

Select Transplant Immunosuppressants

Policy # 00687

Original Effective Date: 08/14/2019

Current Effective Date: 08/01/2026

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Prograf^{®†} granules (tacrolimus), Prograf capsules (tacrolimus), Neoral^{®†} (cyclosporine), Zortress^{®†} (everolimus) and Cellcept^{®†} (mycophenolate mofetil) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Prograf granules (tacrolimus), Prograf capsules (tacrolimus), Neoral (cyclosporine), Zortress (everolimus) or Cellcept (mycophenolate mofetil) will be considered when the following criteria are met:

- For **Prograf granules** requests:
 - Patient is younger than 18 years of age; AND
 - Patient meets ONE of the following:
 - Patient has a gastrostomy tube (G-tube) or is otherwise unable to swallow tablets and/or capsules AND is NOT taking any other medications in tablet and/or capsule form; OR
 - Patient requires a dosage that can ONLY be met with the granule dosage form.
*(Note: The above two patient selection criteria are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met).*
- For **Prograf capsule** requests:
 - Patient has tried and failed (e.g., intolerance or inadequate response) generic tacrolimus capsules unless there is clinical evidence or patient history that suggests the use of generic tacrolimus capsules will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

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- For **Neoral** requests:
 - Patient has tried and failed (e.g., intolerance or inadequate response) generic cyclosporine (modified) unless there is clinical evidence or patient history that suggests the use of generic cyclosporine (modified) will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- For **Zortress** requests:
 - Patient has tried and failed (e.g., intolerance or inadequate response) generic everolimus unless there is clinical evidence or patient history that suggests the use of generic everolimus will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- For **Cellcept** requests:
 - Patient has tried and failed (e.g., intolerance or inadequate response) generic mycophenolate mofetil unless there is clinical evidence or patient history that suggests the use of generic mycophenolate mofetil will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Prograf granules (tacrolimus) when the patient is able to swallow tablets and/or capsules, when the patient is taking other medications in tablet and/or capsule form, or if the patient requires a dosage that can be met with the capsule form to be **not medically necessary.****

Based on review of available data, the Company considers the use of Prograf capsules (tacrolimus), Neoral (cyclosporine), Zortress (everolimus) or Cellcept (mycophenolate mofetil) when the patient has not tried and failed the generic equivalent of the requested drug to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Prograf granules (tacrolimus) in patients 18 years of age or older to be **investigational.***

Background/Overview

Prograf is a calcineurin-inhibitor immunosuppressant indicated for the prophylaxis of organ rejection in adult and pediatric patients receiving allogeneic liver, kidney, heart, or lung transplants, in combination with other immunosuppressants. Prograf is supplied as 0.5, 1, and 5 mg capsules, 5 mg/mL injection, and 0.2 and 1 mg unit dose granule packets. In the package insert, the granules are explicitly mentioned for use in pediatric patients only.

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Neoral (cyclosporine) is a calcineurin-inhibitor immunosuppressant. In transplant recipients, cyclosporine is used for the prophylaxis of organ rejection and may be administered with other immunosuppressive agents in kidney, liver, and heart transplant patients. Neoral is a modified cyclosporine formulation with increased bioavailability compared with SandimmuneTM‡; these products are not bioequivalent and should not be used interchangeably without physician supervision.

Zortress (everolimus) is a mammalian target of rapamycin (mTOR) inhibitor immunosuppressant indicated for the prophylaxis of organ rejection in adult patients receiving a kidney transplant who are at low to moderate immunologic risk and in adult patients receiving a liver transplant. For kidney transplant recipients, Zortress is used in combination with basiliximab induction, reduced-dose cyclosporine, and corticosteroids. For liver transplant recipients, Zortress is administered no earlier than 30 days post-transplant in combination with reduced-dose tacrolimus and corticosteroids. Safety and efficacy have not been established in pediatric patients or in recipients of transplanted organs other than kidney or liver.

Cellcept (mycophenolate mofetil) is an antimetabolite immunosuppressant indicated for the prophylaxis of organ rejection in adult and pediatric recipients 3 months of age and older of allogeneic kidney, heart, or liver transplants, in combination with other immunosuppressants. Cellcept is available as capsules, tablets, oral suspension, and intravenous formulations.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Prograf is a calcineurin-inhibitor immunosuppressant indicated for the prophylaxis of organ rejection in adult and pediatric patients receiving allogeneic liver, kidney, heart, or lung transplants, in combination with other immunosuppressants.

Neoral is indicated for the prophylaxis of organ rejection in kidney, liver, and heart allogeneic transplants. Neoral may be administered with other immunosuppressive agents in kidney, liver, and heart transplant patients.

Zortress is indicated for the prophylaxis of organ rejection in adult patients at low to moderate immunologic risk receiving a kidney transplant, in combination with basiliximab induction, reduced doses of cyclosporine, and corticosteroids. Zortress is also indicated for the prophylaxis of allograft rejection in adult patients receiving a liver transplant and is to be administered no earlier than 30 days post-transplant in combination with reduced doses of tacrolimus and corticosteroids.

Cellcept is indicated for the prophylaxis of organ rejection in adult and pediatric recipients 3 months of age and older of allogeneic kidney, heart, or liver transplants, in combination with other immunosuppressants.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The intent of this policy is to limit the Prograf granule dosage form to pediatric patients who are unable to swallow and are not taking other medications in tablet and/or capsule form, or pediatric patients who require a dose only provided by the granule dosage form. This policy also supports the use of equally effective yet economically sensible products prior to brand products for Prograf capsules, Neoral, Zortress, and Cellcept, unless there is clinical evidence or patient history that suggests the generic equivalent will be ineffective or cause an adverse reaction to the patient.

References

1. Prograf [package insert]. Astellas Pharma US, Inc. Updated July 2021.
2. Neoral [package insert]. Novartis. Updated September 2023.
3. Zortress [package insert]. Novartis. Updated February 2024.
4. Cellcept [package insert]. Genentech. Updated May 2025.

Policy History

Original Effective Date: 08/14/2019

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08/01/2019	Medical Policy Committee review
08/14/2019	Medical Policy Implementation Committee approval. New policy.
08/06/2020	Medical Policy Committee review
08/12/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/05/2021	Medical Policy Committee review
08/11/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2023	Medical Policy Committee review
08/09/2023	Medical Policy Implementation Committee approval. Updated policy to reflect new indication, which now includes prophylaxis of organ rejection in lung transplants.
08/01/2024	Medical Policy Committee review
08/14/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/07/2025	Medical Policy Committee review
08/13/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/21/2026	Pre Pharmacy and Therapeutics Committee review
07/22/2026	Pharmacy and Therapeutics Committee approval. Added Prograf capsules, Neoral, Zortress, and Cellcept to the policy with criteria. Title changed from “Prograf® granules (tacrolimus)” to “Select Transplant Immunosuppressants”.

Next Scheduled Review Date: 07/2027

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***Investigational** – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.