VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

Nulojix (Belatacept)

Effective Date: 12/14/11

Date Developed: 12/14/11 by Albert Reeves MD

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Nulojix (Belatacept) is aSelective T-Cell Costimulation Blocker (Transplant)

Pre-Authorization Criteria:

VCHCP will authorize Nulojix for FDA approved use: Prophylaxis of organ rejection concomitantly with basiliximab, mycophenolate, and corticosteroids in Epstein-Barr virus (EBV) seropositive kidney transplant recipients.

VCHCP requires that Nulojix be prescribed by a Transplant Specialist.

Dosing: Adult

Note: Dosing is based on actual body weight at the time of transplantation; do not modify weight-based dosing during course of therapy unless the change in body weight is >10%. The prescribed dose must be evenly divisible by 12.5 mg to allow accurate preparation of the reconstituted solution using the provided required disposable syringe for preparation. For example, the calculated dose for a 64 kg patient: 64 kg x 10 mg per kg = 640 mg. The nearest doses to 640 mg that are evenly divisible by 12.5 mg would be 637.5 mg or 650 mg; the closest dose to the calculated dose is 637.5 mg, therefore, 637.5 should be the actual prescribed dose for the patient.

Kidney transplant, prophylaxis of organ rejection: I.V.:

Initial phase: 10 mg/kg/dose on Day 1 (day of transplant, prior to implantation) and on day 5 (~96 hours after Day 1 dose), followed by 10 mg/kg/dose given at the end of Week 2, Week 4, Week 8, and Week 12 following transplantation

Maintenance phase: 5 mg/kg/dose every 4 weeks (plus or minus 3 days) beginning at Week 16 following transplantation

Dosing: Geriatric

Refer to adult dosing.

Dosage Forms: U.S.

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Injection, powder for reconstitution:

Nulojix®: 250 mg [contains sucrose 500 mg/vial]

Administration

Administer as an I.V. infusion over 30 minutes using an infusion set with a 0.2-1.2 micron low protein-binding filter. Prior to administration, inspect visually and do not use if solution is discolored or contains particulate matter.

WARNINGS / PRECAUTIONS

Concerns related to adverse effects:

Infections: **[U.S. Boxed Warning]: Risk for infection is increased.** Immunosuppressive therapy may lead to opportunistic infections, sepsis, and/or fatal infections. Tuberculosis (TB) is increased; test patients for latent TB prior to initiation, and treat latent TB infection prior to use.

Latent viral infections: Patients receiving immunosuppressive therapy are at an increased risk of activation of latent viral infections, including John Cunningham virus (JCV) and BK virus infection. Activation of JCV may result in progressive multifocal leukoencephalopathy (PML), a rare and potentially-fatal condition affecting the CNS. Symptoms of PML include apathy, ataxia, cognitive deficiencies, confusion, and hemiparesis. Polyoma virus-associated nephropathy (PVAN), primarily from activation of BK virus, may also occur and lead to the deterioration of renal function and/or renal graft

loss. Risk factors for the development of PML and PVAN include immunosuppression and treatment with immunosuppressant therapy. The onset of PML or PVAN may warrant a reduction in immunosuppressive therapy; however, in transplant recipients, the risk of reduced immunosuppression and graft rejection should be considered.

Lymphoproliferative disorders: **[U.S. Boxed Warning]: Risk of post-transplant lymphoproliferative disorder (PTLD) is increased, primarily involving the CNS,** in patients receiving belatacept compared to patients receiving cyclosporine-based regimens. Degree of immunosuppression is a risk factor for PTLD developing; do not exceed recommended dosing. Patients who are Epstein-Barr virus seronegative (EBV) are at an even higher risk; use is contraindicated in patients without evidence of immunity to EBV. Cytomegalovirus (CMV) infection also increases the risk for PTLD; CMV prophylaxis is recommended for a minimum of 3 months following transplantation. Although CMV disease is a risk for PTLD and CMV seronegative patients are at an increased risk for CMV disease, the clinical role, if any, of determining CMV serology to determine risk of PTLD development has not been determined.

Malignancy: **[U.S. Boxed Warning]: Risk for malignancy is increased.** Malignancy, including skin malignancy and post-transplant lymphoproliferative disease, is associated with the use of immunosuppressants, including belatacept; higher than recommended doses or more frequent dosing is not recommended; patients should be advised to limit their exposure to sunlight/UV light.

DRUG Interactions

(For additional information: Launch Lexi-Interact™ Drug Interactions Program)

BCG: Immunosuppressants may diminish the therapeutic effect of BCG. *Risk X: Avoid combination*

Belimumab: Belatacept may enhance the adverse/toxic effect of Belimumab. *Risk X: Avoid combination*

Coccidioidin Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioidin Skin Test. *Risk C: Monitor therapy*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Mycophenolate: Belatacept may increase serum concentrations of the active metabolite(s) of Mycophenolate. *Risk C: Monitor therapy*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). *Risk C: Monitor therapy*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Vaccinial infections may develop. Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

REFERENCES

1. Durrbach A, Pestana JM, Pearson T, et al, "A Phase III Study of Belatacept versus Cyclosporine in Kidney Transplants from Extended Criteria Donors (BENEFIT-EXT Study)," *Am J Transplant*, 2010, 10(3):547-57. [PubMed 20415898]

2. Latek R, Fleener C, Lamian V, et al, "Assessment of Belatacept-Mediated Costimulation Blockade Through Evaluation of CD80/86-Receptor Saturation," *Transplantation*, 2009, 87(6):926-33. [PubMed 19300198]

3. Levy GA, "Progress in Transplantation," *Ther Drug Monit*, 2010, 32(3):246-9. [PubMed 20418803]

4. Martin ST, Tichy EM, and Gabardi S, "Belatacept: A Novel Biologic for Maintenance Immunosuppression After Renal Transplantation," *Pharmacotherapy*, 2011, 31(4):394-407. [PubMed 21449628]

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