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Coverage Policy Number **IP0033**

Dabigatran

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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. 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

This policy supports medical necessity review for the following dabigatran products:

- **Dabigatran** capsules
- **Pradaxa**® (dabigatran) capsules
- **Pradaxa**® (dabigatran) oral pellets

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the Non-Covered Product Table by the respective plan type and drug list where applicable.

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

Medical Necessity Criteria

Dabigatran (Pradaxa) is considered medically necessary when the following are met:

I. **Dabigatran (dabigatran capsule, Pradaxa capsule).** Individual meets **BOTH** of the following:

1. Diagnosis of **ONE** of the following:
    A. **Atrial Fibrillation (or Atrial Flutter).**
    B. **Deep Vein Thrombosis or Pulmonary Embolism, Treatment.**
    C. **Deep Vein Thrombosis or Pulmonary Embolism, To Reduce the Risk of Recurrence.**
    D. **Deep Vein Thrombosis or Pulmonary Embolism, Prophylaxis Following Hip Replacement Surgery.**
    E. **Deep Vein Thrombosis in Individuals Undergoing Knee Replacement Surgery, Prophylaxis.**
    F. **Treatment or Prevention of Other Thromboembolic-Related Conditions (for example, superficial vein thrombosis, splanchnic vein thrombosis, hepatic vein thrombosis, prophylaxis of venous thromboembolism in high-risk individuals).** Individual meets **ONE** of the following criteria:
        i. Documentation of failure, contraindication or intolerance, to **ONE** of the following: warfarin, fondaparinux injection, a low molecular weight heparin product (for example, enoxaparin injection, Fragmin® [dalteparin injection])
        ii. Currently receiving dabigatran (dabigatran capsules or Pradaxa) for the treatment of an acute thromboembolic condition
2. Non-Covered Product Criteria is met, refer to below table(s)

Employer Group Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Pradaxa 75 mg, 150 mg (dabigatran) capsule	**ONE** of the following: A. There is documentation 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 B. Currently receiving Pradaxa capsules for treatment of thrombosis (for example, deep vein thrombosis or pulmonary embolism) C. Currently receiving Pradaxa capsules for the prophylaxis of deep vein thrombosis or pulmonary embolism after orthopedic surgery (for example, hip or knee replacement surgery)
Pradaxa 110 mg (dabigatran) capsule	**ONE** of the following: A. There is documentation the individual has had an inadequate response, contraindication, or is intolerant to **ONE** of the following: a. Dabigatran capsules [may require prior authorization] b. Eliquis [may require prior authorization] c. Savaysa [may require prior authorization] d. Xarelto [may require prior authorization] B. Individual is less than 18 years of age C. Currently receiving Pradaxa capsules for treatment of thrombosis (for example, deep vein thrombosis or pulmonary embolism) D. Currently receiving Pradaxa capsules for the prophylaxis of deep vein thrombosis or pulmonary embolism after orthopedic surgery (for example, hip or knee replacement surgery)

Individual and Family Plan Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Pradaxa 75 mg, 150 mg (dabigatran) capsule	**ONE** of the following: A. **BOTH** of the following

Non-Covered Product	Criteria
	a. There is documentation 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 [may require prior authorization] b. There is documentation the individual has had an inadequate response, contraindication, or is intolerant to **ONE** of the following: i. Eliquis [may require prior authorization] ii. Xarelto [may require prior authorization] B. Individual is less than 18 years of age C. Currently receiving Pradaxa capsules for treatment of thrombosis (for example, deep vein thrombosis or pulmonary embolism) D. Currently receiving Pradaxa capsules for the prophylaxis of deep vein thrombosis or pulmonary embolism after orthopedic surgery (for example, hip or knee replacement surgery)
Pradaxa 110 mg (dabigatran) capsule	**ONE** of the following: A. There is documentation the individual has had an inadequate response, contraindication, or is intolerant to **ONE** of the following: a. Dabigatran capsules [may require prior authorization] b. Eliquis [may require prior authorization] c. Xarelto [may require prior authorization] B. Individual is less than 18 years of age C. Currently receiving Pradaxa capsules for treatment of thrombosis (for example, deep vein thrombosis or pulmonary embolism) D. Currently receiving Pradaxa capsules for the prophylaxis of deep vein thrombosis or pulmonary embolism after orthopedic surgery (for example, hip or knee replacement surgery)
Dabigatran capsule	**ONE** of the following: A. There is documentation the individual has had an inadequate response, contraindication, or is intolerant to **ONE** of the following: i. Eliquis [may require prior authorization] ii. Xarelto [may require prior authorization] B. Individual is less than 18 years of age C. Currently receiving dabigatran capsules for treatment of thrombosis (for example, deep vein thrombosis or pulmonary embolism) D. Currently receiving dabigatran capsules for the prophylaxis of deep vein thrombosis or pulmonary embolism after orthopedic surgery (for example, hip or knee replacement surgery)

II. **Dabigatran (Pradaxa Oral Pellets) oral pellets.** Individual meets **ALL** of the following:

1. 3 months to 11 years of age
2. Diagnosis of **ONE** of the following:
   A. **Venous Thromboembolic Event (for example, deep vein thrombosis, cerebral venous thrombosis or sinus thrombosis, pulmonary embolism, and central-venous thrombosis) treatment AND the following:**
      i. Treated with a parenteral anticoagulant for at least 5 days
   B. **Venous Thromboembolic Events (for example, deep vein thrombosis, cerebral venous thrombosis or sinus thrombosis, pulmonary embolism, and central-venous thrombosis), To Reduce the Risk of Recurrence in individuals who have previously been treated**

C. **Treatment or Prevention of Other Thromboembolic-Related Conditions (for example, superficial vein thrombosis, splanchnic vein thrombosis, hepatic vein thrombosis, prophylaxis of venous thromboembolism in high-risk individuals).** Individual meets **ONE** of the following criteria:
   i. Documentation of failure, contraindication, or intolerance, to **ONE** of the following: warfarin, fondaparinux injection, a low molecular weight heparin product (e.g., enoxaparin injection, Fragmin® [dalteparin injection])
   ii. Currently receiving Pradaxa Oral Pellets for the treatment of an acute thromboembolic condition

3. Non-Covered Product Criteria is met, refer to below table(s)

Employer Group Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Pradaxa Oral Pellets (dabigatran) oral pellets	**ONE** of the following: A. 8 years of age to 11 years of age, **ONE** of the following: i. Intolerance to generic dabigatran capsules ii. If unable to swallow capsules, failure, contraindication or intolerance to Xarelto oral suspension [may require prior authorization] B. 7 years of age or younger, failure, contraindication or intolerance to Xarelto oral suspension [may require prior authorization] C. Currently receiving Pradaxa oral pellets for treatment of thrombosis (for example, deep vein thrombosis or pulmonary embolism)

Individual and Family Plan Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Pradaxa Oral Pellets (dabigatran) oral pellets	**ONE** of the following: A. Failure, contraindication, or intolerance to Xarelto (tablet, oral suspension) [may require prior authorization] B. Currently receiving Pradaxa oral pellets for treatment of thrombosis (for example, deep vein thrombosis or pulmonary embolism)

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.

Reauthorization Criteria

Continuation of dabigatran (Pradaxa capsules, Pradaxa Oral Pellets, dabigatran capsules) is considered medically necessary for **ALL** covered diagnoses when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Dabigatran (Pradaxa) capsule
Initial approval duration:

- Atrial Fibrillation (or Atrial Flutter): up to 12 months
- Deep Vein Thrombosis or Pulmonary Embolism, Treatment: up to 12 months
- Deep Vein Thrombosis or Pulmonary Embolism, To Reduce the Risk of Recurrence: up to 12 months
- Deep Vein Thrombosis or Pulmonary Embolism, Prophylaxis Following Hip Replacement Surgery: up to 60 days

- Deep Vein Thrombosis in Individuals Undergoing Knee Replacement Surgery, Prophylaxis: up to 60 days
- Treatment or Prevention of Other Thromboembolic-Related Conditions: up to 6 months

Reauthorization approval duration:
- Atrial Fibrillation (or Atrial Flutter): up to 12 months
- Deep Vein Thrombosis or Pulmonary Embolism, Treatment: up to 12 months
- Deep Vein Thrombosis or Pulmonary Embolism, To Reduce the Risk of Recurrence: up to 12 months
- Deep Vein Thrombosis or Pulmonary Embolism, Prophylaxis Following Hip Replacement Surgery: Not applicable
- Deep Vein Thrombosis in Individuals Undergoing Knee Replacement Surgery, Prophylaxis: Not applicable
- Treatment or Prevention of Other Thromboembolic-Related Conditions: up to 6 months

Dabigatran (Pradaxa Oral Pellets) oral pellets
Initial approval duration is up to 2 months
Reauthorization approval duration is up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Prophylaxis of Venous Thromboembolism in Acutely Ill Individuals.** (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]

2. **Prophylaxis of Venous Thromboembolism in Individuals with Factor V Leiden thrombophilia and Antiphospholipid syndrome.** There is limited evidence to the support the use of direct-acting oral anticoagulants (DOACs), including Pradaxa for Factor V Leiden Thrombophilia. Pradaxa and other DOACs are not recommended for use in individuals with triple-positive antiphospholipid syndrome (APS).[1] For individuals with APS (especially those who are triple positive [positive for lupus anticoagulant, anticardiolipin, and anti–beta 2 glycoprotein I antibodies]), treatment with DOACs has been associated with increased rates of recurrent thrombotic events compared with vitamin K antagonist therapy.[1]

Background

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 of age 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 19 (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 December 28, 2022), hospitalized patients with COVID-19 should not be routinely discharged from the hospital while on VTE prophylaxis.[8] For patients at low risk for bleeding and high risk for VTE, continuing anticoagulation with an FDA-approved regimen for extended VTE prophylaxis may be considered, as per protocols for patients without COVID-19. Of note, Xarelto® (rivaroxaban tablets) is FDA-approved for prophylaxis of VTE in acutely ill medical patients; dabigatran 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, CHEST guidelines (2012) suggest anticoagulation for certain patients with superficial vein thrombosis, symptomatic splanchnic thromboses (portal, mesenteric, and/or splenic vein), or symptomatic hepatic vein thrombosis.[2] The guidelines acknowledge the limited available data in these settings, and all are given Grade 2C recommendations (weak recommendation, low-quality evidence). The 2016 CHEST guideline update did not address these conditions or comment on the role of DOACs.[3] 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, agents such as vitamin K antagonists (e.g., warfarin) and low molecular weight heparin have more clinical experience in these settings.

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