Drug Coverage Policy

Effective Date.....03/01/2025
Coverage Policy Number.....IP0033
Policy Title.....Dabigatran

Anticoagulants – Dabigatran

- Pradaxa® (dabigatran etexilate mesylate capsules – Boehringer Ingelheim)
- Pradaxa® Oral Pellets (dabigatran etexilate oral pellets – Boehringer Ingelheim)

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 and have discretion in making individual coverage determinations. 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.

Cigna Healthcare Coverage Policy

Overview
Dabigatran capsules (Pradaxa, generic), a direct thrombin inhibitor, is indicated for the following uses:[1]

- **Non-valvular atrial fibrillation**, to reduce the risk of stroke and systemic embolism in adults.
- **Prophylaxis of deep vein thrombosis (DVT) and pulmonary embolism (PE)**, in adults who have undergone hip replacement surgery.

- **Treatment of DVT and PE** in adults who have been treated with a parenteral anticoagulant for 5 to 10 days, as well as **reduction in the risk of recurrence of DVT and PE** in patients who have been previously treated.
- **Treatment of venous thromboembolic events (VTE)**, in pediatric patients 8 to < 18 years of age who have been treated with a parenteral anticoagulant for at least 5 days, as well as **to reduce the risk of recurrence of VTE** in pediatric patients 8 to < 18 years of age who have been previously treated.

Pradaxa oral pellets, a direct thrombin inhibitor, is indicated for the following uses:[15]

- **VTE**, treatment in pediatric patients 3 months to < 12 years of age who have been treated with a parenteral anticoagulant for at least 5 days, as well as **to reduce the risk of recurrence of VTE** in pediatric patients 3 months to < 12 years of age who have been previously treated.

It is noted in the prescribing information for dabigatran capsules and Pradaxa oral pellets that not all dosage forms are approved for the same indications and age groups.[1,15] Due to differences in bioavailability, the individual products are not substitutable on a mg-per-mg basis. Dabigatran capsules are available in the following strengths: 75 mg, 110 mg, and 150 mg. Pradaxa oral pellets are available in the following strengths per packet: 20 mg, 30 mg, 40 mg, 50 mg, 110 mg, and 150 mg.

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 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 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

Dabigatran has data supporting its use in prophylaxis after knee replacement surgery; these data are limited to adults.[12-14] 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.

Medical Necessity Criteria

Documentation: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes, laboratory tests, claims records, and/or other information.

I. Pradaxa capsules are considered medically necessary when the following are met (1 and 2):

1. Diagnosis of **ONE** of the following (A, B, C, D, E, or F):

FDA-Approved Indications

A. Atrial Fibrillation (or Atrial Flutter). Approve for 1 year if the patient is ≥ 18 years of age.

B. Deep Vein Thrombosis or Pulmonary Embolism, Treatment. Approve for 1 year if the patient is ≥ 8 years of age.

C. Deep Vein Thrombosis or Pulmonary Embolism, To Reduce the Risk of Recurrence. Approve for 1 year if the patient is ≥ 8 years of age.

D. Deep Vein Thrombosis or Pulmonary Embolism in a Patient Undergoing Hip Replacement Surgery, Prophylaxis. Approve for 60 days if the patient is ≥ 18 years of age.

Other Uses with Supportive Evidence

E. Deep Vein Thrombosis in a Patient Undergoing Knee Replacement Surgery, Prophylaxis. Approve for 60 days if the patient is ≥ 18 years of age.

F. Treatment or Prevention of Other Thromboembolic-Related Conditions. Approve for 6 months if the patient meets both of the following (i and ii):
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.

- **i.** Patient is ≥ 8 years of age; AND
- **ii.** Patient meets one of the following (a or b):
  - **a.** Documentation provided that the patient has had failure, contraindication or intolerance 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), or Savaysa (edoxaban tablets) is not required to try warfarin, fondaparinux, or a low molecular weight heparin product.
  - **b.** Patient has been started on dabigatran capsules for the treatment of an acute thromboembolic condition

2. Preferred product criteria is met for the products listed in the below table(s)

II. Pradaxa oral pellets are considered medically necessary when the following are met (1 and 2):

1. Diagnosis of **ONE** of the following (A, B, or C):

FDA-Approved Indications

A. Venous Thromboembolic Events, Treatment. Approve for 1 year if the patient is ≥ 3 months to < 12 years of age.
Note: Examples of venous thromboembolic events include deep vein thrombosis, cerebral venous thrombosis or sinus thrombosis, pulmonary embolism, and central-venous thrombosis.

B. Venous Thromboembolic Events, To Reduce the Risk of Recurrence. Approve for 1 year if the patient is ≥ 3 months to < 12 years of age.
Note: Examples of venous thromboembolic events include deep vein thrombosis, cerebral venous thrombosis or sinus thrombosis, pulmonary embolism, and central-venous thrombosis.

Other Uses with Supportive Evidence

C. Treatment or Prevention of Other Thromboembolic-Related Conditions. Approve for 6 months if the patient meets both of the following (i and ii):
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.

- **i.** Patient is ≥ 3 months to < 12 years of age; AND
- **ii.** Patient meets one of the following (a or b):
  - **a.** Documentation provided that the patient has had failure, contraindication, or intolerance to ONE of the following: 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 Savaysa (edoxaban tablets) is not required to try warfarin, fondaparinux, or a low molecular weight heparin product.
  - **b.** Patient has been started on Pradaxa oral pellets for the treatment of an acute thromboembolic condition.

2. Preferred product criteria is met for the products listed in the below table(s)

Employer Plans and Individual and Family Plans:

Product	Criteria
Pradaxa 75 mg, 110 mg, 150 mg (dabigatran) capsule	**ONE of the following:** 1. The individual has tried **dabigatran capsule** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Patient currently receiving Pradaxa capsules for treatment of thrombosis (for example, deep vein thrombosis [DVT] or pulmonary embolism [PE]) 3. Patient currently receiving Pradaxa capsules for the prophylaxis of deep vein thrombosis [DVT] or pulmonary embolism [PE] after orthopedic surgery (for example, hip or knee replacement surgery)

Product	Criteria
Pradaxa Oral Pellets (dabigatran) oral pellets	**ONE** of the following: 1. Currently receiving Pradaxa oral pellets for treatment of thrombosis (for example, deep vein thrombosis [DVT] or pulmonary embolism [PE]) 2. Patient is ≥ 8 years of age and < 12 years of age, and **ONE** of the following: A. Intolerance to generic dabigatran capsules B. Patient is not able to swallow capsules AND failure, contraindication or intolerance to Xarelto (tablets or oral suspension) 3. Patient is < 8 years of age AND failure, contraindication or intolerance to Xarelto (tablets or oral suspension)

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.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, 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 an individual hospitalized with coronavirus disease 19 [COVID-19]). Xarelto is labeled for prophylaxis of venous thromboembolism in acutely ill medical individuals and is supported in clinical practice guidelines, including guidelines which address prophylaxis of venous thromboembolism in COVID-19 individuals. [8-11]

References

1. Pradaxa® capsules [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; November 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 2.2023 – June 1, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 14, 2024.
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. Available at: https://www.covid19treatmentguidelines.nih.gov/. Accessed on January 14, 2024.
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. Eriksson BI, Dahl OE, Rosencher N, et al, for the RE-MODEL Study Group. Oral dabigatran etexilate vs. subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement: the RE-MODEL randomized trial. *J Thromb Haemost*. 2007;5:2178-2185.
13. RE-MOBILIZE Writing Committee, Ginsberg JS, Davidson BL, Comp PC, et al. Oral thrombin inhibitor dabigatran etexilate vs. North American Enoxaparin regimen for prevention of venous thromboembolism after knee arthroplasty surgery. *J Arthroplasty*. 2009;24(1):1-9.
14. Burness CD, McKeage K. Dabigatran Etexilate. A review of its use for the prevention of venous thromboembolism after total hip or knee replacement surgery. *Drugs*. 2012;72(7):963-986.
15. Pradaxa® oral pellets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; November 2023.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	**Dabigatran capsules:** **Atrial Fibrillation (or Atrial Flutter).** Added an age restriction. **Deep Vein Thrombosis or Pulmonary Embolism, Treatment.** Added an age restriction. **Deep Vein Thrombosis or Pulmonary Embolism, To Reduce the Risk of Recurrence.** Added an age restriction. **Deep Vein Thrombosis or Pulmonary Embolism in a Patient Undergoing Hip Replacement Surgery, Prophylaxis.** Added an age restriction. **Deep Vein Thrombosis in a Patient Undergoing Knee Replacement Surgery, Prophylaxis.** Added an age restriction. **Treatment or Prevention of Other Thromboembolic-Related Conditions.** Added an age restriction.	05/01/2024

	Pradaxa oral pellets: **Venous Thromboembolic Events, Treatment.** Removed the requirement for 5 days of parenteral anticoagulant therapy. **Employer Plans preferred product requirements:** Extended the current Pradaxa 75 mg and 150 mg approach to Pradaxa 110 mg capsules. Clarified the Pradaxa Oral pellets difficulty swallowing option allows for FCI to Xarelto tablets or suspension. **Individual and Family Plans preferred product requirements:** Extended the current Pradaxa 110 mg approach to Pradaxa 75 mg and 150 mg capsules. **Conditions Not Covered:** Removed Prophylaxis of Venous Thromboembolism in Individuals with Factor V Leiden thrombophilia and Antiphospholipid syndrome as a non-covered indication.	
Selected Revision	**Removed** prior authorization requirements for generic dabigatran capsules on all Employer plans and Individual and Family plans.	03/01/2025

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