Clinical Policy: Dabigatran (Pradaxa)

Reference Number: ERX.NPA.64
Effective Date: 06.01.15
Last Review Date: 05.20
Line of Business: Commercial, 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 patients with non-valvular atrial fibrillation (NVAF)
- For the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in patients who have been treated with a parenteral anticoagulant for 5-10 days
- To reduce the risk of recurrence of DVT and PE in patients who have been previously treated
- For the prophylaxis of DVT and PE in patients who have undergone hip replacement surgery

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Pradaxa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Valvular Atrial Fibrillation, Deep Venous Thrombosis, Pulmonary Embolism (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 DVT or PE;
   c. Prophylaxis of DVT or PE in those who have undergone hip replacement surgery;
2. Failure of Eliquis® and Xarelto®, each used for ≥ 30 days at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
3. Dose does not exceed 300 mg (2 capsules) per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Non-Valvular Atrial Fibrillation, Deep Venous Thrombosis, Pulmonary Embolism (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 300 mg (2 capsules) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

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
Xarelto® (rivaroxaban)	**NVAF** 20 mg/day PO QD **Prophylaxis of DVT Following Hip or Knee Replacement Surgery** 10 mg/day PO QD **Treatment of DVT/PE and Reduction in Risk of Recurrent DVT/PE** 15 mg PO BID for 21 days, then 20 mg/day PO QD	30 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	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	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	If CrCl > 30 mL/min: 150 mg PO BID after previous treatment	300 mg/day
Prophylaxis of DVT and PE following hip replacement surgery	If CrCl > 30 mL/min: 110 mg PO on day 1, then 220 mg PO QD	220 mg/day

VI. Product Availability

Capsules: 75 mg, 110 mg, 150 mg

VII. References

1. Pradaxa Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; Novemeber 2019. Available at: https://www.pradaxa.com/. Accessed February 6, 2020.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed February 6, 2020.
3. Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e278S-325S. doi.org/10.1016/j.chest.2015.11.026.
4. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest. 2016 Feb;149(2):315-352. doi: 10.1378/chest.11-2301.
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.
7. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic therapy for atrial fibrillation. Chest 2018; 154(5);1121-1201.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	06.15	06.15
Updated to new template (converted algorithm to bulleted criteria, added background and references).	07.16	09.16
Policy split from ERX.NSST.07 Oral anticoagulants and converted to new template.	07.17	08.17
2Q 2018 annual review: Converted policy from ST to clinical PA; 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
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.06.20	05.20

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.