**PRADAXA DOSING GUIDE**

**STARTING PATIENTS ON PRADAXA**
Assess renal function prior to initiating treatment with PRADAXA.

**INDICATION-SPECIFIC DOSAGE STRENGTHS AVAILABLE:**
75 mg, 110 mg, AND 150 mg

**Dosing information**
- Should be taken with a full glass of water
- Taken with or without food
- No INR monitoring required
- Rapid onset—maximum plasma concentrations achieved 1-3 hours after administration
- Not metabolized by the cytochrome P450 system
- When converting patients to PRADAXA from:
  - Warfarin: Discontinue warfarin and start PRADAXA when the INR is <2.0
  - Parenteral anticoagulants: Start PRADAXA 0 to 2 hours before the time that the next dose of the parenteral drug was to have been administered or at the time of discontinuation of a continuously administered parenteral drug (eg, intravenous unfractionated heparin)

**PERIODICALLY ASSESS RENAL FUNCTION AS CLINICALLY INDICATED AND ADJUST THERAPY ACCORDINGLY**
- Assess more frequently in clinical situations that may be associated with a decline in renal function
- Discontinue PRADAXA in patients who develop acute renal failure and consider alternative anticoagulant therapy
- Generally, the extent of anticoagulation does not need to be assessed. When necessary, use nPT and not INR to assess for anticoagulant activity in patients on PRADAXA

**INDICATIONS AND USAGE**
Pradaxa® (dabigatran etexilate mesylate) capsules is indicated:
- to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation;
- for the treatment of deep venous thrombosis and pulmonary embolism in patients who have been treated with a parenteral anticoagulant for 5-10 days;

**Recommended Dosing**

<table>
<thead>
<tr>
<th>REDUCE STROKE RISK IN NVAF</th>
<th>150 mg Twice Daily</th>
<th>Patients with CrCl &gt;30 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>75 mg Twice Daily</td>
<td>Patients with CrCl 15-30 mL/min</td>
<td></td>
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</tbody>
</table>

<table>
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<tr>
<th>TREAT DVT &amp; PE OR REDUCE RISK OF RECURRENT</th>
<th>150 mg Twice Daily</th>
<th>Patients with CrCl &gt;30 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>110 mg 1-4 hours post-surgery and after achieving hemostasis, then 220 mg Once Daily</td>
<td>Patients with CrCl &gt;30 mL/min</td>
<td></td>
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**Dosing With Concomitant Use of P-gp Inhibitors**

<table>
<thead>
<tr>
<th>REDUCE STROKE RISK IN NVAF</th>
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<th>Patients with CrCl &gt;50 mL/min</th>
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</thead>
<tbody>
<tr>
<td>75 mg Twice Daily</td>
<td>Patients with CrCl 30-50 mL/min with cerivastatin or systemic ketoconazole</td>
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**Dosing recommendation cannot be provided for patients with**
- NVAF: CrCl <30 mL/min or on dialysis
- DVT/PE & Hip: CrCl ≤30 mL/min or on dialysis

**Avoid co-administration in patients with**
- NVAF: CrCl <30 mL/min
- DVT/PE & Hip: CrCl ≤50 mL/min

**(A) PREMATURE DISCONTINUATION OF PRADAXA INCREASES THE RISK OF THROMBOTIC EVENTS**
Premature discontinuation of any oral anticoagulant, including PRADAXA, increases the risk of thrombotic events. If anticoagulation with PRADAXA is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant

Please see additional Important Safety Information about PRADAXA on next page and full Prescribing Information, including boxed WARNING and Medication Guide.
Thromboembolic and Bleeding Events in Patients with Prosthetic Heart Valves

The use of PRADAXA is contraindicated in patients with mechanical prosthetic valves due to a higher risk for thromboembolic events, especially in the post-operative period, and an excess of major bleeding for PRADAXA vs. warfarin. Use of PRADAXA for the prophylaxis of thromboembolic events in patients with AFS in the setting of other forms of valvular heart disease, including bioprosthetic heart valve, has not been studied and is not recommended.

Effect of P-gp Inducers & Inhibitors on Dabigatran Exposure

Concomitant use of PRADAXA with P-gp inducers (e.g., rifampin) reduces exposure to dabigatran and should generally be avoided. P-gp inhibition and impaired renal function are major independent factors in increased exposure to dabigatran. Concomitant use of P-gp inhibitors in patients with renal impairment is expected to increase exposure of dabigatran compared to either factor alone.

Reduction of Risk of Stroke/Thromboembolism in NVAF

- For patients with moderate renal impairment (Ccr 30-50 mL/min), reduce the dose of PRADAXA to 75 mg twice daily when dornedrone or systemic ketoconazole is coadministered with PRADAXA.
- For patients with severe renal impairment (Ccr 15-30 mL/min), avoid concomitant use of PRADAXA and P-gp inhibitors.

Treatment and Reduction in the Risk of Recurrence of DVT/PE & Prophylaxis of DVT/PE following Hip Replacement Surgery

- For patients with Ccr <50 mL/min, avoid use of PRADAXA and concomitant P-gp inhibitors.

ADVERSE REACTIONS

The most common adverse reactions reported with PRADAXA were related to gastrointestinal symptoms and bleeding.

Other Measures Evaluated

In NVAF patients, a higher rate of clinical MI was reported in patients who received PRADAXA (0.7/100 patient-years for 150 mg dose) than in those who received warfarin (0.6).

USE IN SPECIFIC POPULATIONS

Pregnancy: The limited available data on PRADAXA use in pregnant women are insufficient to determine drug-associated risks for adverse developmental outcomes.

Lactation: Breastfeeding is not recommended.

Geriatric: Risk of bleeding increases with age.