**Appendix 6**

**Rituximab Administration**

*Guideline for Management of Patients Attending for Intravenous Rituximab Therapy*

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**Rituximab**

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Adapted from Guideline for Management of Patients Attending Cork University Hospital Infusion Unit

**1 Rituximab**

* 1. **Pre-administration screening**

All patients fbeing considered for Rituximab are screened for suitability prior to commencing first infusion. Investigations may include chest x ray, Mantoux test / Quantiferon, Hepatitis screen, FBC, Renal/Liver/Bone profile, CRP, IgG levels ( if on immunoglobulins).

Ensure patient has had baseline bloods including FBC, Urea and Electrolytes, Liver Function Tests. These should be done no more than 1-2 weeks prior to 1st infusion. Report abnormal results to medical team.

**Prior to infusing Rituximab the patient’s blood results are reviewed and the following parameters require medical review, bolded parameters are the normal ranges:**

* Hb (g/dl) is this <7 or > 16 (12.3-15.3g/dL)
* WCC (x109/l) is this <3.5 or > 15 (4.0-11.0x10^9)
* Neutrophils (x109/l) is this < 1.5 (1.4-6.6g/dL)
* Platelets (x 109/l) is this < 100 (140-440)
* ALT (IU/l) is this > 80 (0.0-41.0)
* Urinalysis – presence of nitrites, blood, protein, leucocytes
* Creatinine >90 (49-90)
  1. **Legal classification**

Rituximab is a monoclonal antibody that binds to the CD20 antigen on B lymphocytes and activates complement-dependent cytotoxicity.

* 1. **Indications, Dosage and Frequency of Administration**

Granulomatosis with polyangiitis and Microscopic polyangiitis

Rituximab, in combination with glucocorticoids, is indicated for the induction of remission in adult patients with severe, active Granulomatosis with polyangiitis (GPA) and Microscopic polyangiitis (MPA).

The recommended dosage of Rituximab for induction of remission therapy of Granulomatosis with polyangiitis and Microscopic polyangiitis is either **1000mg infusions on Day 0 and Day 14 or** **375 mg/m2 body surface area, administered as an intravenous infusion once weekly for 4 weeks (four infusions in total).**

First infusion:

The recommended initial infusion rate for Rituximab is 50 mg/h; subsequently, the rate can be escalated in 50 mg/h increments every 30 minutes to a maximum of 400 mg/h.

Subsequent infusions (number 2 to 4):

Subsequent infusions of Rituximab can be started at a rate of 100 mg/h and increased by 100 mg/h increments every 30 minutes to a maximum of 400 mg/h.

Pneumocystis jiroveci pneumonia (PCP) prophylaxis is recommended for patients with Granulomatosis with polyangiitis or Microscopic polyangiitis during and following Rituximab treatment, as appropriate.

**1.4 Exclusion criteria (Contraindications)**

* Hypersensitivity to the active substance or to any of the excipients used or to murine proteins.
* Active, severe infections e.g. tuberculosis, sepsis and opportunistic infections
* Patients in a severely immunocompromised state e.g. where levels of CD4 or CD8 are very low.
* Severe heart failure (New York Heart Association Class IV) or severe, uncontrolled cardiac disease.

**1.5 Precautions**

Progressive multifocal leukoencephalopathy

All patients treated with Rituximab must be given the patient alert card with each infusion. The alert card contains important safety information for patients regarding potential increased risk of infections, including progressive multifocal leukoencephalopathy (PML).

Serious infections, including fatalities, can occur during therapy with Rituximab. Rituximab should not be administered to patients with an active, severe infection (e.g. tuberculosis, sepsis and opportunistic infections) or severely immunocompromised patients (e.g. where levels of CD4 or CD8 are very low). Physicians should exercise caution when considering the use of Rituximab in patients with a history of recurring or chronic infections or with underlying conditions which may further predispose patients to serious infection, e.g. hypogammaglobulinaemia. It is recommended that immunoglobulin levels are determined prior to initiating treatment with Rituximab

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Patients reporting signs and symptoms of infection following Rituximab therapy should be promptly evaluated and treated appropriately. Before giving a subsequent course of Rituximab treatment, patients should be re-evaluated for any potential risk for infections.

Hepatitis B Infections

Cases of hepatitis B reactivation, including those with a fatal outcome, have been reported in patients receiving Rituximab. Hepatitis B virus (HBV) screening should be performed in all patients before initiation of treatment with Rituximab. At minimum this should include HBsAg-status and HBcAb-status

Immunization

* Physicians should review the patient's vaccination status and follow current immunization guidelines prior to Rituximab therapy. Vaccination should be completed at least 4 weeks prior to first administration of Rituximab.
* The safety of immunization with live viral vaccines following Rituximab therapy has not been studied. Therefore vaccination with live virus vaccines is not recommended whilst on Rituximab or whilst peripherally B cell depleted.
* Patients treated with Rituximab may receive non-live vaccinations. Should non-live vaccinations be required whilst receiving Rituximab therapy, these should be completed at least 4 weeks prior to commencing the next course of Rituximab.

Due to the long retention time of rituximab in B cell depleted patients, women of childbearing potential should use effective contraceptive methods during and for 12 months following treatment with Rituximab.

**1.6 Storage**

Store in a refrigerator (2 °C – 8 °C). Keep the container in the outer carton in order to protect from light.

The prepared infusion solution of Rituximab is physically and chemically stable for 24 hours at 2 °C - 8 °C and subsequently 12 hours at room temperature.

From a microbiological point of view, the prepared infusion solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C – 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

**1.7 Pre-medication**

Rituximab is associated with infusion related reactions (IRR), which may be related to release of cytokines and/or other chemical mediators. Premedication consisting of an analgesic/anti-pyretic drug and an anti-histaminic drug, should always be administered before each infusion of Rituximab.

Patients should receive treatment with 100 mg intravenous methylprednisolone to be completed 30 minutes prior to Rituximab infusions to decrease the incidence and severity of infusion related reactions.

**1.8 Patient observations**

* Patients Temperature, pulse, respirations and blood pressure to be monitored every 15 mins for first hour and every 30 mins thereafter until end of infusion or as patient’s condition indicates.
* The medical team should be contacted if any abnormalities noted or patient become unwell.
* Patients should be closely monitored for the onset of cytokine release syndrome. Patients who develop evidence of severe reactions, especially severe dyspnoea, bronchospasm or hypoxia should have the infusion interrupted immediately.
* Mild or moderate infusion-related reactions usually respond to a reduction in the rate of infusion. The infusion rate may be increased upon improvement of symptoms.

**1.9 Infusion reactions**

Infusion related reactions ( hypertension, nausea, rash, pyrexia, puritis, urticaria, throat irritation, hot flush, hypotension, rhinitis, rigors, tachycardia, fatigue, oropharyngeal pain, peripheral oedema, erythema). The incidence of IRR decreased with subsequent courses.

The reactions reported are usually reversible with a reduction in rate, or interruption, of Rituximab infusion and administration of an anti-pyretic, an antihistamine, and, occasionally, oxygen, intravenous saline or bronchodilators, and glucocorticoids if required. Closely monitor patients with pre-existing cardiac conditions and those who experienced prior cardiopulmonary adverse reactions. Depending on the severity of the IRR and the required interventions, temporarily or permanently discontinue Rituximab. In most cases, the infusion can be resumed at a 50 % reduction in rate (e.g. from 100 mg/h to 50 mg/h) when symptoms have completely resolved.

***See manufacturers information sheet for further information on side effects.***