



CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject **Dabigatran etexilate (Pradaxa®)**

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Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	2
References	3

Hyperlink to Related Coverage Positions

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers dabigatran etexilate (Pradaxa®) as medically necessary to reduce the risk of stroke and systemic embolism in individuals with non-valvular atrial fibrillation and failure, contraindication, and intolerance to warfarin.

FDA Approved Indications

Pradaxa is indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation.

FDA Recommended Dosing

For patients with creatinine clearance (CrCl) >30 mL/min, the recommended dose of Pradaxa is 150 mg taken orally, twice daily, with or without food. For patients with CrCl 15-30 mL/min, the recommended dose is 75 mg twice daily. Dosing recommendations for patients with a CrCL <15 mL/min or on dialysis cannot be provided.

Drug Availability

Pradaxa 75 mg capsules have a light blue opaque cap imprinted with the Boehringer Ingelheim company symbol and a cream-colored opaque body imprinted with "R75". The color of the imprinting is black. The capsules are supplied in bottles of 60 capsules or blister packages containing 60 capsules (10 x 6 capsule blister cards). Pradaxa 150 mg capsules have a light blue opaque cap imprinted with the Boehringer Ingelheim company symbol and a cream-colored opaque body imprinted with "R150". The color of the imprinting is black. The capsules are supplied in bottles of 60 capsules or blister packages containing 60 capsules (10 x 6 capsule blister cards).

General Background

Pharmacology

Dabigatran (Pradaxa) is an oral direct thrombin inhibitor to reduce the risk of thromboembolic events in patients with non-valvular atrial fibrillation. Direct thrombin inhibitors do not require an antithrombin cofactor for thrombin interaction like heparins and can effectively inhibit clot-bound thrombin whereas heparins do not. Dabigatran is a univalent direct thrombin inhibitor which antagonizes only active thrombin and not the other binding sites. Dabigatran reversibly inhibits free and fibrin-bound thrombin, blocking the thrombogenic activity of thrombin.

Dabigatran has a bioavailability of 3-7% after administration. Dabigatran is metabolized through glucuronidation to four different acyl glucuronides. The glucuronides and the parent compound have similar activity. Dabigatran is primarily renally cleared with 80% being excreted in the urine. Dabigatran has a half-life of about 13 hours in patients with good renal function. The half-life increases to approximately 18 hours in patients with creatinine clearance of 31-49 mL/min and 27.5 hours in patients with creatinine clearance of ≤ 30 mL/min.

Guidelines

Guidelines from the American College of Cardiology, American Heart Association, and European Society of Cardiology as well as guidelines from the American College of Chest Physicians recommend the use of antithrombotic therapy based on risk factors for embolic stroke in this patient population. Several risk stratifications for stroke have been published, but the most widely accepted and the one used in both guidelines is the CHADS₂ classification.

Clinical Efficacy

Three published trials evaluated the efficacy of dabigatran compared to warfarin in patients with non-valvular atrial fibrillation. These trials include the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial and two subanalyses of the RE-LY trial. Dabigatran 110 mg (1.54%) was noninferior to warfarin (1.71%) and dabigatran 150 mg (1.11%) was superior to warfarin (1.71%) in the annual reduction of stroke and systemic embolism in patients with non-valvular atrial fibrillation. The rates of intracranial hemorrhage in patients treated with dabigatran 110 mg (0.2%) and dabigatran 150 mg (0.3%) were significantly reduced compared to those treated with warfarin (0.7%). These results were similar regardless of the quality of INR control in patients treated with warfarin, however the benefits of dabigatran appeared to be more pronounced compared to warfarin in patients with poor INR control. The reduction of stroke or systemic embolism with dabigatran versus warfarin was not significantly affected by whether or not a patient had a history of prior stroke or transient ischemic attack (TIA). In a subgroup analysis in this population, no difference occurred between either dose of dabigatran (2.1-2.3%) compared to warfarin (2.8%) in the annual rate of stroke or systemic embolism. Both doses of dabigatran (0.25-0.41%) significantly reduced the annual rate of intracranial bleeding compared to warfarin (1.28%) in patients with a history of stroke or TIA.

Adverse Drug Reactions / Drug Interactions

The most common adverse events associated with dabigatran include bleeding and dyspepsia. Gastrointestinal side effects occur in 35% of patients treated with dabigatran compared to 24% on warfarin. Major bleeding rates for dabigatran and warfarin are similar, although, the annual rates of overall bleeding, intracranial bleeding, and life-threatening bleeding are less frequent with dabigatran. Major gastrointestinal bleeding occurs more frequently with dabigatran compared to warfarin. There is no reversal agent for dabigatran-associated bleeding. Dabigatran is contraindicated in patients with active bleeding or a history of hypersensitivity to the agent.

The risk of bleeding may increase if dabigatran is combined with other anticoagulants. P-glycoprotein inducers reduce the efficacy of dabigatran and should not be used during dabigatran therapy. P-glycoprotein inhibitors may increase dabigatran exposure and increase bleeding risk. Proton pump inhibitors do not significantly decrease dabigatran exposure. Dabigatran is not a cytochrome P450 substrate, inhibitor, or inducer and is not expected to alter the pharmacokinetics of drugs metabolized via this system.

Coding/Billing Information

Note: This section is not in use.

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