Clinical Policy: Dabigatran (Pradaxa)

Reference Number: CP.PMN.49
Effective Date: 05.01.12
Last Review Date: 05.22
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Dabigatran etexilate mesylate (Pradaxa®) is a direct thrombin inhibitor.

FDA Approved Indication(s)

Pradaxa is indicated:

- To reduce the risk of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF)
- 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 3 months 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 3 months to less than 18 years of age who have been previously treated

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 Pradaxa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Valvular Atrial Fibrillation, Venous Thromboembolic Events (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 and risk reduction of VTE (for adults: only DVT or PE are approvable indications*);
   **Non-DVT and non-PE VTEs in adults are off-label indications for which Pradaxa is not covered due to lack of both FDA approval and treatment guideline support.*
   c. Prophylaxis of DVT or PE in those who have undergone hip replacement surgery;
2. For adult members: Failure of Eliquis® used for ≥ 30 days at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

3. Dose does not exceed any of the following (a or b):
   a. Adults: 300 mg (2 capsules) per day;
   b. Pediatrics: 520 mg 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.

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 or b):
   a. Adults: 300 mg (2 capsules) per day;
   b. Pediatrics: 520 mg 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 policy – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CrCl: creatinine clearance
DVT: deep venous thrombosis
FDA: Food and Drug Administration
NVAF: non-valvular atrial fibrillation
PE: pulmonary embolism
VTE: venous thromboembolism

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Eliquis® (apixaban)	**NVAF** 5 mg PO BID **Prophylaxis of DVT Following Hip or Knee Replacement Surgery** 2.5 mg PO BID **Treatment of DVT/PE** 10 mg PO BID for 7 days, then 5 mg PO BID **Reduction in Risk of Recurrent DVT/PE** 2.5 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
  - History of serious hypersensitivity reaction to Pradaxa
  - Mechanical prosthetic heart valve
- Boxed warning(s):
  - Premature discontinuation of Pradaxa increases the risk of thrombotic events

- Spinal/epidural hematoma may occur in patients treated with Pradaxa who are receiving neuraxial anesthesia or undergoing spinal puncture

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NVAF in adult patients	If CrCl > 30 mL/min: 150 mg PO BID If CrCl 15-30 mL/min: 75 mg PO BID	300 mg/day
Treatment of DVT and PE in adult patients	If CrCl > 30 mL/min: 150 mg PO BID after 5-10 days of parenteral anticoagulation	300 mg/day
Reduction in the risk of recurrence of DVT and PE in adult patients	If CrCl > 30 mL/min: 150 mg PO BID after previous treatment	300 mg/day
Prophylaxis of DVT and PE following hip replacement surgery in adult patients	If CrCl > 30 mL/min: 110 mg PO on day 1, then 220 mg PO QD	220 mg/day
Treatment and reduction in risk of recurrence of VTE in pediatric patients	For the treatment of VTE in pediatric patients, treatment should be initiated following treatment with a parenteral anticoagulant for at least 5 days. For reduction in risk of recurrence of VTE, treatment should be initiated following previous treatment. **Age- and weight-based dosing for ORAL PELLETS for patients < 2 years old:** • 3 kg to < 4 kg and 3 to < 6 months old: 30 mg PO BID • 4 kg to < 5 kg and 3 to < 10 months old: 40 mg PO BID • 5 kg to < 7 kg and 3 to < 5 months old: 40 mg PO BID • 5 kg to < 7 kg and 5 to < 24 months old: 50 mg PO BID • 7 kg to < 9 kg and 3 to < 4 months old: 50 mg PO BID • 7 kg to < 9 kg and 4 to < 9 months old: 60 mg (two 30 mg packets) PO BID • 7 kg to < 9 kg and 9 to < 24 months old: 70 mg (one 30 mg packet plus one 40 mg packet) PO BID • 9 kg to < 11 kg and 5 to < 6 months old: 60 mg (two 30 mg packets) PO BID	520 mg/day

Indication	Dosing Regimen	Maximum Dose
	• 9 kg to < 11 kg and 6 to < 11 months old: 80 mg (two 40 mg packets) PO BID • 9 kg to < 11 kg and 11 to < 24 months old: 90 mg (one 40 mg packet plus one 50 mg packet) PO BID • 11 kg to < 13 kg and 8 to < 18 months old: 100 mg (two 50 mg packets) PO BID • 11 kg to < 13 kg and 18 to < 24 months old: 110 mg PO BID • 13 kg to < 16 kg and 10 to < 11 months old: 100 mg (two 50 mg packets) PO BID • 13 kg to < 16 kg and 11 to < 24 months old: 140 mg (one 30 mg packet plus one 110 mg packet) PO BID • 16 kg to < 21 kg and 12 to < 24 months old: 140 mg (one 30 mg packet plus one 110 mg packet) PO BID • 21 kg to < 26 kg and 18 to < 24 months old: 180 mg (one 30 mg packet plus one 150 mg packet) PO BID **Weight-based dosing for ORAL PELLETS for patients 2 to < 12 years old:** • 7 kg to < 9 kg: 70 mg (one 30 mg packet plus one 40 mg packet) PO BID • 9 kg to < 11 kg: 90 mg (one 40 mg packet plus one 50 mg packet) PO BID • 11 kg to < 13 kg: 110 mg PO BID • 13 kg to < 16 kg: 140 mg (one 30 mg packet plus one 110 mg packet) PO BID • 16 kg to < 21 kg: 170 mg (one 20 mg packet plus one 150 mg packet) PO BID • 21 kg to < 41 kg: 220 mg (two 110 mg packets) PO BID • ≥ 41 kg: 260 mg (one 110 mg packet plus one 150 mg packet) PO BID **Weight-based dosing for ORAL CAPSULES for patients 8 to < 18 years old:** • 11 kg to < 16 kg: 75 mg PO BID • 16 kg to < 26 kg: 110 mg PO BID • 26 kg to < 41 kg: 150 mg PO BID	

Indication	Dosing Regimen	Maximum Dose
	• 41 kg to < 61 kg: 185 mg (one 110 mg capsule plus one 75 mg capsule) PO BID • 61 kg to < 81 kg: 220 mg (two 110 mg capsules) PO BID • ≥ 81 kg: 260 mg (one 110 mg capsule plus one 150 mg capsule) PO BID	

VI. Product Availability

- Oral capsules: 75 mg, 110 mg, 150 mg
- Oral pellet packets: 20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg

VII. References

1. Pradaxa Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; June 2021. Available at: https://www.pradaxa.com/. Accessed January 14, 2022.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed January 14, 2022.
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5. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. J Am Coll Cardiol. 2014;64(21):e1-e76.
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.
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9. Stevens SM, Woller SC, Kreuzinger LB, et al. Antithrombotic therapy for VTE disease: Second update of the CHEST guideline and expert panel report. Chest. 2021; 160(6):2247-2259.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: listed out preferred agents Eliquis and Xarelto; changed optional trial of preferred Xa inhibitor or warfarin to trial of both; references reviewed and updated.	02.07.18	05.18
2Q 2019 annual review: removed trial of warfarin per guidelines and specialist feedback; references reviewed and updated.	02.26.19	05.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.06.20	05.20
Per July SDC and prior clinical guidance, removed Xarelto redirection.	07.20.20	
2Q 2021 annual review: no significant changes; references reviewed and updated.	03.01.21	05.21
RT4: added criteria for the newly FDA-approved indication of treatment and reduction of risk of recurrence for pediatric VTEs.	07.13.21	
2Q 2022 annual review: no significant changes; revised pediatric max recommended dose per PI; references reviewed and updated.	01.14.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.07.22	

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.