BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

SAVAYSA™ (edoxaban tosylate) oral
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 SAVAYSA (edoxaban tosylate)

Criteria for Initial Therapy:

Indication
- Nonvalvular atrial fibrillation (NVAF)
- Deep vein thrombosis (DVT) and pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant

Age Requirement
- 18 years or older

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Alternative Therapies

- Failure, contraindication, intolerance, or not a candidate for:
  - Eliquis (apixaban)
  - Xarelto (rivaroxaban)

Brand Specific Criteria

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

Safety

- Creatinine clearance between 15 and 95 mL/minute
- No concomitant drug use with:
  - Anticoagulants (e.g., heparin, enoxaparin, etc.)
  - Antiplatelets (e.g., aspirin, ibuprofen, naproxen, etc.)
  - Thrombolytics (e.g., alteplase, reteplase, etc.)
  - Selective serotonin reuptake inhibitors (e.g., citalopram, fluoxetine, sertraline, etc.)
  - Serotonin norepinephrine reuptake inhibitors (e.g., duloxetine, venlafaxine, etc.)
  - Rifampin
- **NONE** of the following:
  - Mechanical heart valve
  - Moderate to severe mitral stenosis
  - Triple positive antiphospholipid syndrome (positive for lupus anticoagulant, anticardiolipin antibodies, and anti beta 2 glycoprotein I antibodies)
  - Moderate to severe hepatic impairment (Child Pugh Class B and C)
  - FDA label contraindications including active pathological bleeding

Documentation Requirements

- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (including creatinine clearance)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- For NVAF: 12 months OR end of plan year
- For DVT and PE: 6 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

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Clinical Response

- **ONE** of the following:
  - No embolic events in last 12 months for NVAF
  - No embolic events in last 6 months for DVT/PE

Adherence

- Adherence to the prescribed therapy regimen has been documented

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

- FDA label contraindications or significant adverse event including active or severe bleeding
- No concomitant drug use with:
  - Anticoagulants (e.g., heparin, enoxaparin, etc.)
  - Antiplatelets (e.g., aspirin, ibuprofen, naproxen, etc.)
  - Thrombolytics (e.g., alteplase, reteplase, etc.)
  - Selective serotonin reuptake inhibitors (e.g., citalopram, fluoxetine, sertraline, etc.)
  - Serotonin norepinephrine reuptake inhibitors (e.g., duloxetine, venlafaxine, etc.)
  - Rifampin

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use (e.g., creatinine clearance)

Continuation Therapy Criteria Approval Duration

- For NVAF: 12 months OR end of plan year
- For DVT and PE: 6 months OR end of plan year

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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Definitions:

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

Resources:

Savaysa (edoxaban tosylate) product information, revised by Daiichi Sankyo, Inc. 10 2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2025.

Lip GYH, Garcia DA, Stevens SM. Selecting adult patients with lower extremity deep venous thrombosis and pulmonary embolism for indefinite anticoagulation. In: UpToDate, Mandel J, Douketis JD, Finley G (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through May 2025. Topic last updated March 28, 2025. Accessed June 25, 2025.

Manning WJ, Singer DE, Lip GYH. Atrial fibrillation in adults: Selection of candidates for anticoagulation. In: UpToDate, Zimetbaum PJ, Kasner SE, Knight BP, Li H, Yeon SB (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through May 2025. Topic last updated May 29, 2024. Accessed June 25, 2025.

Manning WJ, Singer DE, Lip GYH. Atrial fibrillation in adults: Use of oral anticoagulants. In: UpToDate, Zimetbaum PJ, Kasner SE, Knight BP, Li H, Yeon SB (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through May 2025. Topic last updated September 20, 2024. Accessed June 25, 2025.

Ortel TL, Neumann I, Ageno W, et al.: American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Advances 2020 Oct 13;4(19): 4693-4738. Accessed July 18, 2024. Re-evaluated June 25, 2025.

Stevens SM, Woller SC, Kreuziger LB, et al.: Executive Summary: Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. CHEST 2021 Dec; 160(6):2247-2259. Accessed July 18, 2024. Re-evaluated June 25, 2025.

Joglar JA, Chung MK, Armbruster AL, et al.: 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Available at J Am Coll Cardiol. 2024 Jan 2/9;83 (1):109–279. Accessed June 25, 2025.

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