Prescribing Protocol SESLHDPR/629
Ocrelizumab for Multiple Sclerosis

Health
South Eastern Sydney
Local Health District

Prescribing Protocol	
Title	Ocrelizumab for Multiple Sclerosis
Areas where Protocol/Guideline applicable	Adult Neurology patients in Ambulatory Care areas
Areas where Protocol/Guideline not applicable	All other areas, including inpatient settings
Authorised Prescribers	Neurology Consultants (*note: Neurology Advanced Trainees can prescribe subsequent prescriptions)*
Indication for use	Relapsing-remitting multiple sclerosis as the sole PBS subsidised disease modifying therapy for MS in accordance with PBS Section 100 criteria. For more information see: http://www.pbs.gov.au/medicine/item/11237K-11242Q
Clinical condition	In accordance with PBS criteria: - At initiation patients must be ambulatory (without assistance/support) and have experienced 2 more attacks of neurological dysfunction whilst on a PBS subsidised disease modifying treatment - For continuing treatment patients must not have progression of disability and must tolerate ocrelizumab therapy
Contra-indications	Ocrelizumab is contraindicated in patients with a known hypersensitivity to ocrelizumab or any of the excipients
Precautions	• Vaccination: Consider immunisation needs and give vaccinations at least 6 weeks prior to starting treatment. Efficacy of vaccines during treatment is not known. Live vaccinations are not recommending during treatment or until B cell repletion • Acute Infection: Delay ocrelizumab until any acute infection is resolved. • Chronic Infection: –Risk of reactivation (hepatitis, TB, HIV) • Treatment with other immunosuppresants: Increases risk of serious infection (except corticosteroids for symptomatic relapse treatment) • Active malignancy – avoid use due to increased incidence in clinical trials Pregnancy and Breastfeeding – limited data. Ensure effective contraceptive during treatment and for 6 months after treatment. • Age > 55 years of age: The safety and efficacy in patients > 55 years of age have not been established. • Infusion related reactions are common. Emergency treatment for reactions must be available. • Progressive multifocal leukoencephalopathy (PML): Cases of PML have been associated with ocrelizumab, monitor for any neurological signs or symptoms suggestive of PML and stop treatment immediately if it is suspected
Place in Therapy	Patient must have experienced at least 2 documented attacks of neurological dysfunction, believed to be due to multiple sclerosis, in the preceding 2 years of commencing a PBS-subsidised disease modifying therapy for this condition.

<table>
<tr><td>If part of combination therapy, list other drugs</td><td>Pre-medication is required prior to every infusion.
- Methylprednisolone 100mg IV approximately 30 minutes prior to each dose
- An oral antihistamine approximately 30-60 minutes before each dose
Optional:
- Paracetamol 1g PO may be considered approximately 30-60 minutes before each dose.</td></tr>
<tr><td>Dosage
(Include dosage adjustment for specific patient groups)</td><td>IV infusion, initial dose 300 mg followed by 300 mg 2 weeks later; then, 6 months after the first infusion, give 600 mg every 6 months.(A minimum interval of 5 months should be maintained between each dose of ocrelizumab.)</td></tr>
<tr><td>Duration of therapy</td><td>Ongoing according to response</td></tr>
<tr><td>Important Drug Interactions</td><td>No formal drug interaction studies have been performed as no drug interactions are expected via CYP and other metabolising enzymes or transporters</td></tr>
<tr><td>Administration instructions</td><td>Preparation:
Prepare and administer in line with Work Health and Safety- Monoclonal Antibodies Safe handling and Management SESLHDPR/368 (moderate risk).
Protective gloves, safety glasses and mask must be worn during drug preparation.

Ocrelizumab may contain fine translucent and/or reflective particles associated with enhanced opalescence. Do not use the solution if discoloured or if the solution contains discrete foreign particulate matter.

After dose preparation and dilution, invert the bag and mix gently. Infusion solutions are stable for 8 hours when stored below 25°C and 24 hours when stored between 2-8°C

Prior to the start of the IV infusion, the content of the infusion bag must be at room temperature to avoid an infusion reaction.

Administration:
The diluted infusion solution must be administered using an infusion set with a 0.2 or 0.22 micron in-line filter.

<table>
<tr><th>Infusion Dose</th><th>Dose and dilution with sodium chloride 0.9%</th><th>Infusion Rate</th></tr>
<tr><td>Initial Dose (600mg)
Divided into 2 infusions</td><td>300mg in 250mL

300mg in 250mL (2 weeks later)</td><td>Start the infusion at 30 mL/hr. If well tolerated increase the rate by 30 mL/hr increments every 30 minutes to a maximum rate of 180 mL/hr.
Each 300mg infusion should be given over approximately 2.5 hours</td></tr>
<tr><td rowspan="2">Subsequent Doses (600mg)
Single infusion once every 6 months</td><td>Option 1:
600mg in 500mL</td><td>Start at 40 mL/hr and if well-tolerated increase by 40 mL/hour every 30 minutes to a maximum rate of 200 mL/hour
Each 600mg infusion should be given over approximately 3.5 hours</td></tr>
<tr><td>Option 2 if doses have been well tolerated:
600mg in 500mL</td><td>Start the infusion at 100 mL/hour for the first 15 minutes, increase the rate to 200 mL/hour for the next 15 minutes, then increase to 250 mL/hour for 30 minutes and 300 mL/hour for the last 60 minutes
Each 600mg infusion should be given over approximately 2 hours</td></tr>
</table></td></tr>
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Monitoring requirements	Infusion related reactions (IRR) may occur during any infusion, but are most commonly associated with the first infusion. IRRs may be severe including dyspnoea, pharyngeal or laryngeal oedema, anaphylaxis, hypotension, pyrexia, fatigue, nausea and tachycardia. Other reactions may present as pruritus, rash, urticaria, erythema, throat irritation, oropharyngeal pain, flushing, headache or dizziness. Reactions may occur up to 24 hours after the infusion. Monitor the patient during infusion and for at **least one hour after the infusion**
Management of complications	**Life-threatening IRRs**: Immediately stop Ocrelizumab if there are signs of a life-threatening or disabling IRR during an infusion, such as acute hypersensitivity or acute respiratory distress syndrome. The patient should receive appropriate supportive treatment. Permanently discontinue ocrelizumab in these patients. **Severe IRRs**: If a patient experiences a severe IRR or a complex of flushing, fever, and throat pain symptoms, the infusion should be interrupted immediately and the patient should receive symptomatic treatment. The infusion should be restarted only after all symptoms have resolved. The initial infusion rate at restart should be half the infusion rate at the time of onset of the reaction. **Mild to Moderate IRRs**: If a patient experiences a mild to moderate IRR (e.g. headache), the infusion rate should be reduced to half the rate at the onset of the event. This reduced rate should be maintained for at least 30 minutes. If tolerated, the infusion rate may then be increased according to the patient's initial infusion schedule.
Practice Points	HBV screening should be carried out prior to commencing on treatment. Patients should be informed IRRs can occur within 24 hours of an infusion. If IRR symptoms are noted post-discharge, the patient should be advised to contact their healthcare team immediately **First aid measures** Eye contact - rinse immediately with tap water for at least 20 minutes – open eyelids forcibly begin with medical treatment. Skin contact - remove immediately contaminated clothes, wash affected skin with water and soap - do not use any solvents Inhalation - remove the casualty to fresh air in the event of symptoms get medical treatment
Basis of Protocol/Guideline (including sources of evidence, references)	Ocrevus Product Information Roche PI 170623 AIDH, AMH Introducing OCREVUS® a guide for health professionals Roche Safety Data Sheet OCREVUS® Vials 300 mg/10 mL- Roche
Consultation	Pharmacy dept, POWH

AUTHORISATION	
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GOVERNANCE	
Enactment date Renewal date	August 2018 September 2021
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Chairperson, QUM Committee	Dr John Shephard
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