BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

**PHARMACY COVERAGE GUIDELINE**

# ENVARSUS XR® (tacrolimus extended release) oral tablet Generic Equivalent (if available)

**This Pharmacy Coverage Guideline (PCG):**
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

**Scope**
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

**Instructions & Guidance**
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

## Medical Necessity Requirements for ENVARSUS XR (tacrolimus extended release)

## Criteria for Initial Therapy:

### Prescriber Qualifications
- Prescribed by a Nephrologist or Transplant Specialist or is in consultation with a Nephrologist or Transplant Specialist

### Indication
- Prophylaxis of kidney transplant rejection

ORIGINAL EFFECTIVE DATE: 01/21/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/15/2024

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### Age Requirement
- 18 years of age or older

### Baseline Clinical Evaluation
- Uses other immunosuppressants to prevent organ rejection in kidney transplant

### Alternative Therapies
- Failure (trial for at least three months duration), contraindication per FDA label, intolerance, or is not a candidate for **generic immediate release tacrolimus**

### Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

### Safety
- Will not be used with live vaccines such as intranasal influenza, measles, mumps, rubella, oral polio, Bacillus Calmette Guérin (BCG), yellow fever, varicella, and TY21a typhoid vaccines
- Does not have congenital long QT syndrome

### Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

### Initial Therapy Criteria Approval Duration
- 12 months OR end of plan year

## Criteria for Continuation of Therapy (renewal therapy):
**Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.**

### Prescriber Qualification
- Continues to be seen by a Nephrologist or Transplant Specialist or is in consultation with a Nephrologist or Transplant Specialist

### Clinical Response
- Condition has responded to therapy defined as no organ rejection

### Adherence
- Adherence to the prescribed therapy regimen has been documented

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## Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

## Safety

- Has not developed significant adverse drug effects that may exclude continued use such as:
  - Posterior reversible encephalopathy syndrome
  - Pure red cell aplasia
  - QT prolongation
  - Torsades de pointes
- Will not be used with live vaccines such as intranasal influenza, measles, mumps, rubella, oral polio, Bacillus Calmette Guérin (BCG), yellow fever, varicella, and TY21a typhoid vaccines
- Does not have congenital long QT syndrome

## Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

## Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

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## Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

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## Description:

Envarsus (tacrolimus) XR is a calcineurin inhibitor immunosuppressant indicated for the prophylaxis of organ rejection in *de novo* kidney transplant patients used in combination with other immunosuppressants and for the prophylaxis of organ rejection in kidney transplant patients converted from tacrolimus immediate-release formulations, used in combination with other immunosuppressants. Generic tacrolimus is available as an immediate release formulation in 0.5 mg, 1 mg, and 5 mg capsules and is dosed twice daily. Envarsus XR is dosed once daily.

Information from the product labeling show approval of Envarsus XR was based on a single, published, open label randomized controlled trial designed to show non-inferiority to tacrolimus IR capsules. Patients on stable doses of twice daily tacrolimus IR were randomized to either continue their current regimen or switched to



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Envarsus XR once daily. The two groups were found to be “non-inferior” (no difference detected) in composite efficacy failure endpoints (death, graft failure, locally read biopsy-proven acute rejection, or loss to follow up) within 12 months.

Tacrolimus binds to an intracellular protein, FKBP-12. A complex of tacrolimus-FKBP-12, calcium, calmodulin, and calcineurin (a ubiquitous mammalian intracellular enzyme) is then formed and the phosphatase activity of calcineurin inhibited. Such inhibition prevents the dephosphorylation and translocation of various factors such as the nuclear factor of activated T-cells (NF-AT) and nuclear factor kappa-light-chain-enhancer of activated B-cells (NF-κB).

Tacrolimus inhibits the expression and/or production of several cytokines that include interleukin (IL)-1 beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, IL-10, gamma interferon, tumor necrosis factor-alpha, and granulocyte macrophage colony stimulating factor. Tacrolimus also inhibits IL-2 receptor expression and nitric oxide release, induces apoptosis and production of transforming growth factor-beta that can lead to immunosuppressive activity. The net result is the inhibition of T-lymphocyte activation and proliferation as well as T-helper-cell-dependent B-cell response (i.e., immunosuppression).

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**Definitions:**

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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**Resources:**

Envarsus XR (tacrolimus extended release) tab product information, revised by Veloxis Pharmaceuticals, Inc. 04-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 03, 2025.

Hardinger K, Brennan DC. Kidney transplantation in adults: Maintenance immunosuppressive therapy. In: UpToDate, Tan JC, Sawinski D, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through December 2025. Topic last updated September 30, 2025. Accessed January 19, 2026.



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