

# Rituximab in Neurological Disease

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## 1. Rituximab in neurological disease

### 1.1. Introduction

Rituximab is a monoclonal antibody that binds to and destroys the CD-20 positive B lymphocytes which mature and produce antibodies. Although various mechanisms of action have been postulated the exact mode of action is unknown.

Rituximab was approved by the United States Food and Drug Administration in 1997 for treatment of B cell non-Hodgkin's lymphoma resistant to other chemotherapy regimes(1). In the United Kingdom it is approved for use in resistant follicular non-Hodgkin's lymphoma and in diffuse large B cell lymphoma in combination with a chemotherapy regime (*e.g.* CHOP). In rheumatology, rituximab is licensed for use in combination with methotrexate for severe active rheumatoid arthritis in adults (2).

However, its use in neurological disease is mainly limited to retrospective case studies and case series. They have shown favourable outcomes following treatment in patients with multiple sclerosis, neuromyelitis optica, inflammatory polyneuropathy and vasculitis (3-6).

Rituximab is not licensed for treatment in neuromyelitis optica, vasculitis or other neurological disease so the prescriber and the Trust take full responsibility for its use. This protocol has been compiled based on the evidence available in treatment of neuromyelitis optica and vasculitis. However, patients with other neurological diseases who not respond to standard medical treatment may also be considered for treatment with rituximab where appropriate.

#### **Rituximab in Neuromyelitis optica**

Neuromyelitis optica is a rapidly disabling inflammatory demyelinating relapsing disease which affects the optic nerve and the spinal cord(7). A retrospective multicentre case series looked at 25 patients diagnosed with neuromyelitis optica who were treated with rituximab (5, 6). Follow up showed overall improvement in the post treatment relapse rate and in functional outcome.

#### **Rituximab in Vasculitis**

Vasculitis of the nervous system may occur as part of a multisystem disease or may be isolated.

The RAVE trial demonstrated non-inferiority of rituximab to cyclophosphamide for remission induction in ANCA-associated vasculitis, with the suggestion of superiority in relapsing disease (8). This has led to NICE approval for ANCA-associated vasculitis under the following circumstances:

- (1) further cyclophosphamide treatment would exceed the maximum cumulative cyclophosphamide dose **or**
- (2) cyclophosphamide is contraindicated or not tolerated **or**
- (3) the person has not completed their family and treatment with cyclophosphamide may materially affect their fertility **or**

- (4) the disease has remained active or progressed despite a course of cyclophosphamide lasting 3–6 months **or**
- (5) the person has had uroepithelial malignancy.

The European Vasculitis (EUVAS) Study Group have led on providing evidence based guidelines for vasculitis and have recognised (a) that ANCA may not be detected in the serum of some patients with ANCA associated vasculitis, especially those with localised disease, and (b) that some non-ANCA-associated vasculitides such as essential cryoglobulinaemic vasculitis, a form of immune complex mediated vasculitis, should be treated in the same way as ANCA-associated vasculitis(9). In view of this and the new NICE guideline, rituximab can now be prescribed without individual patient approval for patients at the Walton Centre with nervous system vasculitis that pathophysiologically falls in the ANCA-associated category, even where not clearly ANCA-associated. Other types, for example immune complex mediated vasculitis or those where the type of vasculitis is unclear, will also be eligible for rituximab.

In vasculitis patients where cyclophosphamide is not contraindicated, this will remain first line to induce remission, with subsequent maintenance treatment with another agent such as azathioprine. Should relapse occur following treatment as per the cyclophosphamide guideline (which delivers 6-10 g of cyclophosphamide), then assuming it was well tolerated and remission did occur, cyclophosphamide should be used a second time, perhaps with an alternate maintenance treatment such as methotrexate. Should a second relapse occur, then rituximab should be used instead of further cyclophosphamide for remission induction.

Rituximab is not licensed for treatment in neuromyelitis optica, vasculitis or other neurological disease so the prescriber and the Trust take full responsibility for its use. This protocol has been compiled based on the evidence available in treatment of neuromyelitis optica and vasculitis. However, patients with other neurological diseases who do not respond to standard medical treatment may also be considered for treatment with rituximab where appropriate.

## **1.2. Absolute contraindications**

Heart failure, active infection and hepatitis B (reactivation risk with fulminant hepatitis).

## **1.3. Concomitant use of other immunosuppressant**

Combining rituximab with other immunosuppressants (e.g. azathioprine, mycophenolate, methotrexate) may predispose to infection and thus these are *generally* discontinued when on Rituximab. Rituximab **should not** be given in combination with ciclosporin A or other calcineurin inhibitors due to the increased risk of infection.

## **1.4. Prescribing rituximab**

- (1) If long-term treatment with Rituximab is the plan, then funding must be agreed with NHS England through an individual funding request (IFR). IFR forms for England and Wales are available in the 'other useful documents' folder in the IVIg folder on the S drive. If treatment is urgent, treatment can precede the IFR approval is a

WCFT one-off non-formulary drug application completed and the case has been discussed with management.

- (2) The patient should be informed that this is an unlicensed use of rituximab and given written information (see Appendix I).
- (3) It should be prescribed by a consultant, using the rituximab prescription sheet (Appendix II). This may be done in advance.
- (4) It is prepared only in a controlled environment by the pharmacy Aseptics unit. Pharmacy should be informed when patients are admitted for treatment (or in advance if possible), and the prescription faxed to Aseptics on ext. 5190.
- (5) When patients are admitted, baseline tests must be undertaken.
  - a) ECG (risk of chest pain, fatal cardiac failure, cardiac arrhythmias).
  - b) CXR (risk of reactivation of dormant TB, bronchiolitis obliterans and pneumonitis). Provided a consultant has signed the prescription, any grade of doctor may complete the pre-treatment checklist and sign to declare the patient fit for treatment that day.

### **1.5. Rituximab storage and stability**

Once reconstituted, rituximab must be stored at 2 to 8 degrees Celsius and is stable for 24 hours only. Pharmacy will not usually prepare the rituximab infusion until pre-treatment checks are complete, to prevent wastage if treatment cannot proceed.

### **1.6. Pre-treatment Investigations**

These are usually tested not more than 7 days before infusion start.

1. FBC with differentials (risk of pancytopenia, marrow hypoplasia, late neutropenia).
2. Urea, creatinine, LFT'S, electrolytes.
3. Screen for hepatitis B and C (risk of reactivation).
4. Pregnancy test (remote risk of teratogenicity).
5. ECG (risk of chest pain, fatal cardiac failure, cardiac arrhythmias).
6. CXR (risk of reactivation of dormant TB, bronchiolitis obliterans and pneumonitis).
7. Immunoglobulin levels as a baseline (to assess efficacy and risk of infection (IgG <6g/l), though, treatment can be begun before results return, British Rheumatology Society)(10)

If any of these tests show abnormal results, they should be discussed with the patient's consultant who will decide whether treatment may go ahead or not.

### **1.7. Precautions**

- (1) Anaphylactic reaction to infusion (cardiac arrest trolley should be available on ward).
- (2) Withhold antihypertensive medications 12 hours prior to infusion (as rituximab infusion may drop the blood pressure).
- (3) Female patients should agree to use effective contraceptive methods during and after treatment *i.e.* from day 1 of treatment to 12 months after receiving treatment. (Please refer to patient information leaflet and patient consent form.)

### **1.8. Administration**

Immediately before each rituximab infusion, the following drugs should be given:

- (1) Methylprednisolone 125 mg IV
- (2) Chlorphenamine 10 mg IV
- (3) Paracetamol 1 gram orally

The infusion is started slowly and the rate gradually increased if tolerated. On day 1, start at 50 mg/hour and increase every 30 minutes by 50 mg/hour, up to a maximum rate of 400 mg/hr. On day 15, start at 100 mg/hr and increase every 30 minutes by 100 mg/hr, up to a maximum of 400 mg/hr. (See Appendix II.)

#### 1.8.1 Administration for NMO/other neurological conditions

The recommended dose is 1g in 500ml sodium chloride 0.9% . Two doses are given, two weeks apart, *i.e.* on days 1 and 15. The course is usually repeated every six to twelve months (minimum 16 weeks between courses).

#### 1.8.2 Administration for vasculitis (remission induction)

A dose of 375 mg per square meter of body surface area (BSA) is given every week for 4 weeks. BSA is calculated using weight and height, most commonly with the Du Bois formula:

- $BSA = 0.007184 \times Wt^{0.425} \times Ht^{0.725}$

Steroids are advised alongside rituximab in the form of 1 mg/kg daily prednisolone, with gradual withdrawal over 6 months. 1 to 3 pulses of 1 g methylprednisolone are recommended at the start of treatment, for example with each rituximab infusion.

### 1.9. Observation during infusion

- (1) Regular clinical observation of the patient.
- (2) Blood pressure, oxygen saturation, pulse rate, respiratory rate and temperature every 15 minutes until maximum infusion rate reached then every 30 minutes until 1 hour after completion of infusion.

### 1.10. Management of infusion-related complications

Infusion related reactions include chills, fever, mucosal swelling, breathing difficulty (bronchospasm), skin rash and hypotension (drop in blood pressure by 30mmHg).

#### 1.10.1 Mild infusion-related reaction

- (1) Infusion should be reduced to half the initial infusion rate – (*i.e.* from 100 mg/hr to 50 mg/hr).
- (2) Once reaction resolves, keep reduced rate for an additional 30 minutes.
- (3) If reduced rate is tolerated, infusion rate may be increased to next closest rate on schedule – leave IV line *in situ* 1 hour.

#### 1.10.2 Moderate to severe infusion-related reaction

Infusion should be stopped immediately and appropriate symptomatic treatment administered (*e.g.* fluids support, antihistamines, paracetamol, steroids). The neurology team, on call registrar or outreach team should be called. The infusion should not be restarted until all the symptoms have disappeared and then at half the

rate. If reduced rate is tolerated for 30 minutes, infusion rate may be increased to next highest rate on infusion table. Leave IV line in situ for 1 hour.

### 1.11. Post infusion – follow up blood tests

Check FBC (differential), monthly and treating consultant informed. These tests can be done locally but can be organised at the Walton Centre if required.

Immunoglobulin levels at 4-6 months after infusions and prior to any re-treatment. It is recommended that the possibility of increased risk of infection in patients with low IgG <6g/l be discussed with patient prior to re-treatment with rituximab(10). The role of measuring CD19 counts in rituximab, as a marker of degree of immunosuppression is being evaluated. Patients with NMO should ideally have it done pre infusion and periodically(11).

### 1.12. References

1. Maloney DG, Grillo-Lopez AJ, Bodkin DJ, White CA, Liles TM, Royston I, et al. IDEC-C2B8: results of a phase I multiple-dose trial in patients with relapsed non-Hodgkin's lymphoma. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 1997;15(10):3266-74.
2. Edwards JC, Szczepanski L, Szechinski J, Filipowicz-Sosnowska A, Emery P, Close DR, et al. Efficacy of B-cell-targeted therapy with rituximab in patients with rheumatoid arthritis. *The New England journal of medicine*. 2004;350(25):2572-81.
3. Bar-Or A, Calabresi PA, Arnold D, Markowitz C, Shafer S, Kasper LH, et al. Rituximab in relapsing-remitting multiple sclerosis: a 72-week, open-label, phase I trial. *Annals of neurology*. 2008;63(3):395-400.
4. Cree BA, Lamb S, Morgan K, Chen A, Waubant E, Genain C. An open label study of the effects of rituximab in neuromyelitis optica. *Neurology*. 2005;64(7):1270-2.
5. Jacob A, Weinshenker BG, Violich I, McLinskey N, Krupp L, Fox RJ, et al. Treatment of neuromyelitis optica with rituximab: retrospective analysis of 25 patients. *Archives of neurology*. 2008;65(11):1443-8.
6. Kim SH, Huh SY, Lee SJ, Joung A, Kim HJ. A 5-year follow-up of rituximab treatment in patients with neuromyelitis optica spectrum disorder. *JAMA neurology*. 2013;70(9):1110-7.
7. Jacob A, McKeon A, Nakashima I, Sato DK, Elson L, Fujihara K, et al. Current concept of neuromyelitis optica (NMO) and NMO spectrum disorders. *Journal of neurology, neurosurgery, and psychiatry*. 2013;84(8):922-30.
8. Stone JH, Merkel PA, Spiera R, Seo P, Langford CA, Hoffman GS, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. *The New England journal of medicine*. 2010;363(3):221-32.
9. Mukhtyar C, Guillevin L, Cid MC, Dasgupta B, de Groot K, Gross W, et al. EULAR recommendations for the management of primary small and medium vessel vasculitis. *Annals of the rheumatic diseases*. 2009;68(3):310-7.
10. Bukhari M, Abernethy R, Deighton C, Ding T, Hyrich K, Lunt M, et al. BSR and BHRP guidelines on the use of rituximab in rheumatoid arthritis: *Rheumatology*; 2012 [cited 2012 January 14th 2015]. Available from: <http://rheumatology.oxfordjournals.org/content/suppl/2011/05/04/ker106a.DC1/ker106b.pdf>.
11. Greenberg BM, Graves D, Remington G, Hardeman P, Mann M, Karandikar N, et al. Rituximab dosing and monitoring strategies in neuromyelitis optica patients: creating strategies for therapeutic success. *Multiple sclerosis*. 2012;18(7):1022-6.

12. Chakravarty EF, Murray ER, Kelman A, Farmer P. Pregnancy outcomes after maternal exposure to rituximab. *Blood*. 2011;117(5):1499-506.

## **2. Supporting policies/clinical guidance**

- Cyclophosphamide Administration Guideline, April 2013.

## Appendix 1 – Patient & GP information and consent

The Walton Centre Foundation Trust

### Rituximab Patient Information Leaflet

At The Walton Centre, rituximab is usually prescribed to treat neuromyelitis optica, so this information sheet is based on its use in this condition. Occasionally it may be used for other neurological conditions.

#### What is Rituximab?

Rituximab is a type of medicine known as a monoclonal antibody. It works by damaging white blood cells called B cells. These cells are thought to be attack nerve cells causing neurological symptoms.

Many studies have shown that when rituximab was given to people with neuromyelitis optica, they had a reduction in the number of attacks and symptoms and an improved ability to carry out day to day activities.

Rituximab has been approved licenced in the UK for use in rheumatoid arthritis and for certain types of cancer. It has ***not been formally approved*** for use in any neurological conditions, and studies on its safety and efficacy have only been done with small numbers of patients with these diseases

#### How is it given?

Rituximab is given as a drip (infusion) through a fine tube (cannula) inserted into the vein. Some people can have an allergic reaction to rituximab (detailed below). In order to reduce the risk of this, the first dose will be given slowly over a number of hours. You will be prescribed medicines such as antihistamines and steroids before treatment to help prevent any reaction.

If you develop a reaction, the infusion will be stopped and you will be assessed by the doctor. We will consider whether it is appropriate to restart the treatment when the symptoms have settled. You may need to stay in hospital overnight for the first treatment so that you can be monitored. After that, rituximab can usually be given in the outpatients department and over a shorter period of time. One course of treatment consists of two doses, given two weeks apart (that is, on day 1 and day 15). The course may be repeated at intervals of six to twelve months. For vasculitis, once course of treatment consists of four doses given at weekly intervals.



## **What do you need to tell your doctor before the infusion?**

Please inform your doctor if you have had hepatitis B infection or heart problems. There is a risk of reactivation of the infection. This may cause serious liver damage. Rituximab can rarely worsen heart disease and irregular heart beats. Since the effect of the drug on pregnancy and unborn babies is not known, the drug cannot be used in those who are pregnant or breastfeeding. You should not receive rituximab if you have had a bad reaction to it in the past.

## **Possible immediate side effects**

The reaction to the drug is variable with each person reacting differently. The most common side effects are mentioned below. There may be an immediate or late reaction to the infusion. During the infusion you may develop flu-like symptoms, fever, chills, weakness, muscle aches, tiredness, dizziness and headaches. Rituximab may cause the blood pressure to drop during infusion. Patients who take medication for high blood pressure should not take that medication for at least 12 hours before rituximab is given.

The treatment may cause you to feel sick and occasionally can cause vomiting. We can prescribe anti-sickness drugs to prevent this. You may develop allergic reactions which can manifest as skin rashes, itching, tongue or throat swelling, irritation of the nasal passages, wheezing, and breathlessness.

You will be monitored closely during your treatment, but let your nurse or doctor know if you have any of these symptoms or feel unwell in any way. To help reduce the risk of developing an allergic reaction, antihistamines are given before the infusion. The infusion can also be slowed down or stopped until the reaction is over. Occasionally severe skin reactions can occur, such as painful sores on your skin, in your mouth, ulcers, blisters or peeling of skin.

## **Late onset reactions**

Rituximab can reduce the production of white blood cells by the bone marrow, making you more prone to ***infection***. Your blood cells will be monitored by means of monthly blood tests after you have received rituximab. Please contact your doctor if your temperature goes above 38°C (100.5°F) or even if you feel unwell with a normal temperature. Rituximab can reduce production of ***platelets*** (which help blood to clot) which can lead to bruising or bleeding.

## ***Progressive Multifocal Leukoencephalopathy (PML)***

One of the more serious potential side effects of rituximab is PML which is a rare brain infection caused by the activation of a virus called JC virus. It occurs during or after treatment with

rituximab. The symptoms of PML may be similar to a neuromyelitis optica relapse.

- If you believe your symptoms are getting worse or if you notice any new symptoms, it is important that you speak to your doctor.
- Discuss your treatment with your partner or caregivers. They might see new symptoms that you might not notice.

## **Commonly asked questions**

### ***Can I take other medicines along with rituximab?***

Please inform your doctor if you are prescribed any new treatment.

### ***Can I have immunisations while on rituximab?***

Live vaccines should be avoided.

## **Information for female patients of child bearing age**

Women of child-bearing age **must** use contraception while on rituximab. You must not receive rituximab if you are planning to get pregnant in the near future or if you are not using contraception. The safety of rituximab for an unborn baby is not fully known, and it is also unknown whether it is safe to try for a baby shortly after having rituximab treatment(12). It is generally recommended to allow a gap of 12 months between having rituximab and trying to conceive. Avoid breastfeeding while on rituximab.

**The Walton Centre Foundation Trust  
Rituximab Treatment – Consent Form**

**Name** \_\_\_\_\_

**Date of Birth** \_\_\_\_\_

**Hospital Number** \_\_\_\_\_

I understand that I have been diagnosed with a neurological condition that might possibly benefit from use of the drug rituximab. I confirm that I have read and understood the information sheet provided on rituximab. I have been informed about the side effects associated with rituximab including but not limited to, flu-like symptoms, weakness, muscle aches, tiredness, dizziness, headaches, allergic reactions, breathlessness, painful mouth sores, ulcers, blisters on skin, abnormal blood counts causing anaemia, bleeding, risk of serious infections and death. I will have regular bloods done and should any of the above symptoms occur, I have to contact my doctor.

I understand that by signing this document I am consenting to receive rituximab treatment.

Patient Signature \_\_\_\_\_

Date \_\_\_\_\_

Consultant Signature \_\_\_\_\_

Date \_\_\_\_\_

**The Walton Centre for Neurology and Neurosurgery**

**GP Information Leaflet**

To Dr  
Practice:  
Date:

Patient name:  
D.O.B:  
NHS no:  
Address:

Dear Dr

Re: **Rituximab**

This patient has been diagnosed with \_\_\_\_\_ and has undergone treatment with rituximab. Rituximab is a monoclonal antibody that binds to CD-20+ lymphocyte B cells. Rituximab has been used in treatment of various neurological diseases, though it is not licensed for these indications. Treatment for this condition is based on small case series and there are no randomised clinical trials. Rituximab is widely used in rheumatology and haematological diseases.

I would be happy to provide further information on this drug and the treatment experience so far if you so require. Could you kindly perform full blood count with differentials, liver function tests and urea and electrolytes, 1 week after the first and second infusions, and full blood count with differentials monthly thereafter. Please notify us of any significant abnormality identified. This patient has been provided with written information on rituximab.

Yours sincerely,

Print name and grade:

On behalf of consultant:

## Appendix 2 - Prescription charts and administration records

### WCNN Rituximab Prescription Chart – NMO/Other

<b>Name</b> .....
<b>Unit No</b> .....
<b>Date of birth</b> .....

<b>Ward</b> .....
<b>Consultant</b> .....
<b>Course No</b> .....

	Drug details	Consultant Signature	Date signed
<b>Day 1</b>	<b>Rituximab 1 g in 500 ml saline 0.9%</b> Give by intravenous infusion as per guide overleaf		
<b>Day 15</b>	<b>Rituximab 1 g in 500 ml saline 0.9%</b> Give by intravenous infusion as per guide overleaf		

- Consultant to sign prescription (in advance if necessary).
- Verbal and written information on Rituximab to be given to patient.
- SHO/SpR to review patient and sign below that they are fit for treatment.
- Fax signed prescription to Pharmacy Aseptics on 5190 to order the drug.

**Pre-treatment Checklist:** Tick or note results below; see protocol for further information. A previous course of rituximab should not have been administered within 16 weeks. **Please ensure that patient is fit for infusion before asking pharmacy to prepare the drug.**

	Day 1	Day 15
<b>Date treatment to be given:</b>		
Patient <b>information</b> leaflet given		
Written <b>consent</b> obtained from patient		
<b>CXR</b> (before first infusion or if new chest symptoms)		
<b>Hepatitis B and C</b> (Results)		
U&E within normal (last 7 days)		
<b>FBC</b> within normal (last 7 days)		
<b>LFT</b> within normal (last 7 days)		
<b>ECG</b> (before first ever infusion or if change in medical condition)		
<b>Immunoglobulin</b> levels requested (does not affect treatment)		
<b>Urine</b> – Dipstick (if positive send MSU wait for negative result)		
<b>Reactions</b> to previous doses? Record below		
<b>Premedication</b> prescribed on drug Kardex / EPMA		
Females: <b>pregnancy test</b> negative		
Females: <b>contraception</b> discussed and agreed		
Withhold <b>antihypertensives</b> 12 hours before infusion		
<b>Comments</b>		
<b>Medical officer to sign before infusion started:</b> All pre-treatment checks completed and patient eligible for treatment	Signature Print name	Signature Print name



## WCNN Rituximab Prescription Chart - Vasculitis

<b>Name</b> .....
<b>Unit No.</b> .....
<b>Date of birth</b> .....

<b>Ward</b> .....
<b>Consultant</b> .....
<b>Course No.</b> .....

	Drug details	Consultant Signature	Date signed
Day 1	Rituximab _____ mg in 500 ml Saline 0.9%Methylprednisolone 1 g IV in 100 ml NaCl 0.9%		
Day 15	Rituximab _____ mg in 500 ml Saline 0.9%Methylprednisolone 1 g IV in 100 ml NaCl 0.9%		
Day 15	Rituximab _____ mg in 500 ml saline 0.9% Methylprednisolone 1 g IV in 100 ml NaCl 0.9%		
Day 22	Rituximab _____ mg in 500 ml Saline 0.9%Methylprednisolone 1 g IV in 100 ml NaCl 0.9%		

Consultant to sign prescription (in advance if necessary). Verbal and written information on Rituximab to be given to patient. SHO/SpR to review patient and sign below that they are fit for treatment. Fax signed prescription to Pharmacy Aseptics on 5190 to order the drug.

**Pre-treatment Checklist:** Tick or note results below; see protocol for further information. Repeat following tests FBC, U&E & LFT on day 15. A previous course of rituximab should not have been administered within 16 weeks. **Please ensure that patient is fit for infusion before asking pharmacy to prepare the drug.**

	Day 1	Day 8	Day 15	Day 22
<b>Date treatment to be given:</b>				
Patient <b>information</b> leaflet given				
Written <b>consent</b> obtained from patient				
<b>CXR</b> (before first infusion or if new symptoms)				
<b>Hepatitis B and C</b> (Results)				
<b>LFT</b> within normal (last 7 days)				
<b>U&amp;E</b> within normal (last 7 days)				
<b>FBC</b> within normal (last 7 days)				
<b>ECG</b> (before first infusion or if new symptoms)				
<b>Immunoglobulin</b> levels requested (does not affect treatment)				
<b>Urine</b> – Dipstick (if positive send MSU wait for negative result)				
<b>Reactions</b> to previous doses? Record below				
<b>Premedication</b> prescribed on drug Kardex/EPMA				
Females: <b>pregnancy test</b> negative				
Females: <b>contraception</b> discussed and agreed				
Withhold <b>antihypertensives</b> 12 hours before infusion				
<b>Comments</b>				
<b>Medical officer to sign before infusion started:</b> All pre-treatment checks completed and patient eligible for treatment.	Sign:  Print:	Sign:  Print:	Sign:  Print:	Sign:  Print:

## WCNN Rituximab Administration Record – 1<sup>st</sup> Infusion

**Name:**

**Unit no:**

**Pre-medication:**

Prescribe on drug Kardex, to be given 30 minutes prior to infusion.

1. Paracetamol 1g orally
2. Chlorphenamine 10 mg IV
3. Methylprednisolone 125 mg IV (except in vasculitis – see rituximab prescription)

**Day 1: Rituximab Infusion in sodium chloride 0.9%**

**Date:**

**Instruction:** Start at 50 mg/hr if tolerated, increase by 50 mg/hr every 30 minutes until maximum of 400 mg/hr.

Time	Time since start	Rate mg/hr (*recommended)	Site checked	Reactions	Nurse signatures
<i>Ensure pre-medication has been prescribed and given, and checklist signed by doctor.</i>					
	<b>0</b>	50 mg/hr* (25 ml/hr)			
	<b>30 minutes</b>	100 mg/hr* (50 ml/hr)			
	<b>1 hour</b>	150 mg/hr* (75 ml/hr)			
	<b>1.5 hours</b>	200 mg/hr* (100 ml/hr)			
	<b>2 hours</b>	250 mg/hr* (125 ml/hr)			
	<b>2.5 hours</b>	300 mg/hr* (150 ml/hr)			
	<b>3 hours</b>	350 mg/hr* (175 ml/hr)			
	<b>3.5 hours onwards</b>	400 mg/hr* (200 ml/hr)			

**Observations during infusion**

Blood pressure, pulse rate, respiratory rate, oxygen saturation and temperature every 15 min until maximum infusion rate reached, then every 30 min until 1 hr after completion of infusion.

**Reactions:**

1. Fever temperature > 38.5°C
2. Chills
3. Mucosal swelling
4. Bronchospasm
5. Hypotension (30 mmHg drop)

**Stop infusion and seek medical advice if any reactions occur. If mild, consider restarting after one hour, at half the previous rate, and if symptoms allow, increase rate gradually**



again. If severe, consider restarting once all symptoms have fully resolved, at half the previous rate. If reaction recurs, stop therapy completely.

DRAFT

## WCNN Rituximab Administration Record

### - 2<sup>nd</sup>, 3<sup>rd</sup> & 4<sup>th</sup> Infusions

Name:

Unit no:

#### Pre-medication:

Prescribe on drug Kardex, to be given 30 minutes prior to infusion.

1. Paracetamol 1 g orally
2. Chlorphenamine 10 mg IV
3. Methylprednisolone 125 mg IV (except in vasculitis – see rituximab prescription)

**2<sup>nd</sup>, 3<sup>rd</sup> or 4<sup>th</sup> Infusions: Rituximab in sodium chloride 0.9%**

Date:

**Instruction:** Start at 100 mg/hr, if tolerated increase by 100 mg/hr every 30 minutes till maximum 400 mg/hr. NB if reactions occurred to previous doses, consider increasing rate more slowly e.g. as on day 1.

Time	Time since start	Rate mg/hr (*recommended)	Site checked	Reactions	Nurse signatures
<i>Ensure pre-medication has been prescribed and given, and checklist signed by doctor.</i>					
	<b>0</b>	100 mg/hr* (50 ml/hr)			
	<b>30 minutes</b>	200 mg/hr* (100 ml/hr)			
	<b>1 hour</b>	300 mg/hr* (150 ml/hr)			
	<b>1.5 hours onwards</b>	400 mg/hr* (200 ml/hr)			

#### **Observations during infusion**

Blood pressure, pulse rate, respiratory rate, oxygen saturation and temperature every 15 min until maximum infusion rate reached, then every 30 min until 1 hr after completion of infusion.

#### **Reactions:**

6. Fever temperature > 38.5°C
7. Chills
8. Mucosal swelling
9. Bronchospasm
10. Hypotension (30 mmHg drop)

**Stop infusion and seek medical advice if any reactions occur. If mild, consider restarting after one hour, at half the previous rate, and if symptoms allow, increase rate gradually again. If severe, consider restarting once all symptoms have fully resolved, at half the previous rate. If reaction recurs, stop therapy completely.**