PICS).

Dosing:

1000mg (1g) of Rituximab is given as an infusion on days 0 and 14. In exceptional circumstances (e.g. very low body weight), the dose may be reduced to 500mg. Some patients will receive 1g Rituximab every 6 months as maintenance treatment.

Infusions may be deferred at doctor's discretion due to infection or low white cell count.

See prescribing guidance on renal unit for further information.

The Planned Treatment Schedule on page 7 must be completed**.**

Pre/Post Infusion drugs:

The prescribing of drugs required pre/ post infusion must take place at the time of prescribing the Rituximab Infusion.
Patients should receive pre-medication with

- IV Methylprednisolone 100mg in 100ml Sodium Chloride 0.9% given one hour prior to Rituximab infusion (This may be omitted at Consultant discretion).
- Oral Chlorphenamine 4mg given 30 minutes prior to Rituximab infusion
- Oral Paracetamol 1g given 30 minutes prior to Rituximab infusion - unless patient has taken any Paracetamol containing medications within last 6 hours or patient allergic to Paracetamol.
- In patients who have previously experienced an infusion reaction to Rituximab, intravenous Chlorphenamine may sometimes be used at discretion of treating Consultant.

- Patients should normally receive Co-trimoxazole oral prophylaxis 480mg every other day for 6 months after infusion or indefinitely for those receiving planned maintenance infusions of Rituximab, unless allergic to or intolerant of medication. The prescription should be initiated at the consultation when the decision is made to treat with Rituximab and request made to GP to continue prescription in clinical letter/discharge summary.

Consultant responsibilities prior to admission

- Ensure that the prescription of Rituximab is appropriate for the patient and that the indications and potential side effects of therapy have been explained to the patient. Verbal informed consent obtained and documented on PICS prescription
- Ensure that the patient has received appropriate pregnancy and contraception advice
- Pre screening for Hepatitis B,C and HIV undertaken (annually for those on planned re-treatment regime)
- Pre-screening of Varicella zoster status if not already checked.
- Review patient regarding TB risk: Baseline Chest X-Ray (CXR) if indicated by history and no CXR within last 12 months. Further monitoring at Consultant discretion.
- Liaise with KAT team on Ward 301 or Wellcome Trust CRF(for those in clinical research trials only) via email to confirm availability for required dates.
- Provide details of patient name, date of birth, registration number, diagnosis, number of infusions required.
- Ensure Rituximab is prescribed and the initial authorisation completed on PICS.

Nursing responsibilities before the infusion is commenced.

- Ensure Rituximab is prescribed. Liaise with the Lead Pharmacist for Renal Services (bleep: 1836) or Pharmacy Aseptic Unit (x16216) if there are any problems.
- To prevent delays due to the time taken in the sterile pharmacy lab nursing staff should contact the patient 24 hours prior to the infusion to confirm that they will be attending for the infusion and that they do not have symptoms of infection. If the nurse can confirm that the patient is attending and is fit for infusion the sterile lab can be informed to make up the infusion. If there are any concerns then the sterile lab should not

- be contacted until the patient has been reviewed on admission by the ward nursing staff.
- Review relevant patient correspondence through Portal. The patient must have:
    1. A Rituximab pathway completed for each episode which will be scanned to the portal on completion of treatment course.
    2. Observations recorded through PICS
    3. Documentation of procedure in medical records and as day case episode via PICS.
- Ensure pre-infusion checklist is completed and there are no contraindications to the patient receiving Rituximab.
- If it is possible that the patient may be pregnant, a pregnancy test must be carried out pre-infusion by registered practitioners trained to perform pregnancy testing. The result must be documented and countersigned by both practitioners witnessing the test. If a patient believes she may be pregnant but is unable to provide a urine sample due to renal disease a blood sample must be sent and negative result obtained before infusion commences.
- Take and record: temperature, pulse, blood pressure, oxygen saturations (SaO_2) and respiratory rate and check urinalysis to exclude infection (where patient is not anuric) as a baseline prior to each infusion. Do not proceed with infusion if levels outside normal range for the patient and seek advice from Renal Consultant or Renal SpR
- **If the patient has a fever, send Full Blood Count (FBC), full biochemical profile including CRP and blood cultures**. If the patient is not anuric, a urine sample must also be sent to microbiology for cytometry and culture. **The patient and lab results must be reviewed by medical staff before a decision is made to commence the infusion**. **Patients with suspected significant infection should not receive Rituximab**.
- Ensure a full blood count (FBC) is available within 14 days prior to infusion. If not available, FBC should be sent but the result is not required before starting the Rituximab infusion. Bloods should be taken at the first infusion to include FBC.
- Inform Pharmacy Sterile Lab if patient fit for infusion if not done the day before.
- Ensure cannula inserted.
- Ensure patient has been given pre infusion medications:
    - IV Methylprednisolone,

    - Oral Chlorphenamine and
    - Oral Paracetamol .
- The Intravenous giving set must be primed with Sodium Chloride 0.9% via infusion pump.
- The final authorisation for infusion on PICS should be signed by the nurse who has assessed the patient and has chemotherapy administration privileges on PICS.

Administration of Rituximab infusions.

All areas in which chemotherapy drugs are administered must have the following equipment readily available:

- Emergency bell/telephone
- Resuscitation equipment
- Drugs for management of emergencies; cardiac arrest and anaphylaxis
- Cytotoxic spillage kit
- Access to running water
- Disposal equipment e.g. appropriate sharps bins
- Copies of relevant policies and procedures

Rituximab infusions must be checked and administered in line with:

UHB NHS Foundation Trust Procedure for the Safe Prescribing, Handling and Administration of Cytotoxic and other Chemotherapeutic Agents (Controlled document number 504 current version), and Procedure for the Prescribing, Supply, Dispensing, Handling, Storage, Administration and Disposal of Medicines including Controlled Drugs (Controlled Document Number 443, Current Version)

- One practitioner must be competent in the administration of Chemotherapy Infusions as per Trust Expanded Practice Protocol for the Administration of Intravenous Cytotoxic Drugs by Registered Nurses (Controlled Document Number:249.5 Current version)

The second, checking practitioner must be an intravenous competent registered nurse as per Trust Expanded Practice Protocol for the Administration of Intravenous Drugs and Infusions by Registered Practitioners (Controlled Document Number: 232. Current version) **Registered nurses not competent in the administration of Intravenous Cytotoxic Drugs as per Trust Expanded Practice Protocol for the Administration of Anti Systemic Cancer Therapy must not administer Rituximab infusions.**

Spillage and waste must be dealt with in accordance with: UHB NHS Foundation Trust Procedure for the Safe Prescribing, Handling and Administration of Cytotoxic and other Chemotherapeutic Agents (Controlled document number 504 current version)

Administration **must not commence** or must **STOP** if:

- The patient requests the treatment to stop
- There is any doubt regarding the

- stability of the drug (i.e. possible incorrect storage or precipitation)
- expiry of the infusion
- drug dosage
- pre-treatment investigations

- The environment in which treatment is being administered is deemed unsafe.
- The equipment fails to function effectively.
- There is any doubt regarding the integrity of the venous access device being used.
- Administration must stop if mild to moderate infusion reaction does not resolve
- Patient demonstrates sign of severe infusion reaction.

Rituximab is made as 1000mg in 500ml Sodium Chloride 0.9%. The infusion should be administered as per the below tables. The first infusion is given at a slower rate to reduce the risk of infusion reactions.

In the event of a reaction to the first infusion, the second infusion should be administered following the first infusion guidelines. Most reported reactions occur during first two hours of infusion and so the patient should be closely monitored as the infusion commences and at each infusion rate increase. (RCN 2009).

The infusion rate should not exceed 200ml/hr at this concentration. Alternative regimes will have appropriate regime advised by PICS.

Mild to moderate infusion-related reactions usually respond to a reduction in infusion rate. If a patient develops severe cytokine release syndrome (see clinical observations below) the infusion should be interrupted immediately. On resolution, if the infusion is to continue as directed by Renal Consultant or Renal SpR, the infusion can be resumed at **not more than one-half the previous rate**.

First Rituximab infusion rate (1000mg Rituximab in 500ml sodium chloride 0.9%):

Time of infusion (mins)	INITIAL infusion rate (ml/h)
0-30	25
31-60	50
61-90	75
61-120	100
121-150	125
151-180	150
181-210	175
211-240	200 (MAX rate)
240+	200 (MAX rate)

Second Rituximab infusion rate (1000mg	SECOND infusion rate (ml/h)

rituximab in 500ml sodium chloride 0.9%):Time of infusion (mins)	
0-30	**50**
31-60	**100**
61-90	**150**
61-120	**200 (MAX rate)**
121-150	**200 (MAX rate)**
151-180	**200 (MAX rate)**
181-210	
211-240	
240+	

Clinical Observations for Infusions

During infusion, the patient's vital signs (blood pressure, pulse, respiration and temperature and oxygen saturations) should be monitored every 15 minutes for the first hour, and then if stable every 30 minutes until infusion completed and 30 minutes post infusion. Additional observations should be performed immediately if the patient develops any symptoms or signs suggestive of an infusion reaction and the frequency of observations should be increased appropriately.

Managing Infusion reactions

Any reactions must be managed as per Trust anaphylactic procedure (where anaphylaxis is suspected)
Rituximab can cause an allergic type reaction in some people. Infusion reactions usually occur within the first one to two hours of infusion and less likely with subsequent infusions. Infusion reactions can occur in up to 50% of patients receiving Rituximab. They vary in severity from mild to severe (cytokine release syndrome).)

- Mild symptoms include low grade fevers, chills, hypotension <30mmHg from baseline and rigors in up to 50% of patients. Other symptoms include headache and nausea.

- Initial management of an infusion reaction is to slow the infusion by half (eg from 100mls/hr to 50mls/hr) and consider giving ‘as required’ medication. If the infusion reaction settles the rate of infusion can be increased again after 30 minutes.

- Monitor patient’s vital signs; if the reaction does not resolve or patient demonstrates signs and symptoms of **moderate to severe reaction** (uncommon) eg
    - Fever >38.0^{o}C
    - Tachycardia (>100bpm)
    - Flushing
    - Urticarial rash

- Chills
- Mucosal swelling
- Shortness of breath
- Hypotension >30mmHg from baseline
- Nausea, vomiting

STOP INFUSION, CONTACT RENAL SpR or RENAL CONSULTANT.

- Full anaphylactic shock occurs rarely.
- **In more serious reactions additional IV steroids, IV antihistamines, bronchodilators and oral anti pyretics can be administered.**

The following additional measures should also be undertaken for a **severe or suspected severe** infusion reaction:

- Intravenous chlorphenamine (10mg) and hydrocortisone (100mg) should be administered

- Oxygen should be administered via face mask if the patient complains of breathlessness, oxygen saturations fall below 95%, respiratory rate increases to >26/breath per minute or blood pressure falls (Systolic BP <100mmHg)

  Nebulised salbutamol may be given for bronchospasm (wheezing or severe breathlessness).
- Intravenous sodium chloride 0.9% (250-500ml by rapid infusion) should be administered if the patient develops hypotension (Systolic BP <100mmHg).
- Adrenaline may be considered at the discretion of the attending doctor

Post infusion

- Giving set must be flushed on completion of infusion with 0.9% Sodium Chloride.
- Post infusion observations recorded 30 minutes after completion of infusion.
- Remove cannula when post infusion observations are satisfactory.
- Ensure all waste is disposed of correctly e.g. correct sharps bin.
- Ensure patient has Arthritis Research UK Rituximab leaflet and Rituximab patient alert card (available in clinics and on 301 KAT team) and contact details of Kidney Assessment Team/Renal Inflammatory Disease Clinical Nurse Specialist.
- Inform patient of next infusion date where appropriate and/or follow up appointment as required.
- Once all above is complete patient may be discharged.

- Ensure all components of regime have been signed for (including any drug not given) on PICS and Rituximab infusion is finished on PICS, not doing so will prevent next infusion being prescribed.

ID Label

Prescribing consultant:

Patient Diagnosis:

Treatment Regime: Rituximab 1g at Day 0 and Day 14

Please state if other regime prescribed:

Planned Treatment Schedule

Infusion number	Week	Date	Revised dates if infusion postponed
1	0		
2	2		

RITUXIMAB PRE-ADMINISTRATION CHECKLIST

Patient Name/ID label:……. Unit No:……Date:.....

Dose of Rituximab	Infusion number
	1

On completion of checklist any contraindications or active medical problems must be documented below. Advice must be sought from medical staff before infusion.

Current Health Status/relevant PMH.		
	All criteria must be met for infusion to take place.	
Is/could the patient be pregnant?	Yes/**No**	If yes do not give infusion. See guidance under nurses responsibilities*. Inform medical staff.
History of recent fever, rash, cough, worsening dyspnoea, dental abscess or any other infection? Check patient not on antibiotics other than Co-Trimoxazole prophylaxis. Check CRP on recent blood tests.	Yes/**No**	If yes, check severity & whether on antibiotics. Medical staff to review and confirm whether infusion is to be commenced. If CRP raised above usual level for patient discuss with medical staff before proceeding with infusion.
History of exposure to chicken pox or shingles within 20 days	Yes/**No**	If yes discuss with medical staff and check zoster Immunoglobulin status result if available.
Baseline observations within normal parameters: Temp: Pulse: Resps: O2Sat: BP:	**Yes**/No	If no discuss with medical staff
Urinalysis: (if patient not anuric)	**Yes**/No	If nitrite/leukocyte positive send MSU and discuss with medical staff before commencing infusion.
Appropriate FBC available (see nursing responsibilities on page 4) and within normal parameters for patient.	**Yes**/No	If no bloods available, send to laboratory and proceed with infusion
Patient has been given pre-infusion medication	**Yes**/No	If no, administer pre infusion.
Hepatitis B/C/HIV status checked and negative within last 12 months	**Yes**/No	If no, send sample and proceed with infusion unless Patient Hepatitis B/C/HIV positive in which case consult with prescribing Consultant before proceeding/
Previous reaction to Rituximab	Yes**/No**	If yes ensure Prescribing Doctor aware and premedication including IV Methylprednisolone administered prior to Rituximab if infusion to proceed
FBC sent	**Yes**/No	
Date/Time		Signature

OBSERVATION CHART FOR RITUXIMAB INFUSION

Patient Name/ID label:…….. Unit No:……

First/Second Rituximab Infusion Previous Rituximab Y/N Previous Reactions: Y/N
If yes – document and seek advice as per checklist.

Date	Time	Pulse	Temp	SaO2	Resp Rate	Blood Pressure	Adverse reactions?	Infusion Rate	Signature
	Baseline								

RITUXIMAB PRE-ADMINISTRATION CHECKLIST

Patients Name: **Unit No/Affix ID label** **Date:**

Dose of Rituximab	Infusion number
	2

On completion of checklist any contraindications or active medical problems must be documented below. Advice must be sought from medical staff before infusion.

Current Health Status/relevant PMH.		
	All criteria must be met for infusion to take place.	
Is/could the patient be pregnant?	Yes/**No**	If yes do not give infusion. See guidance under nurses responsibilities*. Inform medical staff.
History of recent fever, rash, cough, worsening dyspnoea, dental abscess or any other infection? Check patient not on antibiotics other than Co-Trimoxazole prophylaxis. Check CRP on recent blood tests.	Yes/**No**	If yes, check severity & whether on antibiotics. Medical staff to review and confirm whether infusion is to be commenced. If CRP raised above usual level for patient discuss with medical staff before proceeding with infusion.
History of exposure to chicken pox or shingles within 20 days (	Yes/**No**	If yes discuss with medical staff and check zoster Immunoglobulin status result if available.
Baseline observations within normal parameters: Temp: Pulse: O2 Sats: BP:	**Yes**/No	If no discuss with medical staff
Urinalysis: (if patient not anuric)	**Yes**/No	If nitrite/leukocyte positive send MSU and discuss with medical staff before commencing infusion.
Appropriate FBC available (see nursing responsibilities on page 4) and within normal parameters for patient.	**Yes/**No	If no bloods available, send to laboratory and proceed with infusion
Hepatitis B/C/HIV status checked and negative within last 12 months	**Yes**/No	If no, send sample and proceed with infusion unless Patient Hepatitis B/C/HIV positive in which case consult with prescribing Consultant before proceeding.
Patient has been given pre-infusion medication	**Yes**/No	If no administer pre infusion.
Previous reaction to Rituximab	Yes/**No**	If yes, ensure Prescribing Doctor aware and premedication including IV Methylprednisolone administered prior to Rituximab if infusion to proceed. Infusion should be given as per First Infusion Schedule. See guidance under nursing responsibilities.
Date/Time		**Signature**

OBSERVATION CHART FOR RITUXIMAB INFUSION

Patient Name/ID label:…….. Unit No:……

Rate of Infusion (s
tate if 1st influsion rate or 2nd infusion rate to be followed) :……

Second Rituximab Infusion Previous Rituximab Y/N Previous Reactions: Y/N If yes – document and seek advice as checklist.

Date	Time	Pulse	Temp	SaO2	Blood pressure	Resp Rate	Adverse reactions?	Infusion Rate	Signature
	Baseline								

RITUXIMAB INFUSION PATHWAY FOR RENAL PATIENTS WITH VASCULITIS or LUPUS

University Hospitals Birmingham NHS
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Patient Name/ID label:…… Date:……..

You have received an infusion of Rituximab today. Your next dose of Rituximab is due

Or

There are no plans for further Rituximab infusions at present.

You should continue to take Prednisolone tablets if prescribed and you should take Co-Trimoxazole 480mg tablets every other day for six months after receiving Rituximab OR on an ongoing basis if you are having planned re-treatments with Rituximab as directed by your medical team.
If you are allergic or intolerant to Co-Trimoxazole then an alternative antibiotic Atovaquone may be prescribed. This treatment is to reduce the risk of severe infection following treatment with Rituximab.

You should carry a Rituximab alert card (given to you by the Infusion Team) and show this to anyone providing medical or dental care for you.

If you experience any fever, or other symptoms of infection or feel unwell following your infusion it is important that you contact us. You may need to be seen by a Doctor and have blood tests taken and may require admission to hospital. Do not delay seeking advice, please contact us urgently on:

- Kidney Assessment Team on 0121 371 3017 or 07766500092 (8am-7pm Mon-Friday, 8am-8pm Sat/Sun/Bank holidays)

- or Sarah Logan, Clinical Nurse Specialist on 0121 627 2518 or 07827232646 Monday to Friday 8.15-4.15

- In case of emergency out of these hours call 0121 371 2000 hospital switchboard and ask for acute renal registrar on call.

Discharging Nurse

Name:……Designation:…….

Please scan a copy of letter to portal and give a copy to the patient