

USE OF RITUXIMAB IN AUTO-IMMUNE CONDITIONS

SAFETY SCREENING AND MONITORING INFORMATION FOR CLINICIANS

Before the use of rituximab, patients need to be screened for infection, their ability to fight infection (including immunisation status) and any contraindications to use. During therapy with rituximab, patients must be monitored for adverse effects, especially infection.

There are three infections of particular concern with rituximab⁽¹⁾:

Hepatitis B (HB)

Pneumocystis jiroveci
pneumonia (PJP)

Progressive Multifocal
Leukoencephalopathy (PML)

Patients with low concentrations of Immunoglobulin G (IgG) before commencing rituximab are at particular risk of infection due to previous immunosuppression or the underlying condition for which they are receiving rituximab. Infection risk also depends on past and current immunosuppression, especially corticosteroid treatment.⁽¹⁾

It is important to treat suspected infections early. If the infection is serious, resistant to treatment or recurrent, check full blood counts, IgG concentrations and contact the patient's specialist for advice.⁽¹⁾

Below is a summary of key safety screening and monitoring that should be performed in **all** patients receiving rituximab as immunosuppressive therapy. There is no consensus about how to screen and this document serves as guidance only. Please use in conjunction with relevant local protocols and resources listed in *References and Resources*.⁽²⁻¹⁰⁾

BEFORE STARTING RITUXIMAB THERAPY

- Assess precautions and contraindications for rituximab use including hypersensitivity, severe immunosuppression, use with other cytokine modulators, and presence of malignancy, cardiovascular and lung diseases, pregnancy and lactation. [Consult Australian Medicines Handbook (AMH) and Rituximab PI].^(6, 8, 11)
- Screen the patient for active and latent infections, especially:
 - Hepatitis B (further information below)
 - Hepatitis C
 - HIV
 - Tuberculosis (TB) (Note: screening requirements determined by local TB epidemiology)
- Seek specialist advice in any patient currently suffering from or with a history of any of the above infections
- Check patient's vaccination status. Vaccination may be recommended prior to initiating rituximab in non-emergency cases- seek specialist advice.
- Measure plasma immunoglobulins^(1, 3), full blood count, liver function tests and creatinine.⁽¹¹⁾
- Consider prophylaxis for *Pneumocystis jiroveci* pneumonia (further information below).⁽⁷⁾

HEPATITIS B

Consult a liver disease specialist to discuss antiviral prophylaxis in patients with positive HB serology before commencing rituximab therapy. Monitor and manage according to guidelines to prevent HB reactivation.^(1, 2, 6)

There is a high risk of reactivation of Hepatitis B Virus (HBV) infection in patients receiving rituximab for non-malignant (and malignant) medical conditions.⁽⁷⁾ Therefore, it is important to note that:

- Rituximab should not be initiated in patients with severe active HB
- Hepatitis B virus (HBV) screening should be performed in all patients before the initiation of rituximab therapy. At a minimum, this should include HB surface antigen (HBsAg) status and Hepatitis B core antigen (anti-HBc) status.⁽⁶⁾
- If required, antiviral prophylactic treatment should begin at least one week before the start of rituximab therapy and generally continued for 12 months after stopping rituximab therapy.^(1, 6)
- Entecavir or tenofovir are generally recommended for antiviral prophylaxis.*
- Repeat investigations may be warranted for subsequent rituximab dosing (e.g. risk of exposure to viral hepatitis).

* For doses see eTG: Treatment of chronic hepatitis B⁽³⁾

PNEUMOCYSTIS JIROVECI PNEUMONIA (PJP)

PJP prophylaxis may be considered in patients receiving rituximab with any of the following factors that increase the risk of PJP infection:

- high glucocorticoid dose (\geq 20mg prednisolone daily [or equivalent] for more than 4 weeks)
- co-administration of steroid-sparing or other immunosuppressive therapy
- presence of T-cell defects
- malignancy
- significant lymphopenia.

Expert advice should be sought regarding PJP prophylaxis before the start of rituximab therapy.⁽⁷⁾

THROUGHOUT RITUXIMAB THERAPY

In conjunction with local protocol requirements, the following monitoring is recommended:

- relevant measures of therapeutic response and disease activity such as measurement of circulating CD19⁺ B cells;
- full blood count and plasma immunoglobulins before each treatment cycle;⁽⁶⁾
- infections (note, in some people B-cell recovery may take up to 2 years);
- progressive multifocal leukoencephalopathy (PML), (see below);^(4, 12)
- other adverse effects;
- vaccination status (ensure this remains up-to-date) including those with travel plans, (see below).

Always reassess precautions and contraindications to rituximab therapy including pregnancy testing (if appropriate) prior to repeat dosing.⁽⁸⁾

PROGRESSIVE MULTIFOCAL LEUCOENCEPHALOPATHY (PML)

Use of rituximab may be associated with an increased risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain, caused by the reactivation of the JC virus, which usually leads to death or severe disability.⁽¹²⁾ Patients must be monitored for any new or worsening neurological symptoms or signs suggestive of PML. If such symptoms occur, rituximab should be immediately stopped until a diagnosis of PML has been excluded. Continue monitoring for at least 12 months after the last dose.⁽⁶⁾

VACCINATIONS

- Vaccination with live vaccines is generally contraindicated for people who are severely immunocompromised.⁽⁵⁾
- Check the current [Australian Immunisation Handbook](#) for inactivated vaccines that are routinely recommended for people who are immunocompromised, and/or seek specialist advice about the most appropriate vaccinations for a patient receiving rituximab taking into account their individual circumstances.⁽⁵⁾⁽⁶⁾
- Refer patients planning to travel to an infectious diseases or travel medicine specialist for advice (vaccination, prevention and treatment of infections).

REFERENCES AND RESOURCES

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See www.nswtag.org.au/off-label-use-of-medicines for information regarding the development of this document.