Original Effective Date: 11/2018
Current Effective Date: 04/04/2025
Last P&T Approval/Version: 01/29/2025
Next Review Due By: 01/2026
Policy Number: C20784-A

Direct Oral Anticoagulants

PRODUCTS AFFECTED

Dabigatran, Eliquis (apixaban), Pradaxa (dabigatran), Savaysa (edoxaban), Xarelto (rivaroxaban)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Non-valvular atrial fibrillation, Treatment of deep vein thrombosis (DVT), Treatment of pulmonary embolism (PE), Prophylaxis of DVT in patients undergoing knee or hip replacement surgery, Coronary artery disease (CAD) or peripheral artery disease (PAD), Prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients, Reduce the risk of recurrence of DVT and PE, Anticoagulation in COVID-19 patients

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

FOR ALL INDICATIONS:

1. Prescriber attests that member is not currently pregnant and does not plan on becoming pregnant
   AND
2. Prescriber attests to evaluating the members current prescription and OTC medication regimen for concurrent use of anticoagulant agents
   AND
3. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial and failure or absolute contraindication to a majority (not more than 3) of the preferred formulary/PDL Direct Factor Xa Inhibitor oral products OR Documentation of recent hospital discharge (within 48 hours) in which therapy was started as an inpatient and member has not yet had follow-up with physician.

A. NONVALVULAR ATRIAL FIBRILLATION:

1. Documentation of diagnosis with non-valvular atrial fibrillation or flutter of < 48 hours duration
   AND
2. Prescriber attests that member has intermediate to high risk for stroke based on the prescriber utilizing a validated scoring tool to assess member's stroke risk (see Appendix)
   AND
3. Documentation the member does NOT have moderate to severe mitral stenosis, mechanical prosthetic valves or bioprosthetic valves. If member DOES have moderate to severe mitral stenosis, mechanical prosthetic valves or bioprosthetic valves, warfarin MUST be used as the anticoagulant.

B. TREATMENT OF DVT AND/OR PE:

1. Documentation of diagnosis of a DVT or PE

C. PROPHYLAXIS OF THROMBOSIS:

1. (a) Documentation member has or is scheduled to have total knee replacement surgery
   OR
   (b) Documentation member has or is scheduled to have total hip replacement surgery
   OR
   (c) Documentation member is at continued risk for recurrent DVT and/or PE after completion of initial treatment lasting at least 6 months
   OR
   (d) Documentation member has congenital heart disease and has had a Fontan procedure

D. CANCER-ASSOCIATED VENOUS THROMBOEMBOLISM:

1. Prescriber attests that member has an acute symptomatic or incidentally detected superficial vein thrombosis, deep vein thrombosis, pulmonary embolism, or splanchnic vein thrombosis
   AND
2. Documentation member has cancer other than basal-cell or squamous cell skin cancer that is active or had been diagnosed within the previous 2 years

E. THROMBOPROPHYLAXIS IN COVID-19 POSITIVE MEMBER (8,9):

1. Documentation member had tested positive for COVID-19 infection and was recently discharged from an inpatient hospital stay or member is receiving acute medical therapy in an outpatient setting
   AND
2. Prescriber provides documentation with medical record that member has a Modified International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) VTE risk score ≥4 and is considered at high-risk for VTE (See appendix)
   AND
3. Therapy requested is rivaroxaban 10mg once daily for 31-39 days
   NOTE: For non-hospitalized members with COVID-19, anticoagulants and antiplatelet therapy should not be initiated for the prevention of VTE or arterial thrombosis unless the member has other indications for

the therapy or is participating in a clinical trial. After hospital discharge, VTE prophylaxis is not recommended for members with COVID-19. For certain high-VTE risk members without COVID-19, post- discharge prophylaxis has been shown to be beneficial.
NIH Antithrombotic Therapy in Patients with COVID-19 Last Updated: October 10, 2023- https://www.covid19treatmentguidelines.nih.gov/adjunctive-therapy/antithrombotic-therapy/

F. REDUCTION OF RISK IN MAJOR CARDIOVASCULAR EVENTS:

1. (a) Documentation of a diagnosis of chronic (>6 months) coronary artery disease AND member is < 65 years of age with documented atherosclerosis or revascularization involving at least 2 vascular beds or at least 2 additional risk factors: 1) Current smoker (within 1 year of request), 2) Diabetes mellitus, 3) Renal dysfunction with estimated glomerular filtration rate <60 ml/min, 4) Heart failure or 5) Non-lacunar ischemic stroke ≥ 1 month ago
   OR
   (b) Documentation of a diagnosis of chronic (>6 months) coronary artery disease AND member is ≥ 65 years of age
   OR
   (c) Documentation of a diagnosis of chronic (>6 months) peripheral artery disease
   AND
2. Documentation member will concurrently be utilizing aspirin 100mg once daily
   AND
3. Member does NOT have any of the following: Need for dual antiplatelet therapy, other non- aspirin antiplatelet therapy or oral anticoagulant therapy, Stroke within 1 month or any history of hemorrhagic or lacunar stroke, Severe heart failure with known ejection fraction <30% or New York Heart Association (NYHA) class III or IV symptoms or Estimated glomerular filtration rate (eGFR) < 15 mL/min

CONTINUATION OF THERAPY:

A. FOR ALL INDICATIONS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation showing continued medical necessity for indication and/or medical history.
   AND
4. Dosing is appropriate for listed diagnosis.

DURATION OF APPROVAL:

Initial authorization:
Prophylactic use DVT and/or PE knee – 12 days
Prophylactic use DVT and/or PE hip replacement -- 35 days
Prophylactic use DVT and/or PE after treatment for acute DVT and/or PE-- 6 months
Deep vein thrombosis, pulmonary embolism treatment -- 6 months
Atrial fibrillation, Stroke prophylaxis – 12 months
Cancer-Associated venous thromboembolism: 3 months
Risk Reduction in CV events: 12 months
Thromboprophylaxis in COVID-19 positive member (Xarelto only): total treatment duration up to 39 days

Continuation of Therapy (for the following indications ONLY): Prophylactic use DVT and/or PE after treatment for acute DVT and/or PE, Deep vein thrombosis, pulmonary embolism treatment: 12 months
Atrial fibrillation, stroke prophylaxis: 12 months
Cancer-Associated venous thromboembolism: 12 months

Risk Reduction in CV events: 12 months

****Duration of therapeutic anticoagulation (first episode, general recommendations): Optimal duration of therapy is unknown and is dependent on many factors, such as whether provoking events were present, member risk factors for recurrence and bleeding, and individual preferences: Provoked venous thromboembolism: 3 months (provided the provoking risk factor is no longer present) [11] Unprovoked pulmonary embolism or deep vein thrombosis (proximal or isolated distal): ≥3 months depending on risk of venous thromboembolism (VTE) recurrence and bleeding. [11, 12, 13]

PRESCRIBER REQUIREMENTS:
No requirements

AGE RESTRICTIONS:
Xarelto ONLY- TREATMENT OF AND REDUCTION IN RISK OF RECURRENT VTE: no limit, THROMBO PROPHYLAXIS WITH CONGENITAL HEART DISEASE: 2 years of age and older
PRADAXA ONLY - Treatment of VTE: 8 years of age and older; Reduction in the Risk of Recurrence of VTE: 8 years of age and older
ALL OTHER INDICATIONS: 18 years of age and older

QUANTITY:
Dosage, frequency, and total treatment duration must be supported by FDA label or compendia supported dosing for prescribed indication

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Direct Factor Xa Inhibitors, Thrombin Inhibitors - Selective Direct & Reversible

FDA-APPROVED USES:
ELIQUIS (apixaban) is indicated:

- to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.
- for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery
- for the treatment of DVT and PE, and for the reduction in the risk of recurrent DVT and PE following initial therapy.

PRADAXA (dabigatran etexilate) is indicated:

- to reduce the risk of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation
- for the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in adult patients who have been treated with a parenteral anticoagulant for 5-10 days
- to reduce the risk of recurrence of DVT and PE in adult patients who have been previously treated
- for the prophylaxis of DVT and PE in adult patients who have undergone hip replacement surgery
- for the treatment of venous thromboembolic events (VTE) in pediatric patients 8 to less than 18 years of age who have been treated with a parenteral anticoagulant for at least 5 days
- to reduce the risk of recurrence of VTE in pediatric patients 8 to less than 18 years of age who have been previously treated

SAVAYSA (edoxaban) is indicated:

- to reduce the risk of stroke and systemic embolism (SE) in patients with nonvalvular atrial fibrillation (NVAF)
- for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) following 5 to 10 days of initial therapy with a parenteral anticoagulant

Limitation 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)

XARELTO (rivaroxaban) is indicated:

- to reduce risk of stroke and systemic embolism in nonvalvular atrial fibrillation
- for treatment of deep vein thrombosis (DVT)
- for treatment of pulmonary embolism (PE)
- for reduction in the risk of recurrence of DVT or PE
- for the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery
- for prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients
- to reduce the risk of major cardiovascular events in patients with chronic coronary artery disease (CAD)
- to reduce the risk of major thrombotic vascular events in patients with peripheral artery disease (PAD), including patients after recent lower extremity revascularization due to symptomatic PAD
- for treatment of VTE and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years
- for thromboprophylaxis in pediatric patients 2 years and older with congenital heart disease after the Fontan procedure

COMPENDIAL APPROVED OFF-LABELED USES:

Cancer-induced VTE, VTE prophylaxis in COVID-19 patients

APPENDIX

APPENDIX:

Appendix 1:

Stroke risk scores for patients with atrial fibrillation (Joglar et al., 2023)

ATRIA indicates Anticoagulation and Risk Factors in Atrial Fibrillation: anemia, renal disease, elderly (age ≥75 y), any previous bleeding, hypertension

CHA_2DS_2-VASc, indicates congestive heart failure, hypertension, age ≥75 y (doubled), diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism (doubled), vascular disease, age 65 to 74 y, sex category

GARFIELD-AF, Global Anticoagulant Registry in the Field-Atrial Fibrillation; and TIA, transient ischemic attack.

Table 8. Three Validated Risk Models for Stroke

Risk Factor	CHA_2DS_2-VASc[2]	ATRIA[1]	GARFIELD[3]
Age ≥85 y		6	0.98
Age ≥75 y	2	5	0.59
Age 65-74 y	1	3	0.20
Female sex	1	1	
Hypertension	1	1	0.16
Renal disease		1	0.35

Risk Factor	CHA_2DS_2-VASc[2]	ATRIA[1]	GARFIELD[3]
Diabetes	1	1	0.21
Current smoking			0.48
Congestive heart failure	1	1	0.23
Previous stroke or TIA	2	2–8*	0.80
Vascular disease	1		0.20
Dementia			0.51
Previous bleeding			0.30
Proteinuria		1	
Low risk score	**0**	**0–5**	**0–0.89**
Intermediate risk score	**1**	**6**	**0.90–1.59**
High risk score	**≥2**	**7–15**	**≥1.60**

Appendix 2:
Modified IMPROVE VTE risk score

VTE risk factor	VTE risk score
Previous VTE	3
Known thrombophilia[a]	2
Current lower limb paralysis or paresis[b]	2
History of cancer[c]	2
ICU/CCU stay	1
Complete immobilization[d] ≥ 1 d	1
Age ≥60 y	1

Abbreviations: CCU, cardiac care unit; ICU, intensive care unit; IMPROVE, International Medical Prevention Registry on Venous Thromboembolism; NIH, National Institutes of Health; VTE, venous thromboembolism. [a]A congenital or acquired condition leading to excess risk of thrombosis (e.g., factor V Leiden, lupus anticoagulant, factor C or factor S deficiency). [b]Leg falls to bed by 5 seconds but has some effort against gravity (taken from NIH stroke scale). [c]Cancer (excluding nonmelanoma skin cancer) present at any time in the past 5 years (cancer must be in remission to meet eligibility criteria). [d]Immobilization is being confined to bed or chair with or without bathroom privileges.

Appendix 3:
NCCN Guidelines Version 02.2024 Cancer Associated Venous Thromboembolic Disease

THERAPEUTIC ANTICOAGULATION FOR VTE

General Guidelines

- Anticoagulation options recommended for management of VTE in patients with cancer include regimens involving only one agent (monotherapy) as well as regimens that use more than one type of agent (combination therapy). This section lists the recommended regimens, including dosing and duration, as well as a list of contraindications and warnings to help guide treatment selection.[1]
  - Duration of Anticoagulation as Recommended by Guideline:
    - Duration should be at least 3 months or as long as active cancer or cancer therapy.
    - For non–catheter-associated DVT or PE recommend indefinite anticoagulation while cancer is active, under treatment, or if risk factors for recurrence persist.
    - For symptomatic catheter-associated DVT, consider anticoagulation treatment for at least 3 months or as long as the catheter is in place.
    - Providers should continue to discuss with patients the risks/benefits of anticoagulation to determine the appropriate duration of therapy. See Elements for Consideration in Decision Not to Treat (VTE-J).
    - Reconsider the role of anticoagulation therapy near the end of life. See Elements for Consideration in Decision Not to Treat (VTE-J).
- Select regimen based on these factors (not in order of importance): Renal failure (CrCl <30 mL/min), hepatic disease (elevated transaminases or bilirubin, Child-Pugh B and C liver impairment, or cirrhosis), inpatient/outpatient status, U.S. FDA approval, cost, patient preference, ease of administration, monitoring, bleeding risk assessment, and ability to reverse anticoagulation. See Contraindications and Warnings on VTE-D, 3 of 6.
- Baseline laboratory testing: CBC with platelet count, renal and hepatic function panel, aPTT, and PT/international normalized ratio (INR).
- Follow institutional standard operating procedures (SOPs) for dosing schedules. If there are no SOPs, then use the American College of Chest Physicians (ACCP) recommendations.[2]
- Following initiation of anticoagulant: hemoglobin, hematocrit, and platelet count at least every 2 to 3 days for the first 14 days while in the inpatient setting and every 2 weeks thereafter or as clinically indicated.
- Direct oral anticoagulants (DOACs), LMWH, and warfarin have all been used to treat patients with SPVT. Although published experience in the treatment of SPVT with DOACs is limited, results appear to be comparable to LMWH and warfarin. Therefore, we suggest that DOACs can be used for long-term treatment of SPVT in appropriate candidates in the recommended doses. In the absence of contraindications, NCCN suggests that DOACs, LMWH, and warfarin can be considered for treatment of SPVT. In patients with cancer, DOACs and LMWH are preferable to warfarin.

THERAPEUTIC ANTICOAGULATION FOR VTE (CONTINUED)

DOACs (preferred for patients without gastric or gastroesophageal lesions)[a]

- Apixaban[b,c]
  - 10 mg PO every 12 hours for 7 days followed by 5 mg PO every 12 hours[3-8]
- Edoxaban[b]
  - Initial therapy with LMWH[d,9,10] or UFH[e,11] for at least 5 days followed by edoxaban 60 mg PO daily (or 30 mg PO daily in patients with Cockcroft-Gault estimated CrCl 30–50 mL/min or weight <60 kg or concomitant potent P-glycoprotein (P-gp) inhibitors)[f,12,13,14]
- Rivaroxaban
  - 15 mg PO every 12 hours for the first 21 days followed by 20 mg daily with food[15-18]

LMWH (preferred for patients with gastric or gastroesophageal lesions)

- Dalteparin[b]
  - 200 units/kg SC daily for 30 days, then switch to 150 units/kg once daily[d,g,10,19,20]
- Enoxaparin
  - 1 mg/kg SC every 12 hours (BMI <40 kg/m^2) or 0.8 mg/kg SC every 12 hours (BMI ≥40 kg/m^2) (can consider decreasing intensity to 1.5 mg/kg daily after first month)[h,9,21,22-24]

DOACs (if above regimens not appropriate or unavailable)[a]

- Dabigatran
  - Initial therapy with LMWH[d,9,10] or UFH[e,11] for at least 5 days followed by dabigatran 150 mg PO every 12 hours[f,25,26]

Fondaparinux[27,28]

- 5 mg SC daily (<50 kg)
- 7.5 mg SC daily (50–100 kg)
- 10 mg SC daily (>100 kg)

UFH (category 2B)[11]

- IV 80 units/kg bolus, followed by 18 units/kg/h adjusted to target aPTT of 2–2.5 X control or per hospital SOPs, followed by SC 250 units/kg every 12 hours (category 2B)
- SC 333 units/kg load, followed by 250 units/kg every 12 hours[29]

Warfarin[i,30-32]

- Start warfarin concurrently with LMWH, fondaparinux, or UFH (see dosing below)
- Warfarin 5 mg daily adjusted to INR 2–3 (2.5 mg daily initial dose for liver disease or use with interacting medications)
  - LMWH[9,10] + warfarin[i] options:
    - Dalteparin 200 units/kg SC daily[10] or 100 units/kg SC every 12 hours
    - Enoxaparin 1 mg/kg SC every 12 hours[9]
  - Fondaparinux + warfarin[i,27,28]
    - 5 mg SC daily (<50 kg)
    - 7.5 mg SC daily (50–100 kg)
    - 10 mg SC daily (>100 kg)
  - UFH[11] + warfarin[i] options:
    - IV 80 units/kg bolus, followed by 18 units/kg/h adjusted to target aPTT of 2–2.5 X control or per hospital SOPs
    - SC 333 units/kg load, followed by 250 units/kg every 12 hours

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Direct Oral Anticoagulants are considered experimental/investigational and therefore, will follow Molina's Off- Label policy.

Contraindications to Eliquis (apixaban) include active pathological bleeding and severe hypersensitivity reaction to Eliquis (apixaban).

Contraindications to Savaysa (edoxaban) include active pathological bleeding.

Contraindications to Xarelto (rivaroxaban) include active pathological bleeding and severe hypersensitivity reaction to rivaroxaban.

BACKGROUND AND OTHER CONSIDERATIONS

Contraindications to Pradaxa (dabigatran) include active pathological bleeding and severe hypersensitivity reaction to dabigatran and mechanical prosthetic heart valve.

Review renal dose adjustment recommendations per label for the requested agent for member's with CrCl > 95 ml/min (Savaysa), ≤ 50 ml/min (Xarelto, Pradaxa) or SCr > 1.5mg/dL (Eliquis).

OTHER SPECIAL CONSIDERATIONS:

Eliquis (apixaban) has a Black Box Warning for premature discontinuation of Eliquis increases the risk of thrombotic events, and spinal/epidural hematoma.

Pradaxa (dabigatran) has a Black Box Warning for premature discontinuation of Pradaxa increases the risk of thrombotic events, and spinal/epidural hematoma.

Savaysa (edoxaban) has a Black Box Warning for reduced efficacy in nonvalvular atrial fibrillation patients with creatinine clearance (CrCl) > 95 ml/min, premature discontinuation of Savaysa increases the risk of ischemic events and spinal/epidural hematoma.

Xarelto (rivaroxaban) has a Black Box Warning for premature discontinuation of Xarelto increases the risk of thrombotic events, and spinal/epidural hematoma.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:

Dabigatran Etexilate Mesylate CAPS 75MG, 110MG, 150MG
Eliquis DVT/PE Starter Pack TBPK 5MG
Eliquis TABS 2.5MG, 5MG
Pradaxa CAPS 75MG, 110MG, 150MG
Pradaxa PACK 20MG, 30MG, 40MG, 40MG, 50MG, 110MG, 150MG
Savaysa TABS 15MG, 30MG, 60MG
Xarelto Starter Pack TBPK 15 & 20MG
Xarelto SUSR 1MG/ML
Xarelto TABS 2.5MG, 10MG, 15MG, 20MG

REFERENCES

1. Eliquis [package insert]. Princeton, New Jersey: Bristol-Myers Squibb Company; April 2021.
2. Savaysa (edoxaban) [prescribing information]. Basking Ridge, NJ: Daiichi Sankyo Inc; October 2023.
3. Xarelto (rivaroxaban) [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals Inc; February

2023.
4. Pradaxa capsules (dabigatran etexilate) [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals Inc; November 2023.
5. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. Lip GYH, Banerjee A, Boriani G, Chiang CE, Fargo R, Freedman B, Lane DA, Ruff CT, Turakhia M, Werring D, Patel S, Moores L - Chest - November 1, 2018; 154 (5); 1121-1201
6. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Members With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2019;Jan 28:[Epub ahead of print].
7. Eikelboom JW, Connolly SJ, Bosch J, et al. Rivaroxaban with or without aspirin in stable cardiovascular disease. N Engl J Med 2017;377:1319-30
8. Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Members With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D) Annie M. Young, Andrea Marshall, Jenny Thirlwall, Oliver Chapman, Anand Lokare, Catherine Hill, Danielle Hale, Janet A. Dunn, Gary H. Lyman, Charles Hutchinson, Peter MacCallum, Ajay Kakkar, F.D. Richard Hobbs, Stavros Petrou, Jeremy Dale, Christopher J. Poole, Anthony Maraveyas, and Mark Levine Journal of Clinical Oncology 2018 36:20, 2017- 2023
9. Agnelli G, Buller H, Cohen A, et al. Oral apixaban for the treatment of venous thromboembolism in cancer members: results from the AMPLIFY trial. J ThrombHeamost 2015; 13: 2187-2191
10. Einstein Investigators, Bauersachs R. Berkowitz SD et al. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med 2010;363:2499-2510
11. Spyropoulos AC, Lipardi C, Xu J, et al. Modified IMPROVE VTE risk score and elevated d- dimer identify a high venous thromboembolism risk in acutely ill medical population for extended thromboprophylaxis. TH Open. 2020;4(1):e59-e65. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32190813.
12. Cohen AT, Harrington RA, Goldhaber SZ, et al. Extended thromboprophylaxis with betrixaban in acutely ill medical patients. N Engl J Med. 2016;375(6):534-544. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27232649.
13. Raskob GE, Spyropoulos AC, Zrubek J, et al. The MARINER trial of rivaroxaban after hospital discharge for medical patients at high risk of VTE. Design, rationale, and clinical implications. Thromb- Haemost 2016;115(06):1240–1248
14. 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. doi: 10.1016/j.chest.2015.11.026.
15. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence- based clinical practice guidelines [published correction appears in Chest. 2012;142(6):1698-1704]. Chest. 2012;141(2)(suppl):e419S-e496S. doi: 10.1378/chest.11-2301.
16. Baglin T, Bauer K, Douketis J, Buller H, Srivastava A, Johnson G; SSC of the ISTH. Duration of anticoagulant therapy after a first episode of an unprovoked pulmonary embolus or deep vein thrombosis: guidance from the SSC of the ISTH. J Thromb Haemost. 2012;10(4):698- 702
17. National Comprehensive Cancer Network. 2022. Cancer-Associated Venous Thromboembolic Disease (Version 1.2022). [online] Available at: < vte.pdf (nccn.org)> [Accessed 4 November 2022].
18. National Comprehensive Cancer Network. 2024. Cancer-Associated Venous Thromboembolic Disease (Version 2.2023). [online] Available at: < vte.pdf (nccn.org)> [Accessed 16 January 2024].
19. Eikelboom, J. W., Connolly, S. J., Bosch, J., Dagenais, G. R., Hart, R. G., Shestakovska, O., … Maggioni, A. P. (2017). Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease. New England Journal of Medicine, 377(14), 1319–1330. https://doi.org/10.1056/nejmoa1709118
20. Choxi, R., Kapoor, K., Mackman, N., & Jovin, I. S. (2022). Direct Oral Anticoagulants and Coronary Artery Disease. Arteriosclerosis, Thrombosis, and Vascular Biology, 42(5). https://doi.org/10.1161/atvbaha.121.317171
21. Joglar, J. A., Chung, M. K., Armbruster, A. L., Benjamin, E. J., Chyou, J. Y., Cronin, E. M., … Linta, K. T. (2023). 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. Circulation, 149(1).

https://doi.org/10.1161/CIR.0000000000001193
22. Van, I. C., Rienstra, M., Bunting, K. V., Casado-Arroyo, R., Caso, V., Harry, … Suwalski, P. (2024). 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). European Heart Journal, 45(36). https://doi.org/10.1093/eurheartj/ehae176

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Drug Class Appendix Available Dosage Forms References	Q1 2025
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Appendix Other Special Considerations Available Dosage Forms References	Q1 2024
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy Duration of Approval Age Restrictions FDA-Approved Uses Appendix Contraindications/Exclusions/Discontinuation Available Dosage Forms	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file