# Prescribing Protocol
# Ravulizumab

Health
South Eastern Sydney
Local Health District

| Prescribing Protocol Template for New Drugs | |
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| **Title** | Ravulizumab Prescribing Protocol |
| **Areas where Protocol/Guideline applicable e.g. District, Hospital, ITU, Ward** | Ambulatory Care Units and Haematology Oncology Day Centres within SESLHD |
| **Areas where Protocol/Guideline not applicable** | Areas other than those above |
| **Authorised Prescribers** | Haematology Consultants and Advanced Trainees |
| **Indication for use** | Ravulizumab is indicated for the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH). |
| **Clinical condition** | Patients with a diagnosis of PNH by flow cytometry<br>AND<br>PNH Granulocyte clone size greater than or equal to 10%<br>AND<br>Lactate dehydrogenase (LDH) greater than or equal to 1.5 x Upper Limit of Normal (ULN)<br>One of the following:<br>Thrombosis requiring therapeutic anticoagulant therapy<br>Anaemia where causes other than haemolysis have been excluded and demonstrated by more than one measure of less than or equal to 70g/L, or by more than one measure of less than or equal to 100g/L with concurrent symptoms of anaemia<br>Pulmonary insufficiency with debilitating shortness of breath and/or chest pain resulting in limitation of normal activity and/or established diagnosis of pulmonary arterial hypertension where causes other than PNH have been excluded<br>Renal insufficiency with eGFR less than or equal to 60mL/min/1.73m$^2$ where causes other than PNH have been excluded. |
| **Contra-indications** | Aplastic anaemia with two or more of:<br>- Neutrophil count <0.5 x $10^9$/L<br>- Platelet count <20 x $10^9$/L<br>- Reticulocytes <25 x $10^9$/L<br>- Severe bone marrow hypocellularity<br>Presence of another life threatening disease or severe disease where the long term prognosis is unlikely to be influenced by therapy (e.g. acute myeloid leukaemia, high risk myelodysplastic syndrome) |
| **Precautions** | Ravulizumab increases the risk of menigococcal infections. Patients must receive meningococcal vaccination prior to or at the time of initiating Ravulizumab. Patients who initiate Ravulizumab treatment less than 2 weeks after receiving a meningococcal vaccine must recive treatment with appropriate prophylactic antibiotics until 2 weeks after vaccination. |
| **Place in Therapy** | First line therapy |

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| If part of combination therapy, list other drugs | Nil |
| **Dosage**<br>(Include dosage adjustment for specific patient groups) | Loading Dose (by patient's actual body weight):<br>≥ 40 to < 60kg - 2400mg<br>≥ 60 to < 100kg - 2700mg<br>≥ 100kg - 3000mg<br>Maintenance doses should be administered at a once every 8-week interval, starting 2 weeks after loading dose administration<br>Maintenance Dose (by patient's actual body weight):<br>≥ 40 to < 60kg - 3000mg<br>≥ 60 to < 100kg - 3300mg<br>≥ 100kg - 3600mg |
| **Duration of therapy** | Ongoing - PNH is a chronic disease and treatment with ravulizumab is recommended to continue for the patient's lifetime. |
| **Important Drug Interactions** | Live vaccines |
| **Administration instructions** | Ravulizumab is administered IV, and must be diluted to a concentration of 5mg/mL with sodium chloride 0.9% prior to use. Please see appendix 1 for information regarding volume of diluent, total volume and infusion rate<br>• Ravulizumab should be prepared by a healthcare professional using aseptic technique. Prepare and administer in line with Work Health and Safety-Monoclonal Antibodies Safe Handling and Management SESLHDPR/368<br>• Ravulizumab must be diluted to a final concentration of 5 mg/mL.<br>• The prescribed dose is determined based on the individual patient's weight (see above).<br>• Each vial should be visually inspected; the solution should be free of any particulate matter or precipitation. Do not use if there is evidence of particulate matter or precipitation.<br>• The calculated volume of should be withdrawn from the appropriate number of vials and diluted into required volume of sodium chloride 0.9% for infusion.<br>• Mix gently, do not shake.<br>**Administration-**<br>• *For intravenous infusion ONLY, Do not administer as an intravenous push or bolus injection.*<br>• The prepared solution should be administered immediately following preparation. If not used immediately after reconstitution, storage times must not exceed 24 hours at 2°C – 8°C or 6 hours at room temperature. |

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| | • Infusion must be administered through a 0.2 micrometre filter<br>• The line should be flushed with sodium chloride 0.9% on completion of the infusion |
| **Monitoring requirements**<br><br>Safety | <u>Safety:</u><br>There must be ongoing evidence of current vaccination for Meningococcal disease<br>• Prior to each infusion patients should be monitored for early signs of meningococcal infections. Contact medical officer immediately if there are concerns regarding infective symptoms such as:<br>  ○ Rash<br>  ○ Fever<br>  ○ Headache<br>  ○ Photophobia<br>  ○ Neck stiffness<br>• Prescribing medical officer is to be contacted to review patient prior to <u>initial</u> infusion commencement and ensure consent for treatment is obtained<br><br>The following bloods are required within one week prior to each infusion for ongoing monitoring by the treating medical officer:<br>• Full Blood Count (FBC),<br>• Lactate Dehydrogenase (LDH),<br>• Liver Function Tests (LFT),<br>• Urea Electrolytes and Creatinine (UEC),<br>• haptoglobin<br>• reticulocyte count<br><br>Observations (Temp / HR / RR / BP / $SpO_2$%) should be completed:<br>• prior to infusion<br>• at the mid-way point of infusion<br>• at completion of infusion<br>• prior to discharge<br><br>Patients must be observed for 1 hour post completion of infusion for signs of infusion related reactions. |
| Effectiveness | <u>Effectiveness:</u><br>Improvement or stabilisation of disease as evidenced by monitoring of blood tests results (including haemoglobin, white cell count, platelet count, neutrophil count, lactate dehydrogenase, urea and electrolytes), granulocyte clone size, as well as clinical criteria (dependent on criteria for initial treatment) of thrombosis, transfusion requirement, anaemia, pulmonary insufficiency, renal insufficiency, or smooth muscle spasm. |
| **Management of complications** | Patients who experience a reaction during the administration of Ravulizumab should be treated according to local guidelines.<br>For a Grade 1 or Grade 2 (mild) infusion reaction, the infusion should be temporarily stopped. Treatment with an antihistamine (e.g. loratidine 10mg orally or equivalent) and paracetamol (1 gram orally) may be considered. If the patient's signs and symptoms resolve (with or without administration of the above medication), the infusion may be restarted. However, the patient should be infused at a slower rate and be monitored closely for |

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| | any signs and symptoms of infusion reactions during the remainder of the infusion.<br>Any patient experiencing an infusion reaction should be observed in the clinic until resolution of the reaction, or until the treating medical officer determines the patient is no longer at risk. |
| **Basis of Protocol/Guideline** (including sources of evidence, references) | Australian Product Information - Ultomiris (Ravulizumab RCH) concentrated solution for intravenous infusion |
| **Groups consulted in development of this protocol** | Haematology department, St George Hospital, Manufacturer, Ambulatory Care Unit, St George Hospital |

| **AUTHORISATION** | |
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| **GOVERNANCE** | |
| Enactment date | October 2020 |
| Expiry date: (maximum 36 months from date of original approval) | 31 October 2023 |
| Ratification date by SESLHD QUM Committee | 01 October 2020 |
| Chairperson, QUM Committee | Dr John Shephard |
| Version Number | 1.0 |

## Appendix 1 – Dosing and Administration Guide

| Dose Type | Body Weight (kg) | Dose (mg) | Ravulizumab Volume (mL) | Sodium chloride 0.9% Volume (mL) | Total Volume (mL) | Minimum Infusion Duration minutes (hours) | Maximum Infusion Rate (mL/hour) |
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| Loading | ≥ 40 to < 60 | 2400 | 240 | 240 | 480 | 114 (1.9) | 253 |
| | ≥ 60 to < 100 | 2700 | 270 | 270 | 540 | 102 (1.7) | 318 |
| | ≥ 100 | 3000 | 300 | 300 | 600 | 108 (1.8) | 333 |
| Maintenance | ≥ 40 to < 60 | 3000 | 300 | 300 | 600 | 140 (2.4) | 250 |
| | ≥ 60 to < 100 | 3300 | 330 | 330 | 660 | 120 (2.0) | 330 |
| | ≥ 100 | 3600 | 360 | 360 | 720 | 132 (2.2) | 328 |