Rituximab in Renal Transplantation
Prescribing Protocol

Areas where applicable	Nephrology. For inpatient use only
Authorised Prescribers:	Consultant renal physicians at Prince of Wales Hospital (POWH) and St George Hospital (SGH).
Indication for use	1. Induction therapy in highly-sensitized renal transplants at risk of antibody-mediated rejection. 2. Treatment of refractory antibody-mediated rejection
Clinical condition	Renal Transplant 1. Recipients of renal transplants at high immunological risk: positive cross-match or donor-specific antibodies by Luminex testing. 2. Antibody-mediated rejection: transplant biopsy histology and immunohistochemistry, donor-specific antibody
Contra-indications	Sepsis
Precautions	Infusion reactions (fever, bronchospasm, rash, myalgia).
Proposed Place in Therapy	1. First line in pre-transplant in highly sensitized recipients (HSR) 2. First or second line for the treatment of biopsy proven refractory antibody-mediated rejection (AMR) with use of plasma exchange and intravenous immunoglobulin (IVIG)
If part of combination therapy, list other drugs	All patients will have received immunosuppression with basiliximab, steroids, mycophenolate, a calcineurin inhibitor and in some patients antithymocyte globulin.
Dosage	Rituximab 375 mg/m^2 used as 1. a single infusion pre-transplant in HSR 2. 1 or 2 infusions for the treatment of AMR
Duration of therapy	1 or 2 doses only
Important Drug Interactions	Nil
Administration instructions	**Take precautions when handling this drug.** **Wear protective clothing including gloves and face mask.** **For IV infusion only**. Dilute in glucose 5% or sodium chloride 0.9% to a concentration of 1 to 4 mg/mL. Diluted solution should be administered immediately after preparation. When prepared by pharmacy under aseptic conditions the diluted solution is stable at 2 to 8 ^{o}C for up to 24 hours. First Infusion should be commenced at a rate of 50 mg/hour. If hypersensitivity or infusion related reactions **do not** occur, escalate the infusion rate by 50 mg/hour increments every 30 minutes, to a maximum of 400 mg/hour. Subsequent Infusions can be administered at an initial rate of 100 mg/hour and increased by 100 mg/hour at 30 minute intervals, to a maximum of 400 mg/hour.

Monitoring requirements Safety Effectiveness	Vital signs during infusion, CD19 cell count as marker of efficacy Monitor during infusion for febrile reactions and subsequently (by clinical assessment) for infection. Resolution of or prevention of rejection (transplant biopsy, serial donor-specific antibody titres, serum creatinine, CD19 cell count)
Management of complications	Premedication with paracetamol, hydrocortisone and/or antihistamine. Slow or stop infusion if infusion reaction occurs. Severe reaction may require treatment as per anaphylaxis. Transient hypotension may occur and consideration should be given to withholding any antihypertensive medication for 6 to 24 hours prior to infusion
Basis of Protocol/Guideline:	Vo AA New England J Med (2008) 359,2 242-251 Vo AA, Transplantation, 2014, 89, 3, 312-319 Pescovitz MD Am J Transplantation (2006) 6 859-866 Pescovitz MD, Diabetes Care, 2014, 37, 2, 453-459 Grafalis M Am J Kid Diseases (2009) 53,3 370-372 Nicholas A, Transplant International, 2013, 26, 6, 563-575 Rituximab monograph, Australian Injectable Drugs Handbook, 6th Edition, Society of Hospital Pharmacists of Australia, Australia, 2015 Product information Mabthera®, Roche products Pty Ltd, last updated 1/8/14, available via Clinical Information Access Project (CIAP)
Groups consulted in development of this guideline	V1: Department of Nephrology, POWH V1: A Fischmann, Renal Pharmacist, POWH V2: Department of Nephrology POWH

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GOVERNANCE	
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Chairperson, Drug and QUM Committee	Dr James Mackie
Process for removal of previous version of Protocol/Guideline completed	Not published for SESLHD. Local paper copies of V1 (SESIAHS) removed and destroyed by transplant coordinators at POWH and SGH
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