SESLHD/MG 117

Medicine Guideline

Belatacept (Nulojix®) for prophylaxis of organ rejection in adult patients receiving/received a kidney transplant

Important information	Belatacept is an unapproved medicine in Australia and is supplied under the Special Access Scheme. The prescribing Medical Officer should therefore ensure completion of the following:- 1. Category B Special Access Scheme (SAS) form. If patient is seriously ill and premature death is reasonably likely to occur in the absence of early treatment, Category A SAS form can be completed. Forms must be submitted electronically via https://compliance.health.gov.au/sas/ 2. Documentation in patient's medical record. Consent for Exceptional Use of Medicine (SEI020025) - to be filed in patient's medical record.
Brand	This Medicine Guideline is for Nulojix® brand.
Areas where Protocol/Guideline applicable	SESLHD inpatient and outpatient settings
Authorised Prescribers:	Nephrologist/Nephrology Registrar after discussion with transplant physician in SESLHD.
Indication for use	Used in lieu of calcineurin inhibitors as a maintenance immunosuppressive agent alongside corticosteroids and mycophenolate mofetil/mycophenolic acid.
Formulary Status	Belatacept is not listed on the SESLHD Medicines Formulary. Individual Patient use (IPU) approval must be sought prior to prescribing.
Clinical condition Patient selection: Inclusion criteria (list investigations necessary and relevant results)	See place in therapy section below
Proposed Place in Therapy State whether drug to be used as first, second or third line. When not first line, describe therapies to be used first. (Consider using algorithm)	Only in specific transplanted individuals after there is consensus across the medical transplant team at Prince of Wales (transplanting centre of SESLHD). These patients include those who have: 1. Been demonstrated to have had an intolerance of, or significant side-effect (including, but not limited to, thrombotic microangiopathy, seizures) of calcineurin inhibitors, OR

	2. those with demonstrated malabsorption of calcineurin inhibitors; AND where replacement of the calcineurin inhibitor with a mammalian target of rapamycin inhibitor (mTORi) is (relatively) contraindicated. Individual Patient Use (IPU) submission and approval required for each individual patient prior to commencing treatment.
Adjunctive Therapy If part of combination therapy, list other drugs	Corticosteroids and mycophenolate mofetil/mycophenolic acid.
Contra-indications	Patients who are EBV seronegative or with unknown EBV serostatus, due to increased risk of Post-Transplant Lymphoproliferative Disorder (PTLD), particularly involving the CNS.
Precautions	- Post-Transplant Lymphoproliferative Disorder (PTLD): increased risk, predominantly involving the CNS; monitor for new or worsening neurological, cognitive, or behavioural signs and symptoms. - Other malignancies: increased risk with all immunosuppressants; appears related to intensity and duration of use. Avoid prolonged exposure to UV light and sunlight. - Progressive Multifocal Leukoencephalopathy (PML): increased risk; consider in the diagnosis of patients reporting new or worsening neurological, cognitive, or behavioural signs and symptoms. Recommended doses of immunosuppressants should not be exceeded. - Other serious infections: increased risk of bacterial, viral, fungal, and protozoal infections, including opportunistic infections and tuberculosis. Some infections were fatal. Polyoma virus-associated nephropathy can lead to kidney graft loss; consider reduction in immunosuppression. Evaluate for tuberculosis and initiate treatment for latent infection prior to NULOJIX use. Cytomegalovirus and pneumocystis prophylaxis are recommended after transplantation. - Liver transplant: use is not recommended. - Acute Rejection and Graft Loss with Corticosteroid Minimization: corticosteroid utilisation should be consistent with the NULOJIX clinical trial experience.
Important Drug Interactions	Antithymocyte globulin (ATG) rabbit (Thymoglobuline®): co-administration of the first belatacept dose with ATG may increase the risk of venous thrombosis of the renal allograft. Immunisations: avoid use of live vaccines during treatment.
Dosage (Include dosage	The total infusion dose of belatacept should be based on the actual body weight of the patient at the time of transplantation and should not be modified during the course of therapy, unless there is a change in body

adjustment for specific patient groups)	weight of greater than 10%. The prescribed dose of belatacept must be evenly divisible by 12.5 mg in order for the dose to be prepared accurately using the reconstituted solution and the silicone-free disposable syringe provided. Evenly divisible increments are 0, 12.5, 25, 37.5, 50, 62.5, 75, 87.5, and 100. For example: A patient weighs 64 kg. The dose is 10 mg per kg. Calculated Dose: 64 kg × 10 mg per kg = 640 mg. The closest doses evenly divisible by 12.5 mg below and above 640 mg are 637.5 mg and 650 mg. The nearest dose to 640 mg is 637.5 mg. Therefore, the actual prescribed dose for the patient should be 637.5 mg. **Dosing regimen:** **A. Induction and maintenance at time of transplant (in combination with basiliximab induction, mycophenolate and corticosteroids):** Initial: 10mg/kg before transplantation on day of surgery (Day 0), repeated on post-transplant Day 4 (approximately 96 hours after the Day 0 dose), Day 13 and Day 27, then at the end of Week 8 and 12. Maintenance phase: 5mg/kg every 4 weeks (± 3 days) starting at the end of Week 16. **B. Switching from calcineurin Inhibitor: 5mg/kg every 2 weeks for 5 doses, then every 4 weeks thereafter. CNI dose should be reduced to 40-60% of baseline dose by day 15, and then to 20- 30% of baseline dose by day 22 and discontinued on day 29.** The dose prescribed for the patient must be evenly divisible by 12.5 mg (see instructions above; e.g., evenly divisible increments are 0, 12.5, 25, 37.5, 50, 62.5, 75, 87.5, and 100). Note that drug vials come with 250mg per vial.
Duration of therapy	Dependent on the scenario, at the discretion of the SESLHD transplant medical team.
Prescribing Instructions	Outpatient Prescribing on the Intravenous Adult Fluid Order Form
Administration	Belatacept is for intravenous infusion only. Patients do not require premedication prior to administration of belatacept.

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Instructions	
	Storage: Powder must be refrigerated (2-8˚C) and protected from light. Reconstituted vials may be refrigerated (2-8˚C), protected from light and used within 24 hours. The reconstituted solution is stable at room temperature, between 20 and 25˚C for up to 4 hours under room light. **Administration:** Intravenous infusion via non-pyrogenic, low-protein-binding filter over 30 mins. Pre-medications: None required. **Equipment for preparation:** • 1 x 18- to 21-gauge needle • 1 x 12mL silicone-free Norm-Ject® syringe (provided with product) (ONE syringe per VIAL) • 2 x 100mL bags of either sodium chloride 0.9% OR glucose 5% • 1 x alcohol swab • 1 x 1.2µm low-protein binding Filter Extension Set (provided with product) • 1 x giving set NB. Belatacept must only be reconstituted with the non-siliconized Norm-Ject® syringe to avoid formation of particulates. The in-line filter is an added safety measure to capture any other particles that may be present during normal aseptic reconstitution. **Handling precautions:** As for other immunosuppressive agents, wear PPE when reconstituting the vial and preparing the infusion solution to minimise exposure (i.e. N95/P2 mask and gloves). **Preparation of dose:** 1. Allow the appropriate number of belatacept vials to stand at room temperature for approximately 5 minutes. 2. Using a 18- to 21-gauge needle and the SILICONE-FREE DISPOSIBLE “NORM-JECT®” SYRINGE provided with each vial, withdraw 10.5mL (per 250mg vial) for reconstitution from the 100mL bag of either sodium chloride 0.9% or glucose 5% which you will be using for the final dilution. Note: A separate syringe should be used for each vial required.

3. Remove flip-top from vial and wipe the top with an alcohol swab.

4. Insert syringe needle through the middle of the rubber stopper and direct the stream down the glass wall of the vial to minimise foaming. Leaving syringe inserted into vial, rotate the vial and invert with gentle swirling to dissolve. DO NOT SHAKE. Note: reconstituting contents of the vial will cause it to become pressurised.

5. Allow the reconstituted solution to stand for a few minutes to allow any foam to dissipate. The solution should be clear colourless to pale yellow, essentially free from particulate matter on visual inspection.

6. Using the same silicone-free syringe for each vial, inject the required contents of the reconstituted 250mg vial(s) into the 100mL bag from Step 1 (note: reconstitution fluid must be the same as the fluid used for final dilution). Gently rotate bag to ensure mixing. Final concentration should be 2-10mg/mL.

7. Connect giving-set and STERILE, NON-PYROGENIC, LOW-PROTEIN-BINDING FILTER (PORE SIZE 1.2µm) and prime with a 100mL bag of fluid (same fluid as used for final dilution) to eliminate bubbles in the line or filter.

8. Connect belatacept infusion bag to line and filter and administer to patient over 30 minutes.

9. Once infusion is complete, flush line with 20 to 30mL of the same fluid used for dilution to ensure all drug is delivered.

**** If a syringe containing silicone is accidentally used the solution may develop a few translucent particles and must be discarded.****

Observations:
Baseline blood pressure and pulse should be performed every 15 minutes during the infusion and for a further 30 minutes after infusion is complete.

Monitoring requirements Safety Effectiveness (state objective criteria)	FBC, UEC, CMP, LFTs, CMV DNA and EBV DNA monthly for the first 6 months, then every 3 months minimum. **Safety:** **Possible infusion reactions (within 1 hour of infusion):** Hypotension, Hypertension, flushing and headache. **Adverse Effects:** Increased susceptibility to infections, increased risk of malignancy (including skin), increased sensitivity to sun light, proteinurea, increased blood creatinine, pyelonephritis, diarrhoea, graft dysfunction, leucopenia, hypophosphataemia, anaemia, dehydration, peripheral oedema, constipation, cough, nausea, vomiting, headache. Post-transplant lymphoproliferative disorder (PTLD). If a patient exhibits new or worsening neurological, cognitive, or behavioural signs or symptoms, PTLD should be considered. Progressive multifocal leukoencephalopathy (PML). If the patient exhibits new or worsening neurological, cognitive, or behavioural signs or symptoms, a diagnosis of PML should be ruled out. **Efficacy:** Estimated renal function by eGFR (calculated on UECs).
Management of Complications	Treating nephrologist at the patient's primary hospital, and at the complex transplant clinic if required.
Basis of Protocol/Guideline: (including sources of evidence, references)	1. https://packageinserts.bms.com/pi/pi_nulojix.pdf 2. Belatacept monograph, Micromedex® 2.0, (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com.acs.hcn.com.au/ (cited: 02/12/2024). 3. Belatacept monograph, Collingwood, Vic: Australian Injectable Drugs Handbook 9th Edition. Updated 2nd December 2024. Accessed 13/12/2024.
Groups consulted in development of this	Prince of Wales acute transplant medical team Prince of Wales renal pharmacist

guideline	

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