Drug Coverage Policy

Effective Date……05/15/2025
Coverage Policy Number……IP0034
Policy Title……Savaysa

Anticoagulants – Savaysa

- Savaysa® (edoxaban tablets – Daiichi Sankyo)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Savaysa, a Factor Xa inhibitor, is indicated for the following uses:[1]

- **Non-valvular atrial fibrillation**, to reduce the risk of stroke and systemic embolism.
- **Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE)**, following 5 to 10 days of initial therapy with a parenteral anticoagulant.

Savaysa has a unique Boxed Warning regarding reduced efficacy in non-valvular atrial fibrillation in patients with a creatinine clearance > 95 mL/min; Savaysa should be avoided in these individuals.[1] Safety and effectiveness of Savaysa in pediatric patients have not been established.

Guidelines

Guidelines are available which support the use of direct oral anticoagulants (DOACs) in their commonly used clinical settings, such as DVT/PE[2-5] and atrial fibrillation[6,7]. In patients who are eligible for a DOAC, these are generally preferred over vitamin K antagonists (e.g., warfarin). It is noted that in the randomized trials in atrial fibrillation, DOACs were consistently at least non-inferior to warfarin regarding the composite of stroke or systemic embolism and were associated with a lower risk of serious bleeding.[7]

Anticoagulants and Coronavirus Disease 2019 (COVID-19)

Several clinical practice guidelines have been published with regard to use of anticoagulant therapy in the management of COVID-19. Per National Institutes of Health treatment guidelines regarding antithrombotic therapy in patients with COVID-19 (updated October 10, 2023), hospitalized patients with COVID-19 should not be routinely discharged from the hospital while on venous thromboembolism (VTE) prophylaxis.[8] For hospitalized patients, anticoagulant or antiplatelet therapy should not be used to prevent arterial thrombosis outside of the usual standard of care for patients without COVID-19. In nonhospitalized patients with COVID-19, it is not recommended to use anticoagulant and antiplatelet therapy for the prevention of VTE or arterial thrombosis, except in a clinical trial. Of note, Xarelto® (rivaroxaban tablets and oral suspension) is FDA-approved for prophylaxis of VTE in acutely ill medical patients; Eliquis is not indicated in this setting. Other guidelines have similar recommendations.[9-11]

Other Uses with Supportive Evidence

Savaysa has data for prophylaxis of VTE after hip replacement surgery.[12] Although data are not robust regarding use of DOACs in other off-label thromboembolic-related conditions, American College of Chest Physicians (CHEST) guidelines (2021) suggest anticoagulation for certain patients (e.g., superficial vein thrombosis, antiphospholipid syndrome).[2] The choice of anticoagulant is often individualized based on patient-specific factors; therefore, for certain patients, DOAC use may be considered in practice. Evidence for DOACs is limited for off-label scenarios; in general, there is more clinical experience with agents such as vitamin K antagonists (e.g., warfarin) and low molecular weight heparin in these settings.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for prescription benefit coverage of Savaysa. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Savaysa is considered medically necessary when ONE of the following criteria are met (1, 2, 3, or 4):

FDA-Approved Indications

1. **Atrial Fibrillation (or Atrial Flutter).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has an estimated creatinine clearance ≤ 95 mL/min; AND
   C) Preferred product criteria is met for the products listed in the below table

2. **Deep Vein Thrombosis or Pulmonary Embolism, Treatment.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Preferred product criteria is met for the products listed in the below table

Other Uses with Supportive Evidence

3. **Deep Vein Thrombosis in a Patient Undergoing Hip Replacement Surgery, Prophylaxis.** Approve for 60 days if the patient meets BOTH of the following (A and B)
   A) Patient is ≥ 18 years of age; AND
   B) Preferred product criteria is met for the products listed in the below table

4. **Treatment or Prevention of Other Thromboembolic-Related Conditions.** Approve for 6 months if the patient meets ALL of the following (A, B, and C):
   Note: Examples of other thromboembolic-related conditions include superficial vein thrombosis, splanchnic vein thrombosis, hepatic vein thrombosis, or prophylaxis of venous thromboembolism in a high-risk patient.
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i or ii):
      i. Patient has tried warfarin, fondaparinux, or a low molecular weight heparin product (e.g., enoxaparin, Fragmin [dalteparin injection]); OR
      Note: A patient who has tried Eliquis (apixaban tablets), Xarelto (rivaroxaban tablets and oral suspension), or Pradaxa (dabigatran capsules) is not required to try warfarin, fondaparinux, or a low molecular weight heparin.
      ii. Patient has been started on Savaysa for the treatment of an acute thromboembolic condition; AND
   C) Preferred product criteria is met for the products listed in the below table

Employer Plans:

Product	Criteria
Savaysa (edoxaban tablets)	**EFFECTIVE 7/1/2025** **ONE** of the following (1, 2, 3, or 4): 1. The patient has tried **ONE** of the following (A, B, or C): A. Dabigatran B. Eliquis C. Xarelto; OR 2. The patient is currently receiving Savaysa for treatment of thrombosis (e.g., deep vein thrombosis [DVT] or pulmonary embolism [PE]); OR 3. The patient is using Savaysa for the treatment of DVT or PE associated with cancer and has tried Eliquis; OR 4. The patient is currently receiving Savaysa for prophylaxis of DVT or PE after orthopedic surgery (e.g., hip replacement surgery)

Individual and Family Plans:

Product	Criteria
Savaysa (edoxaban tablets)	**ONE** of the following (1, 2, 3, or 4): 1. The patient has tried **ONE** of the following (A or B): A. Eliquis B. Xarelto; OR 2. The patient is currently receiving Savaysa for treatment of thrombosis (e.g., deep vein thrombosis [DVT] or pulmonary embolism [PE]); OR 3. The patient is using Savaysa for the treatment of DVT or PE associated with cancer and has tried Eliquis; OR 4. The patient is currently receiving Savaysa for prophylaxis of DVT or PE after orthopedic surgery (e.g., hip replacement surgery)

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Savaysa for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Venous Thromboembolism in an Acutely Ill Medical Patient, Prophylaxis.** (Note: This includes post-discharge thromboprophylaxis for a patient hospitalized with coronavirus disease 2019 [COVID-19]). Xarelto is labeled for prophylaxis of venous thromboembolism in acutely ill medical patients and is supported in clinical practice guidelines, including guidelines which address prophylaxis of venous thromboembolism in COVID-19 patients.[7-9]

References

1. Savaysa® tablets [prescribing information]. Basking Ridge, NJ: Daiichi Sankyo; October 2023.
2. Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease. Second update of the CHEST guideline and Expert Panel Report. *Chest*. 2021;160(6):e545-e608.
3. Key NS, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO guideline update. *J Clin Oncol*. 2023;41:3063-3071.
4. The NCCN Cancer-Associated Venous Thromboembolic Disease Clinical Practice Guidelines in Oncology (version 2.2024 – July 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 7, 2025.
5. Ortel TL, Neumann I, Ageno W, Beyth R, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. *Blood Adv*. 2020;4(19):4693-4738.
6. Lip G, Banerjee A, Boriani G, et al. Antithrombotic therapy for atrial fibrillation: CHEST guideline and expert panel report. *Chest*. 2018;154(5):1121-1201.
7. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guidelines for the diagnosis and management of atrial fibrillation. A report of the American College of Cardiology/American Heart Association Joint Committee on Practice guidelines. Developed in

collaboration and endorsed by the American College of Clinical Pharmacy and the Heart Rhythm Society. *J Am Coll Cardiol*. 2024;83(1):109-279.
8. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Antithrombotic therapy in patients with COVID-19. National Institutes of Health. Updated October 23, 2023.
9. Moores LK, Tritschler T, Brosnahan S, et al. Prevention, diagnosis, and treatment of VTE in patients with Coronavirus Disease 2019: CHEST Guideline and Expert Panel Report. *Chest*. 2020;158(3):1143-1163.
10. Spyropoulos AC, Levy JH, Ageno W, et al. Scientific and Standardization Committee communication: Clinical guidance on the diagnosis, prevention, and treatment of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemost*. 2020;18:1859-1865.
11. Barnes GD, Burnett A, Allen A, et al. Thromboembolic prevention and anticoagulant therapy during the COVID-19 pandemic: updated clinical guidance from the anticoagulation forum. *J Thromb Thrombolysis*. 2022;54:197-210.
12. Raskob G, Cohen AT, Eriksson BI, et al. Oral direct factor Xa inhibition with edoxaban for thromboprophylaxis after elective total hip replacement. A randomized double-blind, dose-response study. *Thromb Haemost*. 2010;104(3):642-649.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**FDA-Approved Indications:** Added age restriction for Savaysa usage across all indications **Other Uses with Supportive Evidence:** Added age restriction for Savaysa usage across all indications **Conditions Not Covered:** Removed criterion regarding prophylaxis of Venous Thromboembolism in Individuals with Factor V Leiden thrombophilia and Antiphospholipid syndrome.	06/01/2024
Annual Revision	**Updated** the preferred product criteria requirements for Individual and Family Plans to also include the following exceptions: The patient is currently receiving Savaysa for treatment of thrombosis (e.g., deep vein thrombosis [DVT] or pulmonary embolism [PE]) and; The patient is currently receiving Savaysa for prophylaxis of DVT or PE after orthopedic surgery (e.g., hip replacement surgery). **Venous Thromboembolism in an Acutely Ill Medical Patient, Prophylaxis. Updated** the statement to remove Bevyxxa, as it has been removed from the market.	05/01/2025
Selected Revision	**Added** preferred product criteria for Employer Plans, effective 7/1/2025.	05/15/2025

The policy effective date is in force until updated or retired.