

Clinical Policy: Edoxaban (Savaysa)

Reference Number: CP.PMN.227

Effective Date: 01.01.20

Last Review Date: 02.24

Line of Business: Medicaid

[RevisionLog](#)

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.

It is the policy of health plans affiliated with Centene Corporation[®] 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[®] used for ≥ 30 days at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
3. If member has NVAf, recent (within the past 90 days) CrCl is ≤ 95 mL/min;
4. Dose does not exceed any of the following (a and b):
 - a. 60 mg per day;
 - b. 1 tablet per day.

Approval duration: 12 months

*Includes off-label use for adults and pediatrics.

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed any of the following (a and b):
 - a. 60 mg per day;
 - b. 1 tablet per day.

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

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 policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

- | | |
|------------------------------------|---|
| CrCl: creatinine clearance | NVAF: non-valvular atrial fibrillation |
| DVT: deep vein thrombosis | NCCN: National Comprehensive Cancer Network |
| FDA: Food and Drug Administration | PE: pulmonary embolism |
| LMWH: low-molecular weight heparin | |

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 for all relevant lines of business 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

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:
 - Administration after completion of at least 5 days of parenteral anticoagulation with a low-molecular weight heparin (LMWH) or unfractionated heparin (UFH) for management of acute DVT, acute catheter-related DVT, acute pulmonary embolism,

- acute superficial vein thrombosis, 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 alternative 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.; October 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/206316s019lbl.pdf. Accessed October 31, 2023.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2023. Available at: <https://www.clinicalkey.com/pharmacology/>. Accessed October 31, 2023.
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. Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guidelines and Expert Panel Report. *Chest* 2021 Dec; 160 (6): e545- e608.
5. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2014; 129: 000-000. Doi: 10.1161/CIR.0000000000000041.
6. 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.

7. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic therapy for atrial fibrillation. *Chest* 2018; 154(5):1121-1201.
8. 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.
9. Edoxaban. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: nccn.org. Accessed October 31, 2023.
10. National Comprehensive Cancer Network. Cancer-Associated Venous Thromboembolic Disease Version 2.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/vte.pdf. Accessed October 31, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created based on SDC decision and prior clinical guidance.	01.01.20	02.20
Per July SDC and prior clinical guidance, removed Xarelto redirection.	07.20.20	
1Q 2021 annual review: added cancer associated venous thromboembolic disease as per NCCN recommendations; 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
Template changes applied to other diagnoses/indications and continued therapy section.	10.06.22	
1Q 2023 annual review: no significant changes; updated appendix D with current NCCN compendium language; updated template language for continued therapy and other diagnoses/indication sections; references reviewed and updated.	09.26.22	02.23
1Q 2024 annual review: no significant changes; references reviewed and updated.	10.31.23	02.24

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering

benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2020 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene[®] and Centene Corporation[®] are registered trademarks exclusively owned by Centene Corporation.