**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;
- to reduce the risk of recurrence 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:**
- Premature discontinuation of PRADAXA increases the risk of thrombotic events.
- 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.

**Additional considerations**
- Determine reversal strategies as medically appropriate:
  - Blood products (prothrombin complex concentrates or recombinant Factor VIIa)†
  - PRADAXA—the only OAC that is dialyzable (~50% of dabigatran can be cleared from plasma over 4 hours)†
  - Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of PRADAXA.
- Half-life of PRADAXA in healthy subjects is 12-17 hours.
- Anticoagulant effect and half-life of PRADAXA are increased in patients with renal impairment.
- If surgery cannot be delayed, there is an increased risk of bleeding and this risk should be weighed against the urgency of the intervention.
- PRADAXA can be restarted as soon as medically appropriate.

**MANAGEMENT OF MEDICAL EMERGENCY*”**

- For emergency surgery/urgent procedures:
  - Discontinue PRADAXA.
  - Clinical evaluation of the need for reversal of anticoagulant effects in patients taking PRADAXA.
  - Initiate use of Praxbind® (idarucizumab).
  - Consider standard supportive measures as medically appropriate†:
    - Surgical hemostasis
    - Volume replacement
    - Transfusion (eg, pRBCs, platelets)

- In life-threatening/uncontrolled bleeding:
  - Discontinue PRADAXA.

*These recommendations are not intended to replace clinical judgment or to dictate individual patient care.

†Coagulation factors and dialysis have not been evaluated in clinical trials and clinical experience for the management of medical emergencies is limited.

**NOTES**

NOAC=novel oral anticoagulant; pRBCs=packed red blood cells; OAC=oral anticoagulant.

Please see additional Important Safety Information about PRADAXA on next page and full Prescribing Information, including boxed WARNING and Medication Guide.
IMPORTANT SAFETY INFORMATION (cont'd)

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 is limited. Prothrombin complex concentrates or recombinant Factor VIIa may be considered but their use 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 dronedarone or systemic ketoconazole is coadministered with PRADAXA.
- For patients with severe renal impairment (CrCl 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 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.

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