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

**Action:**
Direct thrombin inhibitor
Inhibitors of: Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors (SPAF), such as prior stroke, or transient ischemic attack, age > 75 years, or a heart failure (NYHA Class ≥ II); diabetes mellitus; hypertension. Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults (DVT/PE).

**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). SPAF: Recommended daily dose 300 mg taken once a 150 mg capsule twice daily. Therapy should be continued long term. DVT/PE: Recommended daily dose 300 mg taken as one 150 mg twice daily following treatment with parenteral anticoagulant for at least 5 days. Duration of treatment should be individualised after careful assessment of the treatment benefit against risk for bleeding. Short duration of therapy (at least three months) should be based on transient risk factors (e.g. recent surgery, trauma, immobilisation) and longer durations should be based on permanent risk factors or idiopathic DVT or PE. In case of intolerance to dabigatran, patients should be instructed to immediately consult their doctor. If liver enzymes > 2 ULN, or if liver enzymes > 3 ULN after the last dose of Pradaxa, the recommended daily dose is Pradaxa 220 mg taken as 110 mg twice daily. Pradaxa and verapamil should be taken at the same time. For the following patient groups, the daily dose of 300 mg or 220 mg should be selected based on an individual assessment of the thromboembolic risk and risk of bleeding: aged 75 – 80 years; with moderate renal impairment (CrCl 30 – 50 mL/min); with gastritis, oesophagitis or gastroesophageal reflux; other risk of increased bleeding. Close clinical surveillance is recommended in patients with renal impairment. Use is contraindicated in patients with severe renal impairment (CrCl < 30 mL/min). In all patients assess renal function by calculating CrCl prior to initiation to exclude patients with severe renal impairment, or if renal function is not assessed when a heart in renal function is suspected. Additionally in patients > 75 years or with mild to moderate renal impairment, 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 such as coagulation disorders, thrombocytopenia or functional platelet defects, recent biopsies, major trauma, bacterial endocarditis, oesophagitis, gastritis or gastrointestinal reflux. Close clinical surveillance is recommended; caution when co-administered with parenteral anticoagulant wait 12 hours after the last dose of Pradaxa; if switching from parenteral anticoagulant to Pradaxa discontinue the parenteral anticoagulant and start Pradaxa 0.2 hours prior to the time that 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 adjust the starting time of the WAA based on CrCl; if switching from VKA to Pradaxa give Pradaxa 50 mg on the day of switching, then increase the dose to 300 mg daily. Cardioversion: patients can stay on Pradaxa whilst being cardioverted. No relevant use of Pradaxa in the paediatric population in the SPAF indication. In DVT/PE indication safety and efficacy of Pradaxa in ages less than 18 years have not been established. 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 intrasplanchnic or intracranial vascular abnormalities; concomitant treatment with any other anticoagulants e.g. unfractionated heparin (UFH); low molecular weight heparins (enoxaparin, dalteparin etc), heparin derivatives (t fondaparinux etc), oral anticoagulants (warfarin, rivaroxaban, apixaban etc) except under specific circumstances of switching anticoagulant therapy or when UFH is given at doses necessary to maintain an open central venous or arterial catheter; hepatic impairment or liver disease expected to have any impact on survival; concomitant systemic ketonacozone, cyclosporine, iraconazole, prophylactic 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
Capsules containing 75 mg or 110 mg dabigatran etexilate (as mesilate) **Action:**

Direct thrombin inhibitor

**Indications:**

Prevention of venous thromboembolic events in adult patients who have undergone elective total hip or knee replacement surgery.

**Dose and Administration:**

**Fasting function** should be assessed. By calculating CrCL prior to initiation to exclude patients with severe renal impairment (CrCl < 30 mL/min). Recommended dose is 220 mg once daily orally taken as 2 single capsules continuing with 2 capsules once daily for a total of 10 days (knee replacement surgery) or 28 – 35 days (hip replacement surgery). Delay initiation of treatment if haemostasis is not secured. If treatment is not started on the day of surgery, initiate with 2 capsules once daily. For the following groups the recommended daily dose of Pradaxa is 150 mg taken once daily as 2 capsules of 75 mg: patients with moderate renal impairment (CrCl 30–50 mL/min); patients who receive concomitant verapamil, amiodarone, quinine; or aged 75 or above.

In patients with moderate renal impairment and concomitant verapamil, consider 75mg daily. Pradaxa is contraindicated in severe renal impairment (CrCl < 30 mL/min). Assess renal function by calculating CrCL prior to initiation to exclude patients with severe renal impairment. As renal impairment may be frequent in the elderly (>75 years), assess renal function prior to initiation to exclude patients with severe renal impairment. Renal function should also be assessed while on treatment in certain clinical situations when it is suspected that renal function could decline or deteriorate. Not recommended if liver enzymes > 2 Upper Limit of Normal (ULN). No dose adjustment required but close clinical surveillance in patients <50 kg or >110 kg, if switching from Pradaxa to parenteral anticoagulant wait 24 hours after the last dose of Pradaxa; if switching from parenteral anticoagulant to Pradaxa, discontinue the parenteral anticoagulant and start Pradaxa 0-2 hours prior to the time that the next dose of the alternate therapy would be due, or at the time of discontinuation in cases of short-term therapy. Monitor liver enzymes in the paediatric use age group. The recommended use in patients with moderate renal impairment and concomitant use of the parenteral anticoagulant should be determined by the type and extent of the procedure.

Haemorrhagic risk: Close clinical surveillance (signs of bleeding or anaemia) is recommended throughout the treatment period, especially when haemorrhagic risk is increased or risks factors combined. Factors which may increase haemorrhagic risk: age > 75 years; moderate renal impairment (CrCl 30–50 mL/min); P-glycoprotein 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 bleed; 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 an additional risk factor.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.

**Contraindications:**

Hypersensitivity to any component; severe renal impairment (CrCl < 30 mL/min); active clinically significant bleeding; lesion or valves requiring anticoagulant treatment.

**Fertility, pregnancy and lactation:**

Avoid during treatment. Do not use in pregnancy unless clearly necessary. Discontinue breastfeeding during treatment. Avoid pregnancy. Fertility impaired by the medicinal product interactions not expected. Pantoprazole and other proton-pump inhibitors (PPI) were co-administered with Pradaxa in clinical trials and concomitant use does not appear to reduce the efficacy of Pradaxa. Ranitidine administration together with Pradaxa had no clinically relevant effect on the extent of absorption of dabigatran. Fertility, pregnancy and lactation:

**Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.**

**Adverse events should also be reported to Boehringer Ingelheim Drug Safety on 0800 328 1627 (freephone).**
Prescribing Information (UK) PRAXBIND® (idarucizumab) 2.5 g/50 mL solution for injection/infusion. Vials containing 2.5 g idarucizumab in 50 mL solution for injection/infusion.

**Indication:** Praxbind is a specific reversal agent for dabigatran and is indicated in adult patients treated with Pradaxa (dabigatran etexilate) when rapid reversal of its anticoagulant effects is required: for emergency surgery/urgent procedures; in life-threatening or uncontrolled bleeding.

**Dose and Administration:** Restricted to hospital use only. Recommended dose is 5 g (2 x 2.5 g/50 mL), administered intravenously as two consecutive infusions over 5 to 10 minutes each or as a bolus injection. Administration of a second 5 g dose may be considered in the following situations: recurrence of clinically relevant bleeding together with prolonged clotting times; if potential re-bleeding would be life-threatening and prolonged clotting times are observed; patients require a second emergency surgery/urgent procedure and have prolonged clotting times. Restarting antithrombotic therapy: If the patient is clinically stable and adequate haemostasis has been achieved following administration of Praxbind, Pradaxa (dabigatran etexilate) treatment can be re-initiated after 24 hours; other antithrombotic therapy (e.g. low-molecular weight heparin) can be started at any time. No dose adjustment is required in patients with renal or hepatic impairment or in elderly patients aged 65 years and above. Safety and efficacy in children below the age of 18 years have not yet been established. Contraindications: None. Warnings and Precautions: Idarucizumab binds specifically to dabigatran and reverses its anticoagulant effect. It will not reverse the effects of other anticoagulants. Treatment can be used in conjunction with medically appropriate standard supportive measures. In patients with known hypersensitivity (e.g. anaphylactoid reaction) to idarucizumab or to any of the excipients the risk of using Praxbind needs to be weighed cautiously against the potential benefit of the emergency treatment, discontinue use if an anaphylactoid reaction or other serious reaction occurs. The recommended dose of Praxbind contains 4 g sorbitol as an excipient. In patients with hereditary fructose intolerance, parenteral administration of sorbitol has been associated with reports of hypoglycaemia, hypophosphatemia, metabolic acidosis, increase in uric acid, acute liver failure with breakdown of excretory and synthetic function, and death. Consequently, in these patients the risk of treatment with Praxbind must be weighed against the potential benefit, and if Praxbind is administered intensified medical care during and within 24 hours of exposure is required. 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. Contains 2.2 mmol (50 mg) sodium per dose. Praxbind causes transient proteinuria which is not indicative of renal damage but which should be taken into account for urine testing. Interactions: No formal interaction studies have been performed. Based on pharmacokinetic properties and high specificity in binding to dabigatran clinically relevant interactions with other medicinal products are considered unlikely. Fertility, Pregnancy and Lactation: There are no data for use in pregnant women. Praxbind may be used during pregnancy, if the expected clinical benefit outweighs the potential risks. There are no data on the effect on fertility. It is unknown whether idarucizumab is excreted in human milk. Undesirable effects: No adverse reactions have been identified. Pack sizes and NHS price: Carton containing 2 vials £2400. Legal category: POM. MA numbers: EU/1/15/1056/001 Marketing Authorisation Holder: Boehringer Ingelheim International GmbH, Binger Str. 173, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. Prepared in November 2015

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Boehringer Ingelheim Drug Safety on 0800 328 1627 (freephone).