Capsules containing 110 mg or 150 mg dabigatran etexilate (as mesilate)

**Action:** Direct thrombin inhibitor

**Indication:** Prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation with one or more of the following risk factors: Previous stroke, transient ischaemic attack, or systemic embolism (SEE); Left ventricular ejection fraction < 40%; Symptomatic heart failure, ≥ New York Heart Association (NYHA) Class 2; Age ≥ 75 years; Age ≥ 65 years associated with one of the following: diabetes mellitus, coronary artery disease, or hypertension

**Dose and Administration:** Renal function should be assessed by calculating CrCL prior to initiation to exclude patients with severe renal impairment (CrCL < 30 mL/min). Recommended daily dose 300 mg as one 150 mg capsule twice daily. Therapy should be continued long term. In case of intolerance to dabigatran, patients should be instructed to immediately consult their doctor. Elderly: Aged ≥ 80 years 220 mg taken as one 110 mg capsule twice daily; 75 – 80 years consider 220 mg taken as one 110 mg capsule twice daily. As renal impairment may be frequent in the elderly (> 75 years), assess renal function by calculating CrCL prior to initiation and examine patients with severe renal impairment (CrCL < 30 mL/min). Renal function should also be assessed at least once a year or more frequently as needed in certain clinical situations when it is suspected that the renal function could decline or deteriorate. Patients with an increased risk of bleeding: closely monitor clinically looking for signs of bleeding or anaemia. Dose adjustment should be decided at the discretion of the physician, following assessment of the potential benefit and the risks of anticoagulation test may help identify increased risk patients. Patients with gastritis, oesophagitis, or gastroesophageal reflux consider 220 mg taken as one 110 mg capsule twice daily due to the elevated risk of major gastro-intestinal bleeding. Renal impairment: contraindicated in severe renal impairment (CrCL < 30 mL/min); patients with renal impairment and a high risk of bleeding consider 220 mg taken as one 110 mg capsule twice daily. Close clinical surveillance is recommended in patients with renal impairment. As above assess renal function prior to initiation to exclude patients with severe renal impairment and assess renal function at least once a year or more frequently as needed. Concomitant verapamil 220 mg taken as one 110 mg capsule twice daily; Pradaxa and verapamil should be taken at the same time. No dose adjustment required but close clinical surveillance in patients < 50 kg. Not recommended if liver enzymes > 2 Upper Limit of Normal (ULN). If the next dose of the alternate therapy would be due, or at the time of dronedarone; prosthetic heart valves requiring anticoagulant treatment. Systemic ketoconazole, cyclosporine, itraconazole, tacrolimus, or liver disease expected to have any impact on survival; concomitant systemic ketoconazole, cyclosporine, itraconazole, tacrolimus, drenodarone; prosthetic heart valves requiring anticoagulant treatment.

**Warnings and Precautions:** Not recommended if liver enzymes > 2 ULN.

Haemorrhagic risk: Close clinical surveillance (signs of bleeding or anaemia) is recommended throughout the treatment period, especially when haemorrhagic risk is increased or risk factors combined. Factors which may increase haemorrhagic risk: age ≥ 75 years; moderate renal impairment (CrCL 30 – 50 mL/min); Pyglycoprotein inhibitor co-medication; body weight < 50 kg: acetylsalicylic acid (aspirin); NSAID; clopidogrel; selective serotonin re-uptake inhibitors (SSRIs) or selective serotonin norepinephrine re-uptake inhibitors (SNRIs); other drugs which may impair haemostasis; diseases/procedures associated with a risk of bleeding such as coagulation disorders, thrombocytopenia or functional platelet defects, recent biopsy, major trauma, bacterial endocarditis, oesophagitis, gastritis or gastroesophageal reflux. Concomitant use of ticagrelor. The measurement of dabigatran related anticoagulation may be helpful to avoid excessive high exposure to dabigatran in the presence of additional risk factors. Patients who develop acute renal failure must discontinue Pradaxa. If severe bleeding occurs, discontinue treatment and investigate the source of the bleeding. Avoid or use with caution medicinal products which may increase the risk of haemorrhage.

The use of fibrinolitic medicinal products for the treatment of acute ischaemic stroke may be considered if the patient presents with a dTT, ECT or aPTT not exceeding the ULN according to the local reference range. Avoid concomitant administration with P-gp inducers.

Patients on dabigatran etexilate who undergo surgery or invasive procedures are at increased risk for bleeding if other anticoagulant or antiplatelet interventions may require the temporary discontinuation of dabigatran etexilate; prescribers should consult the Summary of Product Characteristics for further information. Procedures such as spinal anaesthesia may require complete haemostatic function. The risk of spinal or epidural haematoma may be increased in cases of traumatic or repeated puncture and by the prolonged use of epidural catheters. After removal of a catheter an interval of at least 2 hours should elapse before the administration of the first dose of dabigatran etexilate; these patients require frequent observation for neurological signs and symptoms of spinal or epidural haematoma. Treat with caution patients at high surgical mortality risk and with intrinsic risk factors for thromboembolic events. Myocardial infarction. Contains Sunset Yellow (E110) which may cause allergic reactions. **Interactions:** Anticoagulants and antiplatelet aggregation medicinal products; P-gp inhibitors e.g. amiodarone, quinidine, verapamil, clarithromycin, ticagrelor co-administration (close clinical surveillance); verapamil co-administration - reduce Pradaxa dose to 220 mg (see above); not recommended for concomitant treatment posaconazole, protease inhibitors including ritonavir and its combinations with other protease inhibitors; avoid with P-gp inducers e.g. rifampicin, St John’s wort, carbamazepine, phenytoin; avoid with ritonavir and its combinations with other protease inhibitors; avoid with P-gp inducers.

**Monitoring:** ECT or aPTT not exceeding the ULN according to the local reference range. Assess renal function at least once a year or more frequently as needed. As above assess renal function prior to initiation to exclude patients with severe renal impairment and assess renal function at least once a year or more frequently as needed. Concomitant verapamil 220 mg taken as one 110 mg capsule twice daily; Pradaxa and verapamil should be taken at the same time. No dose adjustment required but close clinical surveillance in patients < 50 kg. Not recommended if liver enzymes > 2 Upper Limit of Normal (ULN). If the next dose of the alternate therapy would be due, or at the time of discontinuation in case of continuous treatment; if switching from Pradaxa to VKA switch starting time with switching from VKA to Pradaxa stop VKA and give Pradaxa once INR < 2.0. Cardioversion patients can stay on Pradaxa whilst being cardioverted. No relevant use of Pradaxa in the paediatric population in the indication. Indication. Pradaxa can be taken with or without food. Pradaxa should be swallowed as a whole with a glass of water to facilitate delivery to the stomach. Patients should be instructed not to open the capsule as this may increase the risk of bleeding. **Contraindications:** Hypersensitivity to any component; severe renal impairment (CrCL < 30 mL/min); active clinically significant bleeding; lesion or condition, if considered a significant risk factor for major bleeding. This may include current or recent gastrointestinal ulceration, presence of malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities; concomitant treatment with any other anticoagulants e.g. unfractionated heparin (UHF), low molecular weight heparins (enoxaparin, dalteparin etc), heparin derivatives (fondaparinux etc), oral anticoagulants (warfarin, rivaroxaban, apixaban etc) except under the circumstances of switching therapy to or from Pradaxa or when UHF is given at doses necessary to maintain an anticoagulant venous or arterial catheter; hepatic impairment or liver disease expected to have any impact on survival; concomitant systemic ketoconazole, cyclosporine, itraconazole, tacrolimus, drenodarone; prosthetic heart valves requiring anticoagulant treatment.

**Adverse events:**

Most commonly reported adverse reactions are

≥ 1/100 to < 1/10: anaemia; epistaxis; gastrointestinal haemorrhage; abdominal pain; diarrhoea; dyspepsia; nausea; skin haemorrhage; genitourinary haemorrhage, including haematuria.

**Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, Bircher Str. 170, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for further information on side effects.

**Pack sizes and NHS price:**

110 mg 60 capsules £65.90 150 mg 60 capsules £65.90 Legal category POM MA numbers: 110 mg EU/1/08/442/007 (60 capsules) 150 mg EU/1/08/442/011 (60 capsules) Marketing Authorisation Holder: Boehringer Ingelheim Drug Safety on 0800 328 1627 (freephone).