Intermountain Healthcare

Medication Information Sheet

October 2013

Dabigatran Etexilate (PRADAXA®)

REASON FOR FACT SHEET:

Dabigatran etexilate (Pradaxa®) was approved by the FDA in October of 2010 as an alternative to warfarin to reduce the risk of stroke in patients with non-valvular atrial fibrillation. Dabigatran was reviewed by the P&T Committee and added to the formulary on January 19, 2011. This sheet is designed to give providers information regarding the use of this medication. For the purpose of this information sheet, dabigatran etexilate (Pradaxa®) will just be referred to as dabigatran.

INDICATIONS AND USAGE:

Dabigatran is a direct thrombin inhibitor indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation.

DOSAGE AND ADMINISTRATION

For patients with CrCl >30 mL/min: 150 mg orally, twice daily

Initiating dabigatran among patients with CrCl <30 ml/min should generally be avoided and is considered contraindicated by the American College of Chest Physicians' recommendations in Antithrombotic Therapy and Prevention of Thrombosis, 9th edition (AT9).[3]

Instruct patients not to chew, break, or open capsules

IMPORTANT, PLEASE NOTE: The oral bioavailability of dabigatran increases by 75% when the pellets are taken without the capsule shell compared to the intact capsule formulation. Dabigatran capsules should therefore **not be broken, chewed, or opened before administration.** There is no option for feeding tube administration.

CONTRAINDICATIONS

Dabigatran is contraindicated in patients with: Active pathological bleeding, history of a serious hypersensitivity reaction to dabigatran (e.g., anaphylactic reaction or anaphylactic shock), patients with mechanical prosthetic heart valves, or CrCl < 30 ml/min (according to AT9).

CONVERTING BETWEEN DABIGATRAN AND PARENTERAL ANTICOGULANTS

Note: No clinical trial data exist for the below recommendations, rather they are based on dabigatran pharmacokinetics. Clinical judgment should be utilized to individualize the approach to each patient.

For patients currently receiving a parenteral anticoagulant, start dabigatran 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 (e.g., intravenous un-fractionated heparin).

For patients currently taking dabigatran, wait 12 hours (if CrCl ≥30 mL/min) or 24 hours (if CrCl <30 mL/min) after the last dose of dabigatran before initiating treatment with a parenteral anticoagulant

Surgery and Interventions: If possible, discontinue dabigatran 1 to 2 days (if CrCl ≥50 mL/min) or 3 to 5 days (if CrCl <50 mL/min) before invasive or surgical procedures because of the increased risk of bleeding. Consider longer times for patients undergoing major surgery, spinal puncture, or placement of a spinal or epidural catheter or port, in whom complete hemostasis may be required

Dabigatran Etexilate (PRADAXA®)

If surgery cannot be delayed, there is an increased risk of bleeding. This risk of bleeding should be weighed against the urgency of the intervention. Bleeding risk and anticoagulant of dabigatran activity can be approximated by the aPTT test.

TEMPORARY DISCONTINUATION OF DABIGATRAN

Interruption of anticoagulants, including dabigatran, for active bleeding, elective surgery, or invasive procedures places patients at an increased risk of stroke. Lapses in therapy should be avoided, and if anticoagulation with dabigatran must be temporarily discontinued for any reason, therapy should be restarted as soon as possible. Note that the timing of dabigatran interruption is based on assessment of pharmacodynamics and has not been the subject of clinical trials. Clinical judgment should be exercised in timing doses.

PREGNANCY AND NURSING

Pregnancy: Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women.
Nursing Mothers: It is not known whether dabigatran is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when dabigatran is administered to a nursing woman.

IN CASE OF BLEEDING:

1. Initiate appropriate clinical support.
2. Discontinue treatment with dabigatran, and investigate the source of bleeding. Dabigatran is primarily excreted in the urine therefore, maintain adequate diuresis. Dabigatran can be dialyzed (Protein binding is low), with the removal of about 60% of drug over 2 to 3 hours.
3. Consider surgical hemostasis or the transfusion of fresh frozen plasma or red blood cells.
4. No specific antidote is proven to reverse the anticoagulant effect of dabigatran. Possible consideration may be given to the following:
    a. Consider activated prothrombin complex concentrates (e.g., FEIBA), or recombinant factor VIIa, or concentrates of coagulation factors II, IX or X.
    b. Consider administration of platelet concentrates in cases where thrombocytopenia is present or long-acting antiplatelet drugs have been used. Measurement of aPTT may help guide therapy.

SPECIAL CONCERNS: INCREASED INR

Because dabigatran can contribute to an elevated INR, the INR will better reflect warfarin's effect after dabigatran has been stopped for at least 2 days.

DRUG INTERACTIONS

The concomitant use of dabigatran with P-gp inducers (e.g., rifampin, St. John's Wort) reduces exposure to dabigatran and should generally be avoided. P-gp inhibitors, ketoconazole, verapamil, amiodarone, dronedarone, quinidine, and clarithromycin could result in increased dabigatran exposure but do not require dose adjustments.

PHARMACOKINETICS:

Absorption: The absolute bioavailability of dabigatran following oral administration of dabigatran etexilate is approximately 3 to 7%. Cmax occurs at 1 hour post-administration in the fasted state.
Distribution: Dabigatran is approximately 35% bound to human plasma proteins. The volume of distribution of dabigatran is 50 to 70 L.
Elimination: Dabigatran is eliminated primarily in the urine. Renal clearance of dabigatran is 80% of total clearance after intravenous administration. The half-life of dabigatran in healthy subjects is 12 to 17 hours.

HOW SUPPLIED/STORAGE AND HANDLING & COST

Once opened, the product must be used within 4 months. Store in the original bottle and keep tightly closed to protect from moisture. Dabigatran has a Tier 3 co-pay with Select Med. Have your patients check with their insurance company prior to dispensing for specifics. Cash cost to the patient: Approximately $320 per 30 day supply.

References:

1- www.pradaxa.com full prescribing information. Accessed September 24, 2013.

2- Ageno W, Gallus AS, Wittkowsky A, Crowther M, Hylek EM, Palareti G ; American College of Chest Physicians. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e44S-88S. doi: 10.1378/chest.11-2292.

3- Guyatt GH, Akl EA, Crowther M, Gutterman DD, Schuünemann HJ; American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. Executive summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):7S-47S. doi: 10.1378/chest.1412S3