Safety first—Immediate reversal available nationwide$^{1,2}$
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

General 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

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

Indications and Usage for PRADAXA
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

Select safety information about PRADAXA

Boxed 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

Recommended dose for NVAF
PRADAXA 150 mg twice daily for patients with CrCl >30 mL/min

Reduced dose
PRADAXA 75 mg twice daily for patients with CrCl 15–30 mL/min

In patients with moderate renal impairment (CrCl 30–50 mL/min):
Reduce dose to 75 mg twice daily if given with P-gp inhibitors dronedarone or systemic ketoconazole

Dose adjustments
- In patients with CrCl <30 mL/min: Avoid concomitant use of PRADAXA and P-gp inhibitors
- For patients with CrCl <15 mL/min or on dialysis: Dosing recommendations cannot be provided

Select safety information about PRADAXA

(B) Spinal/Epidural Hematoma (cont’d)
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.

Please see Important Safety Information about PRADAXA and PRAXBIND throughout this brochure. Please see accompanying full Prescribing Information for PRADAXA, including boxed WARNING and Medication Guide, as well as full Prescribing Information for PRAXBIND.
PRADAXA—Dosing for DVT & PE patients
Uniform dosing for the treatment of DVT & PE

Recommended dose for DVT and PE
PRADAXA 150 mg twice daily for patients with CrCl >30 mL/min

Parenteral anticoagulant
PRADAXA 150 mg twice daily

0
5-10 days

PRADAXA 150 mg twice daily

- Initial treatment with parenteral anticoagulant for 5-10 days
- Patients can start PRADAXA on Day 6
- No bridging necessary

Dosing information

- In patients with CrCl <50 mL/min: Avoid concomitant use of PRADAXA and P-gp inhibitors
- For patients with CrCl ≤30 mL/min or on dialysis: Dosing recommendations cannot be provided

For the reduction in risk of recurrence of DVT and PE

Recommended dose for DVT and PE
PRADAXA 150 mg twice daily for previously treated patients with CrCl >30 mL/min

Dosing information

- No parenteral anticoagulation necessary

- In patients with CrCl <50 mL/min: Avoid concomitant use of PRADAXA and P-gp inhibitors
- For patients with CrCl ≤30 mL/min or on dialysis: Dosing recommendations cannot be provided

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

For the prophylaxis of DVT & PE

PRADAXA—Dosing in patients following hip replacement surgery

Recommended dose following hip replacement surgery
PRADAXA 220 mg once daily for patients with CrCl >30 mL/min

PRADAXA 220 mg once daily

1-4 hours post-surgery
Hemostasis
28-35 days

Dosing information

- Initiate PRADAXA with 110 mg taken orally 1-4 hours after surgery and after hemostasis has been achieved
- Start PRADAXA 220 mg once daily for 28-35 days
- If PRADAXA is not started on the day of surgery, after hemostasis has been achieved, initiate treatment with 220 mg once daily

- In patients with CrCl <50 mL/min: Avoid concomitant use of PRADAXA and P-gp inhibitors
- For patients with CrCl ≤30 mL/min or on dialysis: Dosing recommendations cannot be provided

SELECT SAFETY INFORMATION ABOUT PRADAXA
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.

Please see Important Safety Information about PRADAXA and PRAXBIND throughout this brochure. Please see accompanying full Prescribing Information for PRADAXA, including boxed WARNING and Medication Guide, as well as full Prescribing Information for PRAXBIND.
Converting patients on PRADAXA to & from other anticoagulants

Warfarin

Converting from warfarin

Discontinue warfarin and start PRADAXA when the INR is <2.0

Adjust the starting time of warfarin based on CrCl as follows:

- **Recommended start of warfarin before discontinuing PRADAXA**: 3 days, 2 days, 1 day, No recommendations can be made
- **Creatinine clearance**:
  - 3 days: ≥50 mL/min
  - 2 days: 30-50 mL/min
  - 1 day: 15-30 mL/min
  - No recommendations can be made: <15 mL/min

- Because PRADAXA can increase INR, the INR will better reflect warfarin’s effect only after PRADAXA has been stopped for at least 2 days.

Converting to warfarin

*SELECT SAFETY INFORMATION ABOUT PRADAXA*

**WARNINGS & PRECAUTIONS**

**Risk of Bleeding (cont'd)**

- **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.

**Parenteral anticoagulants**

**Administration of parenteral anticoagulant**

- Scheduled dosing: 0 to 2 hours before time of next dose
- Continuous infusion (eg, intravenous unfractionated heparin): At the time of discontinuation

**Recommended starting time of PRADAXA**

- **CrCl ≥30 mL/min**: Wait 12 hours after last dose of PRADAXA
- **CrCl <30 mL/min**: Wait 24 hours after last dose of PRADAXA

**Converting from parenteral anticoagulants**

- **Recommended start of warfarin before discontinuing PRADAXA**
  - Creatinine clearance ≥50 mL/min: 3 days
  - Creatinine clearance 30-50 mL/min: 2 days
  - Creatinine clearance 15-30 mL/min: 1 day
  - Creatinine clearance <15 mL/min: No recommendations can be made

**Converting to parenteral anticoagulants**

Before initiating treatment with a parenteral anticoagulant:

- **CrCl ≥30 mL/min**: Wait 12 hours after last dose of PRADAXA
- **CrCl <30 mL/min**: Wait 24 hours after last dose of PRADAXA

*SELECT SAFETY INFORMATION ABOUT PRADAXA*

**WARNINGS & PRECAUTIONS**

**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.
Assessing anticoagulation activity of PRADAXA

**General guidelines**
- INR is relatively insensitive to dabigatran exposure and cannot be interpreted the same way for warfarin monitoring.
- When assessment is necessary, use aPTT and not INR to assess for anticoagulant activity in patients on PRADAXA.
- PRADAXA prolongs aPTT at therapeutic doses.
- When possible, determine time of last dose of PRADAXA relative to time of blood sampling.

**Anticoagulant effect**
- aPTT provides an approximation of anticoagulant effect.
- Prolongation of aPTT occurs with increasing PRADAXA plasma concentration.
- In the RE-LY® Trial, median (10th to 90th percentile) trough aPTT in patients receiving PRADAXA 150 mg was 52 (40 to 76) seconds.
- The degree of anticoagulant activity can also be assessed by the ECT—a more specific measure of dabigatran effect.

**Average time course for effects of dabigatran on aPTT in patients with various degrees of renal impairment**

![Average time course for effects of dabigatran on aPTT in patients with various degrees of renal impairment](image)

- While advice cannot be provided on the level of recovery of aPTT needed in any particular clinical setting, curves in the aPTT time course can be used to estimate time to reach a particular level of aPTT recovery—even when time since the last dose of PRADAXA is not precisely known.
- Plasma concentration levels decline relatively quickly following discontinuation in patients with normal renal function.

**SELECT SAFETY INFORMATION ABOUT PRADAXA**

**WARNINGS & PRECAUTIONS**

**Effect of P-gp Inducers & Inhibitors on Dabigatran Exposure (cont’d)**

*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 ≤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.

**SELECT SAFETY INFORMATION ABOUT PRADAXA**

**ADVERSE REACTIONS**

The most serious adverse reactions reported with PRADAXA were related to bleeding.

**NVAF**
- Most frequent adverse reactions leading to discontinuation of PRADAXA were bleeding & gastrointestinal (GI) events.
- PRADAXA 150 mg resulted in higher rates of major and any GI bleeds compared to warfarin.
- In patients ≥75 years of age, the risk of major bleeding may be greater with PRADAXA vs warfarin.
- Patients on PRADAXA 150 mg had an increased incidence of GI adverse reactions. These were dyspepsia (including abdominal pain upper, abdominal pain, abdominal discomfort, and epigastric discomfort) and gastritis-like symptoms (including GERD, esophagitis, erosive gastritis, gastric hemorrhage, hemorrhagic gastritis, hemorrhagic erosive gastritis, and GI ulcer).

Please see Important Safety Information about PRADAXA and PRAXBIND throughout this brochure. Please see accompanying full Prescribing Information for PRADAXA, including boxed WARNING and Medication Guide, as well as full Prescribing Information for PRAXBIND.
Discontinuing PRADAXA before scheduled surgery & interventions

### SELECT SAFETY INFORMATION ABOUT PRADAXA

#### ADVERSE REACTIONS

**DVT/PE**
- Rates of any GI bleeds were higher in patients receiving PRADAXA 150 mg vs warfarin and placebo
- In the active-controlled studies, there was a higher rate of clinical myocardial infarction (MI) in PRADAXA patients [20 (0.66/100 patient-years)] vs warfarin [5 (0.17/100 patient-years)]. In the placebo-controlled study, there was similar rate of non-fatal and fatal clinical MI in PRADAXA patients [1 (0.32/100 patient-years)] vs placebo [1 (0.34/100 patient-years)]
- GI adverse reactions were similar in patients receiving PRADAXA 150 mg vs warfarin. They were dyspepsia (including abdominal pain upper, abdominal pain, abdominal discomfort, and epigastric discomfort) and gastritis-like symptoms (including gastritis, GERD, esophagitis, erosive gastritis and gastric hemorrhage)

**DVT/PE After Hip Replacement Surgery**
- Rate of major GI bleeds in patients receiving PRADAXA 220 mg and enoxaparin was the same; rate of any GI bleeds was higher in patients receiving PRADAXA 220 mg vs enoxaparin
- GI adverse reactions were the same in patients receiving PRADAXA 220 mg vs enoxaparin. These were dyspepsia (including abdominal pain upper, abdominal pain, abdominal discomfort, and epigastric discomfort) and gastritis-like symptoms (including gastritis, GERD, esophagitis, erosive gastritis and gastric hemorrhage)
- Clinical MI was reported in 2 (0.1%) patients who received PRADAXA 220 mg and 6 (0.3%) patients who received enoxaparin

### Half-life

- Healthy subjects: 12-17 hours

- Due to an increased risk of bleeding, PRADAXA should be discontinued before invasive or surgical procedures, if possible:
  - Discontinue 1-2 days before procedure
  - Discontinue 3-5 days before procedure

<table>
<thead>
<tr>
<th>CrCl ≥50 mL/min</th>
<th>CrCl &lt;50 mL/min</th>
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<tbody>
<tr>
<td>Discontinue 1-2 days before procedure</td>
<td>Discontinue 3-5 days before procedure</td>
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### Additional guidance

- **Risk of bleeding**
  - If surgery cannot be delayed, there is an increased risk of bleeding
  - This risk of bleeding should be weighed against urgency of intervention
  - Use the specific reversal agent Praxbind® (idarucizumab) in case of emergency surgery or urgent procedures when reversal of the anticoagulant effect of dabigatran is needed
  - Refer to the prescribing information for PRAXBIND for additional information
  - Restart PRADAXA as soon as medically appropriate

### Discontinuation and increased risk of thrombotic events

- 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, consider coverage with another anticoagulant and restart PRADAXA as soon as medically appropriate

### SELECT SAFETY INFORMATION ABOUT PRADAXA

#### 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).

Please see Important Safety Information about PRADAXA and PRAXBIND throughout this brochure. Please see accompanying full Prescribing Information for PRADAXA, including boxed WARNING and Medication Guide, as well as full Prescribing Information for PRAXBIND.
Additional instructions for patients

- Tell patients to take PRADAXA exactly as prescribed
- Remind patients not to discontinue PRADAXA without talking to the healthcare provider who prescribed it
- Instruct patients to remove only 1 capsule from the opened bottle at the time of use. The bottle should be immediately and tightly closed
- Advise patients not to chew or break the capsules before swallowing them and not to open the capsules and take the pellets alone
- Advise patients that the capsule should be taken with a full glass of water
- If GI symptoms develop, consider having the patient take PRADAXA within 30 minutes after a meal or adding a PPI

Storage & handling of PRADAXA

Bottles and blister packs:

- Store at 25°C (77°F)
- Excursions permitted to 15°-30°C (59°-86°F)
- Store in original package to protect from moisture
- Patients should not place product in pill boxes or pill organizers

Bottles only:

- Patients should only open 1 bottle at a time
- Keep the bottle tightly closed
- Must be used within 4 months of opening

Safety first—Immediate reversal available nationwide\(^1,2\)

PRAXBIND is indicated in patients treated with PRADAXA when reversal of the anticoagulant effects of dabigatran is needed:

- For emergency surgery/urgent procedures
- In life-threatening or uncontrolled bleeding

This indication is approved under accelerated approval based on a reduction in unbound dabigatran and normalization of coagulation parameters in healthy volunteers. Continued approval for this indication may be contingent upon the results of an ongoing cohort case series study.

RE-VERSE AD™ Trial: Multicenter, multinational, single-cohort case series trial for the reversal of PRADAXA\(^2\)

Primary Endpoint:

- To determine the maximum percentage reversal of the anticoagulant effect of dabigatran within 4 hours after the administration of PRAXBIND, based on central laboratory determination of dTT or ECT:

  - In patients who presented with PRADAXA-related life-threatening or uncontrolled bleeding (Group A)
  - In patients who required emergency surgery or urgent procedures (Group B)

Methodology:

- The interim analysis included data for 123 patients (66 patients in Group A and 57 patients in Group B) currently taking PRADAXA who were administered PRAXBIND 5 g
- Results of central laboratory evaluations were available for a subset of 90 patients (51 patients in Group A and 39 patients in Group B)
- Median age was 77 years and median CrCl was 55 mL/min
- Approximately 67% and 63% of the patients in groups A and B, respectively, had been treated with 110 mg of PRADAXA twice daily prior to PRAXBIND administration

SELECT SAFETY INFORMATION ABOUT PRAXBIND

WARNINGS & PRECAUTIONS

Thromboembolic Risk

- Dabigatran-treated patients have underlying diseases predisposing them to thromboembolic events. Reversing dabigatran therapy exposes patients to the thrombotic risk of their underlying disease. To reduce this risk, resumption of anticoagulant therapy should be considered as soon as medically appropriate.
PRAXBIND—Flexible administration for immediate reversal

Ready to use immediately
- One recommended dose for all PRADAXA patients
- No reconstitution needed

Flexible administration
Intravenously administer the dose of 5 g (2 vials, each containing 2.5 g) as:

Option 1: Infusion
- Hang vials and administer as 2 consecutive infusions.

Option 2: Bolus Injection
- Inject both vials consecutively via syringe.

- Do not mix with other medicinal products
- A pre-existing intravenous line may be used for administration of PRAXBIND. The line must be flushed with 0.9% Sodium Chloride Injection, USP solution prior to infusion
- No other infusion should be administered in parallel via the same intravenous access

Quickly & specifically binds to PRADAXA
- Not expected to bind to other endogenous targets

SELECT SAFETY INFORMATION ABOUT PRAXBIND

WARNINGS & PRECAUTIONS
Re-elevation of Coagulation Parameters
- Elevated coagulation parameters (e.g., activated partial thromboplastin time or ecarin clotting time) have been observed in a limited number of PRAXBIND-treated patients. If reappearance of clinically relevant bleeding together with elevated coagulation parameters is observed or if patients requiring a second emergency surgery/urgent procedure have elevated coagulation parameters, an additional full dose may be considered.

Please see Important Safety Information about PRADAXA and PRAXBIND throughout this brochure. Please see accompanying full Prescribing Information for PRADAXA, including boxed WARNING and Medication Guide, as well as full Prescribing Information for PRAXBIND.

In a phase 1 trial in healthy volunteers,

PRAXBIND—Immediate, complete, & long-lasting effect over 24 hours*†
- Reduction observed over the entire observation period of ≥24 hours†
- In a limited number of patients, re-distribution of dabigatran from the periphery to plasma led to re-elevation of dTT, ECT, aPTT, and TT

Cases with partial reversal were identified with laboratory assessment.

SELECT SAFETY INFORMATION ABOUT PRAXBIND

WARNINGS & PRECAUTIONS
Hypersensitivity Reactions
- There is insufficient clinical experience evaluating risk of hypersensitivity to idarucizumab, but a possible relationship could not be excluded. Risk of hypersensitivity (e.g., anaphylactoid reaction) to idarucizumab or excipients needs to be weighed cautiously against the potential benefit. If serious allergic reaction occurs, immediately discontinue PRAXBIND and institute appropriate treatment.

Please see Important Safety Information about PRADAXA and PRAXBIND throughout this brochure. Please see accompanying full Prescribing Information for PRADAXA, including boxed WARNING and Medication Guide, as well as full Prescribing Information for PRAXBIND.

TT=thrombin time; ETP=endogenous thrombin potential; ULN=upper limit of normal.
*Immediate reversal=effect of dabigatran reversed to below the ULN directly after infusion of PRAXBIND.
†Complete reversal=mean clotting time returned to below the ULN.
In an interim analysis of an ongoing trial in actively treated patients of RE-VERSE AD™,

**PRAXBIND—Immediate, complete, & long-lasting effect over 24 hours**

- Median maximum reversal was 100% in the first 4 hours (primary endpoint; n=90)‡
- 9 out of 10 patients achieved complete reversal (n=90)‡
- In a limited number of patients, elevated coagulation parameters (eg, aPTT or ECT) have been observed 12-24 hours post-dose

[Graph showing change of ECT from baseline in PRADAXA-treated patients from RE-VERSE AD]

**SELECT SAFETY INFORMATION ABOUT PRAXBIND**

**WARNINGS & PRECAUTIONS**

**Risk in Patients with Hereditary Fructose Intolerance**

- PRAXBIND contains 4 g sorbitol as an excipient. When prescribing PRAXBIND in patients with hereditary fructose intolerance consider the total daily amount of sorbitol/fructose consumption from all sources as serious adverse reactions (e.g. hypoglycemia, hypophosphatemia, metabolic acidosis, increase in uric acid, acute liver failure and death) may occur.

Please see Important Safety Information about PRADAXA and PRAXBIND throughout this brochure. Please see accompanying full Prescribing Information for PRADAXA, including boxed WARNING and Medication Guide, as well as full Prescribing Information for PRAXBIND.

**SELECT SAFETY INFORMATION ABOUT PRAXBIND**

**ADVERSE REACTIONS**

- The most frequently reported adverse reaction in ≥5% of idarucizumab-treated healthy volunteers was headache (12/224). The most frequently reported adverse reactions in ≥5% of patients were hypokalemia (9/123), delirium (9/123), constipation (8/123), pyrexia (7/123) and pneumonia (7/123).

- 5 patients reported thrombotic events in RE-VERSE AD (5/123)
  - 1 report was 2 days after PRAXBIND administration
  - 4 reports were ≥7 days after PRAXBIND administration
  - Events occurred in the absence of antithrombotic therapy and could be attributed to the patients’ underlying medical condition

[Graph showing change of aPTT from baseline in PRADAXA-treated patients from RE-VERSE AD]

h=hour(s).

*Please see the RE-VERSE AD Trial on page 13.
†Determined by mean clotting time below the ULN as measured by ECT and dTT.
‡Blood samples were obtained at baseline, after the first infusion, at 10-30 minutes after the second infusion, and at 1, 2, 4, 12, and 24 hours.
In an interim analysis of an ongoing trial in actively treated patients of RE-VERSE AD™ (n=123),

PRAXBIND—Every minute matters

Normalization of serious bleeding observed as early as 12 minutes after administration**†1 (Group A: 48 of 66 patients in Group A were evaluable; 44 of 48 patients had normalization of bleeding within 72 hours.)
- Median time to bleeding cessation: 9.8 hours
- Range: 0.2 hours to 62 days

92% of patients who underwent an urgent procedure or emergency surgery had normal blood clotting†1 (Group B: 52 of 52 patients in Group B were evaluable; 48 of 52 patients had normal blood clotting.)

Clinical relevance of findings from Groups A and B is undetermined.†

SELECT SAFETY INFORMATION ABOUT PRAXBIND
ADVERSE REACTIONS (cont’d)
- As with all proteins there is a potential for immunogenicity with idarucizumab. In treated patients, treatment-emergent antibodies with low titers were observed (9/224).

OAC = oral anticoagulant.
*Please see the RE-VERSE AD Trial on page 13.
†Cessation and normalization assessments were subjective and based upon investigator visualization or measurement.
‡Emergency surgery or urgent procedure is defined as a procedure that cannot be delayed for a minimum of 8 hours.
§Life-threatening or uncontrolled bleeding is defined as overt bleeding that is judged by the treating clinician to require a reversal agent.

Be ready for any emergency—Flexibility in reversal use²

Management of medical emergency‡

1. For emergency surgery/urgent procedures†
2. In life-threatening/uncontrolled bleeding†

- Discontinue PRADAXA
- Clinical evaluation of the need for reversal of anticoagulant effects in patients taking PRADAXA
- Initiate use of PRAXBIND

Consider standard supportive measures as medically appropriate†:
- Surgical hemostasis
- Volume replacement/blood products
  - Prothrombin complex concentrates or recombinant Factor VIIa
  - Platelet concentrates (with thrombocytopenia or long-acting antiplatelets)
- PRADAXA is the only OAC that is dialyzable; ~50% of dabigatran can be cleared from plasma over 4 hours§

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

Additional considerations
- Anticoagulant effect and half-life of PRADAXA are increased in patients with renal impairment
- PRAXBIND has no effect on other anticoagulant or antithrombotic therapies
- PRADAXA can be reinitiated after 24 hours

²These recommendations are not intended to replace clinical judgment or to dictate individual patient care.

SELECT SAFETY INFORMATION ABOUT PRAXBIND
USE IN SPECIFIC POPULATIONS
Pregnancy and Nursing Mothers
- PRAXBIND should be given to a pregnant or nursing woman only if clearly needed.

Please see Important Safety Information about PRADAXA and PRAXBIND throughout this brochure. Please see accompanying full Prescribing Information for PRADAXA, including boxed WARNING and Medication Guide, as well as full Prescribing Information for PRAXBIND.
Safety first—Immediate reversal available nationwide¹,²

Quick, flexible administration

- Fast-acting reversal in a single 5-g dose (2 vials, each containing 2.5 g)*
  - One recommended dose for all PRADAXA patients
  - Can be administered as an infusion OR bolus injection

PRAXBIND has shown no procoagulant effect

- Measured as ETP

PRADAXA can be reinitiated after 24 hours

For more information or to locate PRAXBIND near you, please call 1-800-542-6257 (opt 1) or visit PRAXBIND.com


Please see Important Safety Information about PRADAXA and PRAXBIND throughout this brochure. Please see accompanying full Prescribing Information for PRADAXA, including boxed WARNING and Medication Guide, as well as full Prescribing Information for PRAXBIND.