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Last P&T Approval/Version: 10/25/2023
Next Review Due By: 10/2024
Policy Number: C9968-A

Nulojix (belatacept)

PRODUCTS AFFECTED

Nulojix (belatacept)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Prophylaxis of organ rejection

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

PLEASE CONSULT TRANSPLANT TEAM FOR COORDINATION OF RENAL TRANSPLANT APPROVALS
A. PROPHYLAXIS OF ORGAN REJECTION PRE-TRANSPLANT:

1. Documentation of history of renal transplant or scheduled transplant within the next 14 days.
   AND
2. Documentation member is Epstein-Barr virus (EBV) seropositive [DOCUMENTATION REQUIRED]
   AND
3. Documentation member is using in combination with basiliximab induction, mycophenolate mofetil and corticosteroids
   AND
4. Documentation member was evaluated for tuberculosis and treatment (if needed) for latent infection was initiated prior to Nulojix
   AND
5. For patients continuing therapy after inpatient stay for transplant: See transplant team approval- PROVIDE REFERRAL DATA

CONTINUATION OF THERAPY:

A. PROPHYLAXIS OF ORGAN REJECTION:

1. Documentation member is responsive to therapy demonstrated by no signs or symptoms of acute/chronic kidney rejection
   AND
2. Prescriber attests to continued use of mycophenolate and corticosteroid utilization is consistent with the Nulojix clinical trial experience (i.e., taper to 10mg per day for the first 6 months post transplant)

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a transplant specialist or nephrologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Initial Phase, 10 mg/kg IV on day 1 (day of transplant, prior to implantation), day 5, and end of weeks 2, 4, 8, and 12 after transplant.
Maintenance Phase: 5 mg/kg IV at the end of week 16 and every 4 weeks (plus or minus 3 days) thereafter

PLACE OF ADMINISTRATION:

The recommendation is that infused medications in this policy will be for medical benefit coverage administered in a place of service that is a non-hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Intravenous

DRUG CLASS:

Selective T-Cell Costimulation Blockers

FDA-APPROVED USES:

Indicated for prophylaxis of organ rejection in adult patients receiving a kidney transplantation in combination with basiliximab induction, mycophenolate mofetil, and corticosteroids.

Limitations of use: Use only in patients who are EBV seropositive. Use has not been established for the prophylaxis of organ rejection in transplanted organs other than the kidney.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Nulojix powder, lyophilized, for solution for Intravenous injection; a selective T-cell co stimulation blocker indicated for prophylaxis of organ rejection in adult patients receiving a kidney transplant. It is used in combination with basiliximab induction, mycophenolate mofetil, and corticosteroids. Some limitations of use are that it can only be used in patients who are EBV seropositive, and it safe use has not been established for the prophylaxis of organ rejection in transplanted organs other than the kidney. Nulojix should never be used in patients with unknown aerostats or EBV seronegative. Use in patients with history of liver transplant is not recommended and only physicians experienced in immunosuppressive therapy and management of kidney transplant patients should prescribe Nulojix. See table 1 below for dosing recommendation. Doses higher than or more frequent than recommended should be avoided due to the increased risk of infection or malignancy. It should only be administered intravenously over a 30-minute period and only the silicone-free disposable syringe enclosed in the package should be used for administration.
Nulojix comes with boxed warning for Post-transplant lymphoproliferative disorder (PTLD), other malignancies, and serious infections. There is an increased risk for Progressive Multifocal Leukoencephalopathy (PML) with Nulojix. Corticosteroid utilization should be consistent with Nulojix clinical trial experience as acute rejection and graft loss might result with corticosteroid minimization In the Belatacept Evaluation of Nephroprotection and Efficacy as First-line Immunosuppression Trial (BENEFIT), 686 recipients of a living or standard-criteria deceased donor kidney transplant were randomly assigned to more intensive (MI) belatacept, less intensive (LI) belatacept, or cyclosporine, in conjunction with mycophenolate and glucocorticoids; all patients received basiliximab as induction therapy [126,128,131,132,134,137]. At 12 months, patients treated with belatacept experienced a higher incidence and grade of acute rejection episodes (22 and 17 versus 7 percent in the MI, LI, and cyclosporine arms, respectively) but had superior renal function, a benefit that was sustained at seven years posttransplant (estimated glomerular filtration rate [eGFR] of 70 and 72 versus 45 mL/min/m2, respectively). In addition, rates of death or allograft loss were significantly lower at seven years in patients assigned to belatacept (12.7 and 12.8 versus 21.7 percent). Posttransplant lymphoproliferative disorder (PTLD) was more common with belatacept, particularly among EBV- seronegative patients.
The BENEFIT-EXT trial compared the efficacy and safety of belatacept with that of cyclosporine in extended criteria donor (ECD) kidney transplant recipients, using the same study design as the one used in BENEFIT [127,128,130,133,138]. At 12 months, acute rejection rates were similar between groups. Similar to BENEFIT, patients treated with belatacept had better renal function at one, two, five, and seven years compared with those treated with cyclosporine. Rates of PTLD were also higher among patients treated with belatacept.
A randomized, controlled trial compared belatacept with a tacrolimus-based, steroid-avoiding maintenance immunosuppression regimen [129]. Recipients of living and deceased donor renal allografts were randomly assigned to treatment with belatacept-mycophenolate mofetil (belatacept- MMF), belatacept- sirolimus, or tacrolimus-MMF. All patients received induction with rabbit antithymocyte globulin (rATG)- Thymoglobulin and a short course of glucocorticoids. Acute rejection rates were highest in the belatacept- MMF arm (12 percent), and the calculated GFR was 8 to 10 mL/min higher with either belatacept regimen than with tacrolimus-MMF.
Another randomized, controlled trial of 40 kidney transplant recipients compared belatacept with a

tacrolimus-based, steroid-containing maintenance regimen [139]. Patients were randomly assigned to belatacept or tacrolimus, combined with MMF and prednisolone; all patients received basiliximab as induction therapy. At one-year posttransplant, the incidence of acute rejection was higher among patients who received belatacept compared with those who received tacrolimus (55versus 10 percent, respectively). Graft loss, due to rejection, occurred in three patients, all in the belatacept group. There was no difference in graft function between the two groups.

Risk of Rejection with Conversion From a CNI Based Maintenance Regimen

Conversion from calcineurin inhibitor (off-label dosing) (Grinyo 2012; Grinyo 2016; Rostaing 2011): IV: Initial phase: 5 mg/kg on transition days 1, 15, 29, 43, and 57, Maintenance phase: 5 mg/kg every 4 weeks beginning 4 weeks after completion of the initial phase. Note: Taper calcineurin inhibitor dose slowly over 1 month (no reduction on day 1, 40% to 60% reduction on day 15, 70% to 80% reduction on day 23; discontinue on day 29 and beyond).

Conversion of patients receiving a CNI based maintenance regimen to a NULOJIX based maintenance regimen increases the risk of acute rejection. In two randomized controlled studies, kidney transplant recipients at least six months post-transplant and stable on a CNI based regimen who were converted to a belatacept based regimen experienced higher rejection rates mostly during the first year post-conversion than patients maintained on their CNI based regimens. Conversion of stable kidney transplant recipients from a CNI based maintenance therapy to a belatacept based maintenance therapy is not recommended unless the patient is CNI intolerant.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Nulojix (belatacept) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Nulojix (belatacept) include: transplant recipients who are Epstein-Barr virus (EBV) seronegative or with unknown EBV serostatus [due to the risk of post-transplant lymphoproliferative disorder (PTLD), predominantly involving the central nervous system (CNS)], prolonged exposure to UV light and sunlight, use of live vaccines during treatment.

OTHER SPECIAL CONSIDERATIONS:

Nulojix (belatacept) has a Black Boxed warning for post-transplant lymphoproliferative disorder, other malignancies, and serious infections.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J0485	Injection, belatacept 1mg

AVAILABLE DOSAGE FORMS:

Nulojix SOLR 250MG single-use vial

REFERENCES

1. Nulojix® for injection [prescribing information]. Princeton, NJ: Bristol- Myers Squibb Company; July 2021.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO Clinical

Practice Guideline for the Care of Kidney Transplant Recipients. Am J Transplant. 2009;9(Suppl 3):S1–S157. Accessed at: https://kdigo.org/wpcontent/uploads/2017/02/KDIGO- 2009- Transplant-Recipient-Guideline- English.pdf.

3. Klintmalm GB, Feng S, Lake JR, et al. Belatacept-Based Immunosuppression in De Novo Liver Transplant Recipients: 1-Year Experience From a Phase II Randomized Study. Am J Transplant. 2014;14:1817-1827.
4. Josephson, M. A., Becker, Y. T., Budde, K., Kasiske, B. L., Kiberd, B. A., Alexandre Loupy, … Zeier, M. (2023). Challenges in the management of the kidney allograft: from decline to failure: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney International. https://doi.org/10.1016/j.kint.2023.05.010

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy References	Q4 2023
REVISION- Notable revisions: Required Medical Information Prescriber Requirements Quantity Background Contraindications/Exclusions/Discontinuation	Q4 2022
Q2 2022 Established tracking in new format	Historical changes on file