YOUR CONTROL THEIR FUTURE

PRADAXA—THE ONLY NOAC WITH A SPECIFIC REVERSAL AGENT

MANAGEMENT OF MEDICAL EMERGENCY *

For emergency surgery/urgent procedures

Discontinue PRADAXA

In life-threatening/uncontrolled bleeding

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 (e.g., pRBCs, platelets)

Additional considerations

• Determine reversal strategies as medically appropriate:
  • Blood products (prothrombin complex concentrates or recombinant Factor VIIa)¹
  • PRADAXA—the only OAC that is dialyzable (~50% of dabigatran can be cleared from plasma over 4 hours)¹²
  • 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

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

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: (A) PREMATURE DISCONTINUATION OF PRADAXA INCREASES THE RISK OF THROMBOTIC EVENTS. (B) SPINAL/EPIDURAL HEMATOMA (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

(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. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

• use of indwelling epidural catheters
• concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants
• a history of traumatic or repeated epidural or spinal punctures
• a history of spinal deformity or spinal surgery
• optimal timing between the administration of PRADAXA and neuraxial procedures is not known

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.

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 VIII 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 (Ccr 30-50 mL/min), reduce the dose of PRADAXA to 75 mg twice daily when dornedorenone 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 <30 mL/min, avoid use of PRADAXA and concomitant P-gp inhibitors

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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