Pradaxa (dabigatran etexilate mesylate) capsules   U.S. Fact Sheet

What is Pradaxa?

- PRADAXA 150mg twice daily is approved in the U.S. for the reduction of stroke and systemic embolism in patients with non-valvular atrial fibrillation (AFib).\(^1\)
- Treatment with PRADAXA does not require blood monitoring or related dose adjustments and has no recommended dietary restrictions.\(^1\)
- PRADAXA 75mg twice daily is also approved for the small subset of patients who have severe renal impairment (creatinine clearance 15-30 mL/min).\(^1\)

How Does PRADAXA Work?

- PRADAXA is an oral direct thrombin inhibitor (DTI),\(^1\) which helps prevent the formation of clots by blocking thrombin, a key component of the clotting process.\(^1\)
- All anticoagulants exert their effects by reducing the effects of thrombin, either directly or indirectly.\(^1,2\) PRADAXA can bind to both free and clot-bound thrombin\(^1\) by directly blocking its activity.\(^1\)

Stroke Prevention in Atrial Fibrillation Clinical Trial Program

The safety and efficacy of PRADAXA for stroke prevention in AFib has been established in nearly 19,000 patients through five Phase II and Phase III trials, including RE-LY\(^\text{®}\), PETRO and PETRO-EX.\(^3,4,5\)

RE-LY\(^\text{®}\) was a global, Phase III, randomized PROBE (prospective, randomized, open-label, blinded endpoint evaluation)\(^6\) trial of 18,113 patients with non-valvular atrial fibrillation\(^6\) enrolled in 951 centers in 44 countries.\(^3\) The trial investigated whether PRADAXA (two blinded doses) was as effective as well-controlled warfarin (open label) – INR 2.0 - 3.0 – for the prevention of stroke and systemic embolism.\(^6\)

The RE-LY\(^\text{®}\) trial found:

- Primary Efficacy Endpoint: Stroke and Systemic Embolism
  - PRADAXA was shown to significantly reduce the incidence of stroke (including hemorrhagic) and systemic embolism by 35 percent compared to warfarin (PRADAXA 150mg 2.2%/yr; warfarin 3.4%/yr; \(p<0.0001;\)).\(^1\)
• Bleeding Endpoints from RE-LY®
  o There was no significant difference in the rate of major bleeding for PRADAXA 150mg (3.3%/yr) compared to warfarin (3.6%/yr).¹
  o PRADAXA 150mg reduced the risk of intracranial hemorrhage (.3%/yr) by 59 percent compared to warfarin (.8%/yr).¹
  o The rate of major gastrointestinal (GI) bleeding was significantly greater with PRADAXA 150mg (1.6%/yr) than warfarin (1.1%/yr) and a higher rate of any GI bleeds (6.1% vs. 4.0%, respectively).¹

• Adverse Reactions from RE-LY®
  o Patients on PRADAXA 150mg had an increased incidence of gastrointestinal adverse reactions (35%/yr) compared to warfarin (24%/yr).¹
    ▪ These were commonly 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 gastrointestinal ulcer).¹
  o The discontinuation rate due to drug-related adverse events was 21 percent for PRADAXA 150mg and 16 percent for warfarin.¹

The RELY-ABLE® trial is a Phase III, long-term safety study of PRADAXA in patients with AFib who completed the RE-LY® trial and a cluster randomized trial to assess the effect of a knowledge translation intervention on patient outcomes.⁷

• RELY-ABLE® enrolled an estimated 6,200 patients⁷
• RELY-ABLE® is currently ongoing and expected to be completed in July 2011⁷

About Pradaxa® (dabigatran etexilate) capsules

INDICATIONS AND USAGE
PRADAXA is a prescription medicine used to reduce the risk of stroke and blood clots in people who have a medical condition called atrial fibrillation.

IMPORTANT SAFETY INFORMATION ABOUT PRADAXA
PRADAXA can cause bleeding that can be serious and lead to death.

Do not take PRADAXA if you have certain types of abnormal bleeding. Do not take PRADAXA if you have ever had an allergic reaction to it.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements.

Some medications, including aspirin and aspirin containing products, non-steroidal anti-inflammatory drugs (NSAIDs), and blood thinners can increase your chance of bleeding if you take them with PRADAXA.

You may have a higher risk of bleeding with PRADAXA if you are over 75 years old, if you have kidney problems, or if you have a condition that causes bleeding, like a stomach ulcer.
Seek medical care immediately for any unexpected bleeding or signs of bleeding such as unusual bruising, coughing up or vomiting blood, or changes in the color of your urine or stools.

Tell your doctor if you are planning to have any surgery, or medical or dental procedure, as you may have to stop taking PRADAXA for a short time.

Take PRADAXA exactly as prescribed by your doctor. Do not stop taking PRADAXA unless your doctor tells you to as this could increase your risk of having a stroke.

In addition to bleeding, PRADAXA can cause stomach upset or burning, and stomach pain.

For full PRADAXA prescribing information, please visit www.pradaxa.com or contact Boehringer Ingelheim’s Drug Information Unit at 1-800-542-6257.

1 Praxaxa Prescribing Information.
4 Ezekowitz, MD et al. “Dabigatran With or Without Concomitant Aspirin Compared with Warfarin Alone in Patients with Nonvalvular Atrial Fibrillation (PETRO Study).” American Journal of Cardiology. 2007; 100:1419-1426.