**Scottish Paediatric & Adolescent Rheumatology Network**

**Guideline for Rituximab Use**

Rituximab is an anti-inflammatory monoclonal antibody, derived from human and mouse cells. Rituximab removes B cells, therefore reducing the amount of auto-antibodies such as rheumatoid factor (RF), double stranded DNA (dsDNA) and anti-neutrophil cytoplasmic antibodies

(MPO/PR3 ANCA) and thereby reduce disease activity.

B cells reappear 4-12 months after therapy; however memory B cells can remain suppressed for up to 2 years. It has been shown to be effective in the management of many paediatric rheumatological conditions including:

* Patients with Juvenile onset Systemic Lupus Erythematosus (JSLE)
* Dermatomyositis
* Rheumatoid factor positive juvenile idiopathic arthritis (JIA)
* Systemic vasculitis who have not responded to standard treatments, such as azathioprine, mycophenolate mofetil, methotrexate and corticosteroids.
* First line treatment for patients with ANCA positive vasculitis and systemic lupus erythematosus with severe major organ involvement eg. renal or central nervous system (CNS)

**Contra-indications:**

* History of hypersensitivity to rituximab, other murine proteins or to any of the excipients
* Tuberculosis
* Severe infections e.g. sepsis, abscesses and opportunistic infections
* Moderate or severe heart failure
* Patients in a severely immunocompromised state
* Pregnancy

**Cautions:**

* History of cardiovascular disease or renal impairment (dose adjustment may be required)
* History of malignancy
* Chronic hepatitis B infection
* Heart failure
* Severe needle phobia and potential vascular access problems

**Pre-assessment considerations:**

* Full clinical history
* Height, weight, body surface area, pubertal status
* Immunisation history – Consider delaying infusion until 4 weeks post administration of live vaccinations as per green book guidance: [Greenbook\_chapter\_6.pdf (publishing.service.gov.uk)](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/655225/Greenbook_chapter_6.pdf)
* Consider COVID-19 vaccination status as per BSR guidance available at following link [COVID-19 guidance | British Society for Rheumatology](https://www.rheumatology.org.uk/improving-care/covid-19-guidance)
* Bloods including FBC, ESR, U&E, LFT, creatinine, CRP.
* Lymphocyte subsets (CD19/CD20)
* Immunoglobulins
* Disease specific antibodies:

 Antinuclear antibodies (ANA) and dsDNA in JSLE

 RF and cyclic citrullinated peptide (CCP) in JIA

 Myeloperoxidase (MPO) and proteinase 3 ANCA (PR3 ANCA) in ANCA positive vasculitis

 Myositis specific antibodies in JDM

* Varicella Zoster serology, hepatitis B and C status, HIV status, EBV and CMV IgG should be checked if not done previously and only repeated if thought to be clinically relevant.
* Chest X-ray: To be performed and resulted prior to commencing if not performed in the last 3 months and if no relevant symptoms have developed in the interim.
* Pregnancy test for all females over 12 years of age who have reached menarche.
* Patient information to be given and discussed with the patient and carers

**Dosage**

Rituximab is administered as an intravenous (IV) infusion. Dose and frequency may vary according to underlying clinical condition and clinician’s discretion.

Options include a dose of 750mg/m2 (maximum dose 1000mg) 2 weeks apart.

It may also be given at 375mg/m2 weekly for 4 weeks.

It can then be given as a single dose 6-monthly thereafter, again dose may differ according to clinical situation and clinician’s discretion.

**Premedication**

All patients will receive premedication with chlorphenamine and paracetamol, administered 60 minutes prior to infusion commencing. Methylprednisolone IV infusion is administered immediately prior to the rituximab infusion.

Paracetamol and chlorphenamine oral dosing as per BNFC.

Methylprednisolone IV injection dosing:

Children aged 1 - 5 years 50mg

Children 6 years and over 100mg

**Monitoring Prior to Infusion**

Ensure the following is complete before commencing the infusion:

* Pregnancy test for all females over 12 years of age who have reached menarche.
* Ensure there is no underlying infection.
* Site an intravenous cannula in an appropriate vein.
* Take bloods to check FBC, U&E’s, LFTs, CRP, and ESR – do not wait for blood results before starting.
* Baseline temperature, pulse, respiratory rate, blood pressure. Record these immediately prior to commencing the infusion.

**Preparation(6)**

Rituximab is prepared by pharmacy in aseptic units.

**Administration:**

* Prior to starting the infusion ensure emergency drugs are available in the ward area in case of any adverse reaction.
* All medications should be given in accordance with [hospital Safe Use of Medicines Policy](http://intranet.lothian.scot.nhs.uk/NHSLothian/Healthcare/ClinicalGuidance/General/Medicines%20Policy%20and%20procedures%20-%20December%202009.pdf).
* Check all prescribed doses of rituximab are correct for the patient.
* Administer premedication.
* Administer the rituximab infusion using an infusion set with an in-line, sterile, non-pyrogenic, low protein-binding filter (pore size 1.2 micron or less).
* Visually inspect the infusion for particulate matter, discolouration or foreign particles.
* Infuse at the prescribed, 30 minute, stepwise rate.
* Flush with 30ml of Sodium Chloride 0.9% at the end of the rituximab infusion.
* The IV Infusion rate will gradually increase during the infusion

**Monitoring**

**During the infusion**

* Monitor pulse, temperature, respiratory rate and blood pressure every 15 minutes during the patients first rituximab infusion. If well tolerated subsequent infusion monitoring can be every 30 minutes.
* Acute infusion reactions may develop anytime during or after the infusion.
* Patients should take oral prednisolone for 3 days after the infusion; Day 1 - 30mg OD, Day 2 - 20mg OD and Day 3- 10mg OD) and then continue with their normal maintenance prednisolone dose.

**Post infusion**

* Monitor pulse, temperature, respiratory rate and blood pressure every 15 minutes for 1 hour the patients first infusion
* Monitor pulse, temperature, respiratory rate and blood pressure every 30 minutes for 30 minutes post a patients second infusion.
* Advise patients and carers to report any signs of infection or possible side effects. Delayed hypersensitivity-like reactions may appear 1-14 days after the infusion.
* Advise patients and carers to seek immediate medical advice if hypersensitivity symptoms occur. Delayed reactions are more likely to occur if a patient has had a previous course of infliximab.
* Immunoglobulins and lymphocyte subsets (CD19/CD20) will be followed up at day 28 post infusion and should be checked approximately 2 monthly until B cells normalise

**Possible side effects**

See BNFc or Summary of Product Characteristics for full list of side effects.(2,5)

**Common or very common**

* Anaemia
* Constipation
* Depression
* Fever
* Gastrointestinal discomfort
* Hypertension/hypotension
* Increased risk of infection
* Infusion related reaction
* Night sweats

**Uncommon**

* Haemolytic anaemia
* Progressive multifocal leukoencephalopathy

**Rare or very rare**

* Hepatitis reactivation

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*NOTE*

*This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient’s case notes at the time the relevant decision is taken.*