

Clinical Policy: Edoxaban (Savaysa)

Reference Number: ERX.NPA.63

Effective Date: 06.01.15

Last Review Date: 02.22

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

Edoxaban (Savaysa®) is a factor Xa inhibitor.

FDA Approved Indication(s)

Savaysa is indicated:

- To reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF)
- For the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant

Limitation(s) of use: For NVAF, Savaysa should not be used in patients with creatinine clearance (CrCL) > 95 mL/min because of increased risk of ischemic stroke compared to warfarin at the highest dose studied (60 mg).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Savaysa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Valvular Atrial Fibrillation, Deep Venous Thrombosis, Pulmonary Embolism* (must meet all):

1. Prescribed for one of the following conditions (a, b, or c):
 - a. Reduction of the risk of stroke and systemic embolism in member with NVAF;
 - b. Treatment of DVT or PE;
 - c. Cancer associated venous thromboembolic disease (*see Appendix D*);
2. Failure of Eliquis® and Xarelto®, each used for ≥ 30 days at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
3. If member has NVAF, recent (within the past 90 days) CrCl is ≤ 95 mL/min;
4. Dose does not exceed 60 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Non-Valvular Atrial Fibrillation, Deep Venous Thrombosis, Pulmonary Embolism (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 60 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CrCl: creatinine clearance

DVT: deep vein thrombosis

FDA: Food and Drug Administration

LMWH: low-molecular weight heparin

NCCN: National Comprehensive Cancer Network

NVAF: non-valvular atrial fibrillation

PE: pulmonary embolism

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Eliquis® (apixaban)	NVAF 5 mg PO BID Treatment of DVT/PE 10 mg PO BID for 7 days, then 5 mg PO BID	20 mg/day
Xarelto® (rivaroxaban)	NVAF 20 mg/day PO QD Treatment of DVT/PE 15 mg PO BID for 21 days, then 20 mg/day PO	30 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Active pathological bleeding
- Boxed warning(s):
 - Reduced efficacy in nonvalvular atrial fibrillation patients with CrCl > 95 mL/min
 - Premature discontinuation of Savaysa increases the risk of ischemic events
 - Spinal/epidural hematoma may occur in patients treated with Savaysa who are receiving neuraxial anesthesia or undergoing spinal puncture

Appendix D: General Information

- Savaysa should not be used in NVAF patients with CrCl > 95 mL/min due to reduced efficacy. In the ENGAGE AF-TIMI 48 study, NVAF patients with CrCl > 95 mL/min had an increased rate of ischemic stroke with Savaysa 60 mg once daily compared to patients treated with warfarin. In these patients, another anticoagulant should be used.

- Per National Comprehensive Cancer Network (NCCN) guidelines for cancer-associated venous thromboembolic disease, edoxaban is recommended for:
 - Administer after completion of at least 5 days of parenteral anticoagulation with a low-molecular weight heparin (LMWH) or unfractionated heparin for management of acute DVT, acute catheter-related DVT, acute pulmonary embolism, management of splanchnic vein thrombosis, acute thrombosis, and consider for treatment of chronic thrombosis in cancer patients with no contraindication to anticoagulation (preferred for patients without gastric or gastroesophageal lesions)
 - Anticoagulation for cancer patients following therapeutic anticoagulation failure with heparin sodium, low-molecular weight heparin, fondaparinux or warfarin sodium
 - Initial treatment for suspected or confirmed heparin-induced thrombocytopenia following discontinuation of heparin-based products in clinically stable patients with no contraindications and without hemodynamically unstable pulmonary embolism, limb-threatening thrombosis, or planned invasive procedures
 - Transition to oral therapy (direct oral anticoagulants preferred) for patients with heparin-induced thrombocytopenia who have been stabilized on initial treatment with a direct thrombin inhibitor or fondaparinux and have no contraindications or invasive procedures planned

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NVAF	If CrCl > 50 to ≤ 95 mL/min: 60 mg PO QD If CrCl 15-50 mL/min: 30 mg PO QD	60 mg/day
Treatment of DVT and PE	If CrCl > 50 mL/min: 60 mg PO QD If CrCl 15-50 mL/min or body weight ≤ 60 kg: 30 mg PO QD	60 mg/day

VI. Product Availability

Tablets: 60 mg, 30 mg, 15 mg

VII. References

1. Savaysa Prescribing Information. Basking Ridge, NJ: Daiichi Sankyo, Inc.; March 2021. Available at: www.savaysa.com. Accessed November 23, 2021.
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3. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest. 2016; 149(2): 315-352.
4. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. J Am Coll Cardiol. 2014;64(21):e1-e76.
5. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. J Am Coll Cardiol. 2019; 140:e125-e151.
6. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic therapy for atrial fibrillation. Chest 2018; 154(5):1121-1201.
7. 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 Adv. 2020 Oct 13;4(19):4693-38.
8. Edoxaban. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed November 6, 2020.
9. National Comprehensive Cancer Network. Cancer-Associated Venous Thromboembolic Disease Version 3.2021. Available at: <http://www.nccn.org>. Accessed November 23, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from ERX.NSST.07 Oral anticoagulants and converted to new template.	07.17	08.17
2Q 2018 annual review: Converted policy from ST to clinical PA. References reviewed and updated.	03.19.18	05.18
2Q 2019 annual review: removed trial of warfarin per guidelines and specialist feedback; references reviewed and updated.	02.26.19	05.19
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.06.20	05.20
1Q 2021 annual review: added cancer associated venous thromboembolic disease as per NCCN recommendations; added Appendix D; references reviewed and updated.	11.06.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.23.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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