Prescribing Information (SPAF - UK) – PRADAXA® (dabigatran etexilate) Capsules containing 110 mg or 150 mg dabigatran etexilate (as mesilate) Indication: Direct thrombin inhibitor Action: Preventation of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as prior stroke, or transient ischaemic attack; age ≥ 75 years; heart failure (NYHA Classes II to IV); diabetes mellitus; 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 taken as one 150 mg capsule twice daily. Therapy should be continued long term. In case of intolerability to dabigatran, patients should be instructed to immediately consult their doctor. For patients aged 80 years or above, or those receiving concomitant verapamil, 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 gastrooesophageal 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. Renal function should also be assessed when a decline 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: closely monitor clinically looking for signs of bleeding or anaemia. A coagulation test may help identify increased risk patients. No dose adjustment required but close clinical surveillance in patients < 50 kg. Not recommended if liver enzymes ≥ 2 Upper Limit of Normal (ULN). If switching from Pradaxa to 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 VKA based on CrCl; if switching from VKA to Pradaxa stop VKA and give Pradaxa once INR <2.0. Cardioversion: patients can stay on Pradaxa whilst being cardioverted. Catheter ablation for atrial fibrillation: Can be conducted in patients on 150 mg twice daily Pradaxa treatment - treatment does not need to be interrupted. No data available for 110 mg twice daily Pradaxa treatment. No relevant use of Pradaxa in the paediatric population in the 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 intrasplenic or intracerebral vascular abnormalities; concomitant treatment with any other anticoagulants e.g. unfractionated heparin (UFH), low molecular weight heparins (enoxaparin, dalteparin etc), heparin derivatives (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 leukaemia, lymphoma, carcinoma, bronchial, bronchiolar or prostatic carcinoma; thrombotic or embolic events. 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. For situations of life-threatening or uncontrolled bleeding, when rapid reversal of anticoagulation effect of dabigatran is required, the specific reversal agent (Praxbind, idarucizumab) is available. 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 biopsy, major trauma, bacterial endocarditis, oesophagitis, gastritis or gastrooesophageal 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 fibrinolytic medicinal products for the treatment of acute ischaemic stroke may be considered if the patient presents with a dT, 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 therefore surgical interventions may require the temporary discontinuation of dabigatran etexilate. In emergency surgery or urgent procedures, when rapid reversal of the anticoagulation effect is required the specific reversal agent (Praxbind, idarucizumab) to dabigatran is available. Prescribers should consult the Summary of Product Characteristics for full prescribing information. 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) close clinical surveillance is recommended; caution when co-administered with posaconazole; not recommended for concomitant treatment tacrolimus, protease inhibitors including ritonavir and its combinations with other protease inhibitors; avoid with P-gp inducers e.g. rifampicin, St John’s wort, carbamazepine, phenyltoin, SSRIs or SNRIs. Dabigatran etexilate and dabigatran are not metabolised by cytochrome CYP450 system, therefore related medicinal product interactions not expected. Pantoprazole and other proton-pump inhibitors (PPI) were co-administered with Pradaxa in clinical trials and concomitant PPI treatment did 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: Avoid pregnancy during treatment. Do not use in pregnancy unless clearly necessary. Discontinue breast-feeding during treatment. Undesirable effects: Most commonly reported adverse reactions are bleedings occurring in total in approximately 16.6 % in patients with atrial fibrillation treated for the prevention of stroke and SEE. Common (≥ 1/100 to < 1/10): anaemia; epistaxis; gastrointestinal haemorrhage; abdominal pain; diarrhoea; dyspepsia; nausea; skin haemorrhage; genitourinary haemorrhage, including haematuria. Prescribers should consult the Summary of Product Characteristics for further information on side effects. Pack sizes and NHS price: 110 mg 60 capsules £51.00 150 mg 60 capsules £51.00 Legal category POM MA numbers: 110 mg EU/08/442/007 (60 capsules) 150 mg EU/08/442/011 (60 capsules) 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 2017.
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. 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 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. **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**