Clinical Policy: Dabigatran (Pradaxa)
Reference Number: CP.PMN.49
Effective Date: 05.01.12
Last Review Date: 05.20
Line of Business: Medicaid

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.

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, 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 both are contraindicated or clinically significant adverse effects are experienced;
      3. Dose does not exceed 300 mg (2 capsules) per day.
      Approval duration: 12 months

   B. Other diagnoses/indications
      1. Refer to CP.PMN.53 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 Centene benefit 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 Centene benefit and documentation supports positive response to therapy.  
   Approval duration: Duration of request or 12 months (whichever is less); or  
   2. Refer to CP.PMN.53 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 – 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

   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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eliquis® (apixaban)</td>
<td>NVAF 5 mg PO BID</td>
<td>20 mg/day</td>
</tr>
<tr>
<td>Prophylaxis of DVT Following Hip or Knee Replacement Surgery 2.5 mg PO BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment of DVT/PE 10 mg PO BID for 7 days, then 5 mg PO BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduction in Risk of Recurrent DVT/PE</td>
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<td></td>
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</table>
CLINICAL POLICY
Dabigatran

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<thead>
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<th>Dosing Regimen</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5 mg PO BID</td>
<td>Xarelto&lt;sup&gt;®&lt;/sup&gt; (rivaroxaban)</td>
<td></td>
</tr>
<tr>
<td>NVAF 20 mg/day PO QD</td>
<td>Prophylaxis of DVT Following Hip or Knee Replacement Surgery 10 mg/day PO QD</td>
<td>30 mg/day</td>
</tr>
<tr>
<td>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</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVAF</td>
<td>If CrCl &gt; 30 mL/min: 150 mg PO BID If CrCl 15-30 mL/min: 75 mg PO BID</td>
<td>300 mg/day</td>
</tr>
<tr>
<td>Treatment of DVT and PE</td>
<td>If CrCl &gt; 30 mL/min: 150 mg PO BID after 5-10 days of parenteral anticoagulation</td>
<td>300 mg/day</td>
</tr>
<tr>
<td>Reduction in the risk of recurrence of DVT and PE</td>
<td>If CrCl &gt; 30 mL/min: 150 mg PO BID after previous treatment</td>
<td>300 mg/day</td>
</tr>
<tr>
<td>Prophylaxis of DVT and PE following hip replacement surgery</td>
<td>If CrCl &gt; 30 mL/min: 110 mg PO on day 1, then 220 mg PO QD</td>
<td>220 mg/day</td>
</tr>
</tbody>
</table>

VI. Product Availability
Capsules: 75 mg, 110 mg, 150 mg

VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Updated FDA approved indications, updated criteria to include the additional indication and trial/fail of preferred factor Xa inhibitor.</td>
<td>05.15</td>
<td>05.15</td>
</tr>
<tr>
<td>Converted to new template; Added newly approved indication of prophylaxis of DVT or PE in those who have undergone hip replacement surgery; Updated references.</td>
<td>02.16</td>
<td>05.16</td>
</tr>
<tr>
<td>Converted to new template Removed age criteria as age is not an absolute contraindication per FDA labeling Updated references</td>
<td>03.17</td>
<td>05.17</td>
</tr>
<tr>
<td>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.</td>
<td>02.07.18</td>
<td>05.18</td>
</tr>
<tr>
<td>2Q 2019 annual review: removed trial of warfarin per guidelines and specialist feedback; references reviewed and updated.</td>
<td>02.26.19</td>
<td>05.19</td>
</tr>
<tr>
<td>2Q 2020 annual review: no significant changes; references reviewed and updated.</td>
<td>02.06.20</td>
<td>05.20</td>
</tr>
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</table>

**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
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