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 aPTT and not INR to assess for anticoagulant activity in patients on PRADAXA

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

PRADAXA DOSING GUIDE

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

Recommended Dosing

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>DOSAGE</th>
<th>CRCL RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>REDUCE STROKE RISK IN NVAF</td>
<td>150 mg Twice Daily</td>
<td>Patients with CrCl &gt;30 mL/min</td>
</tr>
<tr>
<td>TREAT DVT &amp; PE OR REDUCE RISK OF RECURRENT</td>
<td>150 mg Twice Daily</td>
<td>Patients with CrCl &gt;30 mL/min</td>
</tr>
<tr>
<td>REDUCE DVT &amp; PE RISK AFTER HIP REPLACEMENT SURGERY</td>
<td>110 mg 1-4 hours post-surgery and after achieving hemostasis, then 220 mg Once Daily for 28-35 days</td>
<td>Patients with CrCl &gt;30 mL/min</td>
</tr>
</tbody>
</table>

Dosing recommendation cannot be provided for patients with:
- NVAF: CrCl <15 mL/min or on dialysis
- DVT/PE & HIP: CrCl ≤30 mL/min or on dialysis

INDICATIONS AND USAGE
Pradaxa® (dabigatran etexilate) 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 previously treated;
- for the prophylaxis of deep vein thrombosis and pulmonary embolism in patients who have undergone hip replacement surgery

IMPORTANT SAFETY INFORMATION ABOUT PRADAXA
WARNING: (A) PREMATURE DISCONTINUATION OF PRADAXA INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

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.
(B) SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas may occur in patients treated with PRADAXA who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis.

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary. Consider the benefits and risks before neuraxial intervention in patients who are or will be anticoagulated.

CONTRAINDICATIONS

PRADAXA is contraindicated in patients with:
- active pathological bleeding;
- known serious hypersensitivity reaction to PRADAXA (e.g., anaphylactic reaction or anaphylactic shock);
- mechanical prosthetic heart valve

WARNINGS & PRECAUTIONS

Increased Risk of Thrombotic Events after Premature Discontinuation

Premature discontinuation of any oral anticoagulant, including PRADAXA, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. If PRADAXA is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant and restart PRADAXA as soon as medically appropriate.

Risk of Bleeding

• PRADAXA increases the risk of bleeding and can cause significant and, sometimes, fatal bleeding. Promptly evaluate any signs or symptoms of blood loss (e.g., a drop in hemoglobin and/or hematocrit or hypotension). Discontinue PRADAXA in patients with active pathological bleeding.
• Risk factors for bleeding include concomitant use of medications that increase the risk of bleeding (e.g., anti-platelet agents, heparin, fibrinolytic therapy, and chronic use of NSAIDs). PRADAXA’s anticoagulant activity and half-life are increased in patients with renal impairment.
• Reversal of Anticoagulant Effect: A specific reversal agent (idarucizumab) for dabigatran is available when reversal of the anticoagulant effect of dabigatran is needed;
  • For emergency surgery/urgent procedures
  • In life-threatening or uncontrolled bleeding
  • Hemodialysis can remove dabigatran; however clinical experience for hemodialysis as a treatment for bleeding has not been evaluated. Protamine sulfate and vitamin K are not expected to affect dabigatran anticoagulant activity.
  • Consider administration of platelet concentrates where thrombocytopenia is present or long-acting antiplatelet drugs have been used.

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 AFib 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/Systemic Embolism in NVAF

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

Increased Risk of Thrombosis in Patients with Triple-Positive Antiphospholipid Syndrome

There is an increased risk of thrombosis in patients with triple-positive antiphospholipid syndrome. PRADAXA use is not recommended.

ADVERSE REACTIONS

The most common adverse reactions reported with PRADAXA were related to gastritis-like 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.

Please see additional Important Safety Information about PRADAXA on previous page and full Prescribing Information, including boxed WARNING and Medication Guide.