Prescribing Information (SPAF and DVT/PE - UK)

PRADAXA® (dabigatran etexilate)

Capsules: 75, 150, 225 mg as (mesilate) Action: Direct thrombin inhibitor Indications: Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) with one or more risk factors (SPAF), including: Patients with NVAF (SPAF): Can be conducted in patients on 150 mg twice daily Pradaxa treatment. Catheter ablation for atrial fibrillation (SPAF): Patients with non-valvular atrial fibrillation (SPAF), such as prior stroke, or transient ischaemic attack (TIA); age ≥ 75 years; heart failure (NYHA-Class ≥ 3); diabetes mellitus; numerous risk factors for thromboembolic events. Direct acting Oral Anticoagulants (DOACs) including dabigatran etexilate are not recommended for patients with a history of thrombosis who are diagnosed with antiphospholipid syndrome. Myocardial infarction. Efficacy and safety have not been established for DVT/PE patients with active cancer. Interactions: P-gp inhibitors - close clinical surveillance and dose reductions may be required (see above): contraindicated – ketoconazole, dronedarone, itraconazole, cyclosporine, glicapreprox/pioperatinsav; not recommended – tacrolimus; use with caution – valproam, amiodarone, quinidine, clarithromycin, ticagrelor, posaconazole. P-gp inducers e.g. rifampicin, St John’s wort, cimetidine or phenytoin - use should be avoided. Prostate inhibitors e.g. ritorone and its combinations with other prostate inhibitors – use not recommended. Anticoagulants and antiplatelet aggregation medicinal products. SSRIs or SNRIs. Pantoprazole and other proton-pump inhibitors (PPIs) were co-administered with Pradaxa in clinical trials and concomitant PPI treatment did not appear to reduce the efficacy of Pradaxa. Rivaroxaban administration together with Pradaxa had no clinically relevant effect on the extent of absorption of dabigatran. Dabigatran etexilate and dabigatran are not metabolised by cytochrome CYP450 system, therefore related medicinal product interactions are not known. Fertility, pregnancy and lactation: Avoid Pradaxa treatment as sex steroids and anticoagulant therapy would be due, or at the time of discontinuation in case of continuous treatment; if switching to or from VKA therapy, the starting dose of Pradaxa should be based on the average expected CrCL from VKA to Pradaxa stop VKA and give Pradaxa once INR < 2.0. Cardioversion (SPAF): patients can stay on Pradaxa whilst being cardioverted. Catheter ablation for atrial fibrillation (SPAF): Patients with non-valvular atrial fibrillation (SPAF) and DVT/PE prevention trial RE-MEDY and in 10.5% of patients in DVT/PE prevention trial RE-SONATE. Adverse reactions identified from the study in prevention of thromboembolic and systemic embolism in patients with atrial fibrillation and the studies in DVT/PE prevention are listed with frequency using the following convention: common (≥ 1/100 to < 1/10), uncommon (≥ 1/1000 to < 1/1000), not known (cannot be estimated from the available data).

Stoke and SEE:

Common: anaemia; epistaxis; gastrointestinal haemorrhage; abdominal pain; diarrhoea; dyspepsia; nausea; skin haemorrhage; gastrointestinal ulcer. Uncommon: haemoglobin decreased; thrombocytopenia; drug hypersensitivity; rash; pruritus; intracranial haemorrhage; haematoma; haemorrhage; haemoptysis; rectal haemorrhage; haemorrhoidal ulcer; gastrointestinal ulcer; gastrointestinal haemorrhage; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; gastrointestinal ulcer; 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Desirable effects: Most commonly reported adverse reactions are bleedings occurring in total in approximately 14% of patients treated short-term for elective hip or knee replacement surgery; major bleedings, including wound site bleedings < 2%. Adverse reactions are listed with frequency using the following convention: common (≥ 1/10 to < 1/100), uncommon (≥ 1/1,000 to < 1/10,000), rare (≥ 1/10,000 to < 1/100,000), very rare (cannot be estimated from the available data). Common: haemoglobin decreased; hepatic function abnormal/liver function test abnormal. Uncommon: anaemia; haematocrit decreased; drug hypersensitivity; haemorrhagic shock; haemorrhage, including haematuria; traumatic haemorrhage; post procedural haematoma; haemorrhoidal haemorrhage; diarrhoea; nausea; vomiting; alanine aminotransferase increased; aspartate aminotransferase increased; hepatic enzyme function test abnormal. Rare: thrombocytopenia; anaphylactic reaction; angioedema; urticaria; rash; pruritus; intracranial haemorrhage; haemorrhoids; gastrointestinal haemorrhage; diarrhoea; nausea; vomiting; alinineaminotransferase increased; aspartateaminotransferase increased; hepatic enzyme increased; hyperbilirubinaemia; skin haemorrhage; haemorrhagenesis; gerontological disorders; renal impairment; haematocrit decreased; decreased platelet count; bleeding; haemorrhage; including haematuria; traumatic haemorrhage; post procedural haematoma; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post procedural haemorrhage; post proced...
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 dabigatran or 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 anaphylactic 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 £2,400.

**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.