Anticoagulant Advancements for VTE in All Ages and NVAF in Adult Patients

INDUSTRY PRODUCT SYMPOSIUM

11:30–12:45 BST, Saturday 9 July 2022

ICC Capital Suite 10+11, ExCel London

Program

Chair: Sam Schulman

DOACs, Data, and Dosing in Adults: Practical Tips for NVAF and VTE Management	Sam Schulman, Canada
Caring for Pediatric Patients: DOACs for Acute VTE Treatment and Secondary Prophylaxis	Heleen van Ommen, Netherlands
Anticoagulant Effects of DOACs in Children: Coagulation Assay Responses	Lesley Mitchell, Canada
Hands-on Hints for Anticoagulation Reversal: Insight From Patient Cases	Peter Verhamme, Belgium

A satellite symposium held during the International Society on Thrombosis and Haemostasis Congress, 9–13 July 2022, London, United Kingdom

The symposium is organized and funded by Boehringer Ingelheim and is intended for healthcare professionals only; product-related information will be discussed

Prescribing information and adverse event reporting for Great Britain can be found on pages 2 to 5

For more information or to access the current prescriber guide and Summary of Product Characteristics, please visit www.medicines.org.uk/emc

Prescribing information may vary depending on local approval in each country. Prior to prescribing, always refer to the local product label

In Great Britain and the European Union:

Pradaxa® (dabigatran etexilate) (110mg and 150mg hard capsules) is indicated for the prevention of stroke and systemic embolism in adult patients with NVAF, with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA); age ≥75 years; heart failure (NYHA Class ≥II); diabetes mellitus; hypertension.

Pradaxa® (110mg and 150mg hard capsules) is indicated for the treatment of DVT and PE, and prevention of recurrent DVT and PE in adults. Pradaxa® (75mg, 110mg and 150mg hard capsules) is indicated for the treatment of VTE and prevention of recurrent VTE in paediatric patients from birth to less than 18 years of age, and can be used in patients aged 8 years or older who are able to swallow the capsules whole.

Praxbind® (idarucizumab) 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.

DOACs, direct oral anticoagulants; DVT, deep vein thrombosis; NVAF, non-valvular atrial fibrillation; PE, pulmonary embolism; VTE, venous thromboembolism

Boehringer Ingelheim

SC-CRP-10730
PC-GB-106860 V2
Date of preparation: May 2022

Prescribing information

Prescribing Information (SPAF and DVT/PE - Great Britain)

PRADAXA® (dabigatran etexilate)

Capsules containing 110 mg or 150 mg dabigatran etexilate (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), such as prior stroke or transient ischaemic attack (TIA); age ≥ 75 years; 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 creatinine clearance (CrCL) prior to initiation to exclude patients with severe renal impairment (CrCL < 30 mL/min). SPAF: Recommended daily dose is 300 mg taken as one 150 mg capsule twice daily. Therapy should be continued long term. DVT/PE: Recommended daily dose is 300 mg taken as one 150 mg capsule 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 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 dabigatran etexilate 220 mg taken as 110 mg twice daily. Dabigatran etexilate 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 increased risk of 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 and especially the elderly (> 75 years) 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. If switching from dabigatran etexilate to parenteral anticoagulant wait 12 hours after the last dose of dabigatran etexilate; if switching from parenteral anticoagulant to dabigatran etexilate discontinue the parenteral anticoagulant and start dabigatran etexilate 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 dabigatran etexilate to VKA adjust the starting time of the VKA based on CrCL; if switching from VKA to dabigatran etexilate stop VKA and give dabigatran etexilate once INR < 2.0. Cardioversion (SPAF): patients can stay on dabigatran etexilate while being cardioverted. Catheter ablation for atrial fibrillation (SPAF): Can be conducted in patients on 150 mg twice daily dabigatran etexilate treatment - treatment does not need to be interrupted. No data available for 110 mg twice daily dabigatran etexilate treatment. Percutaneous coronary intervention (PCI) with stenting (SPAF): Patients with NVAF who undergo a PCI with stenting can be treated with dabigatran etexilate in combination with antiplatelets after haemostasis is achieved. No relevant use of dabigatran etexilate in the paediatric population in the SPAF indication. This medicinal product is for oral use and can be taken with or without food. The capsules 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 the active substance or to any of the excipients; 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 (UFH), low molecular weight heparins (enoxaparin, dalteparin etc), heparin derivatives (fondaparinux etc), oral anticoagulants (warfarin, rivaroxaban, apixaban etc) except under specific circumstances. These are switching anticoagulant therapy, when UFH is given at doses necessary to maintain an open central venous or arterial catheter or when UFH is given during catheter ablation for atrial fibrillation; hepatic impairment or liver disease expected to have any impact on survival; concomitant treatment with the following strong P-glycoprotein (P-gp) inhibitors: systemic ketoconazole, cyclosporine, itraconazole, dronedarone and the fixed-dose combination glecaprevir/pibrentasvir; 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 if 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 idarucizumab is available. Haemodialysis can remove dabigatran. Fresh whole blood or fresh frozen plasma, coagulation factor concentration (activated or non-activated), recombinant factor VIIa or platelet concentrates are other possible options. 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) and other platelet aggregation inhibitors such as clopidogrel; NSAIDs; selective serotonin re-uptake inhibitors (SSRIs) or selective serotonin norepinephrine re-uptake inhibitors (SNRIs); other medicinal products 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. The measurement of dabigatran related anticoagulation may be helpful to detect excessive high exposure to dabigatran in the presence of additional risk factors. Patients who

Prescribing information for Praxbind® (idarucizumab) and paediatric VTE can be found on the following pages

develop acute renal failure must discontinue dabigatran etexilate. When severe bleeding occurs, discontinue treatment, investigate the source of the bleeding and use of the specific reversal agent idarucizumab may be considered. Haemodialysis can remove dabigatran. 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 dTT, ECT or aPTT not exceeding the upper limit of normal (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 idarucizumab to dabigatran is available. Haemodialysis can remove dabigatran. Prescribers should consult the Summary of Product Characteristics for further information relating to surgery and interventions. 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. 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, glecaprevir/pibrentasvir; not recommended – tacrolimus; use with caution – verapamil, amiodarone, quinidine, clarithromycin, ticagrelor, posaconazole. P-gp inducers e.g. rifampicin, St John's wort, carbamazepine or phenytoin - use should be avoided. Protease inhibitors e.g. ritonavir and its combinations with other protease inhibitors – use not recommended. Anticoagulants and antiplatelet aggregation medicinal products. SSRIs or SNRIs. Pantoprazole and other proton-pump inhibitors (PPI) were co-administered with dabigatran etexilate in clinical trials and concomitant PPI treatment did not appear to reduce the efficacy of dabigatran etexilate. Ranitidine administration together with dabigatran etexilate 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 not expected. **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 systemic embolism (SEE) and 14.4 % in adult patients treated for DVT/PE. Bleeding occurred in 19.4% of patients in DVT/PE prevention trial RE-MEDY (adult patients) and in 10.5% of patients in DVT/PE prevention trial RE-SONATE (adult patients). Adverse reactions identified from the study in prevention of thromboembolic stroke and systemic embolism in patients with atrial fibrillation and the studies in DVT/PE treatment and in DVT/PE prevention are listed with frequency using the following convention: common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), not known (cannot be estimated from the available data). *Stroke and SEE:* Common: anaemia; epistaxis; gastrointestinal haemorrhage; abdominal pain; diarrhoea; dyspepsia; nausea; skin haemorrhage; genitourological haemorrhage, including haematuria. Uncommon: haemoglobin decreased; thrombocytopenia; drug hypersensitivity; rash; pruritus; intracranial haemorrhage; haematoma; haemorrhage; haemoptysis; rectal haemorrhage; haemorrhoidal haemorrhage; gastrointestinal ulcer, including oesophageal ulcer; gastroesophagitis; gastroesophageal reflux disease; vomiting; dysphagia; hepatic function abnormal/ liver function test abnormal; alanine aminotransferase increased; aspartate aminotransferase increased. Rare: haematocrit decreased; anaphylactic reaction; angioedema; urticaria; hepatic enzyme increased; hyperbilirubinaemia; haemarthrosis; injection site haemorrhage; catheter site haemorrhage; traumatic haemorrhage; incision site haemorrhage. Not known: neutropenia; agranulocytosis; bronchospasm; alopecia. *DVT/PE:* Common: epistaxis; gastrointestinal haemorrhage; dyspepsia; rectal haemorrhage; skin haemorrhage; genitourological haemorrhage, including haematuria. Uncommon: anaemia; drug hypersensitivity; rash; pruritus; haematoma; haemorrhage; haemoptysis; abdominal pain; diarrhoea; nausea; haemorrhoidal haemorrhage; gastrointestinal ulcer, including oesophageal ulcer; gastroesophagitis; gastroesophageal reflux disease; vomiting; hepatic function abnormal/ liver function test abnormal; alanine aminotransferase increased; aspartate aminotransferase increased; hepatic enzyme increased; haemarthrosis; traumatic haemorrhage. Rare: thrombocytopenia; anaphylactic reaction; angioedema; urticaria; intracranial haemorrhage; dysphagia; injection site haemorrhage; catheter site haemorrhage; incision site haemorrhage. Not known: haemoglobin decreased; haematocrit decreased; neutropenia; agranulocytosis; bronchospasm; hyperbilirubinaemia; alopecia. 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* PLGB 14598/0217 *150 mg* PLGB 14598/0218 **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, Binger Str. 173, 55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in** January 2022.

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 for Praxbind® (idarucizumab) and paediatric VTE can be found on the following pages

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 vials of 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 idarucizumab, 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 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 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/metabolites are 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** October 2020.

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 (paed VTE - Great Britain)

PRADAXA® (dabigatran etexilate)

Capsules containing 75 mg, 110 mg or 150 mg dabigatran etexilate (as mesilate) **Action:** Direct thrombin inhibitor **Indication:** Treatment of venous thromboembolic events (VTE) and prevention of recurrent VTE in paediatric patients from birth to less than 18 years of age. **Dose and Administration:** Prior to the initiation of treatment, the estimated glomerular filtration rate (eGFR) should be estimated using the Schwartz formula. Treatment with dabigatran etexilate in paediatric patients with eGFR <50 mL/min/1.73m^2 is contraindicated. Pradaxa capsules can be used in paediatric patients aged 8 years or older who are able to swallow the capsules whole. For the treatment of VTE in paediatric patients, treatment should be initiated following treatment with a parenteral anticoagulant for at least 5 days. For prevention of recurrent VTE, treatment should be initiated following previous treatment. Dabigatran etexilate capsules should be taken twice daily, one dose in the morning and one dose in the evening, at approximately the same time every day. The dosing interval should be as close to 12 hours as possible. The recommended dose of dabigatran etexilate capsules is based on the patient's age and weight. Prescribers should consult the Summary of Product Characteristics for further information on dosing. While on treatment, renal function should be assessed in certain clinical situations when it is suspected that the renal function could decline or deteriorate (such as hypovolemia, dehydration, and with certain co-medications, etc). The duration of therapy should be individualised based on the benefit risk assessment. A forgotten dabigatran etexilate dose may still be taken up to 6 hours prior to the next scheduled dose. From 6 hours prior to the next scheduled dose onwards, the missed dose should be omitted. A double dose to make up for missed individual doses must never be taken. Dabigatran etexilate treatment should not be discontinued without medical advice. Patients or their caregivers should be instructed to contact the treating physician if the patient develops gastrointestinal symptoms such as dyspepsia. If switching from dabigatran etexilate to a parenteral anticoagulant, it is recommended to wait 12 hours after the last dose of dabigatran etexilate; if switching from parenteral anticoagulant to dabigatran etexilate, discontinue the parenteral anticoagulant and start dabigatran etexilate 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 dabigatran etexilate to Vitamin K antagonists (VKA), patients should start

VKA 3 days before discontinuing dabigatran etexilate. Because dabigatran etexilate can impact the International Normalised Ratio (INR), the INR will better reflect VKA's effect only after dabigatran etexilate has been stopped for at least 2 days. Until then, INR values should be interpreted with caution. If switching from VKA to dabigatran etexilate, the VKA should be stopped, dabigatran etexilate can be given as soon as the INR is <2.0. This medicinal product is for oral use and can be taken with or without food. The capsules 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 the active substance or to any of the excipients; eGFR <50 mL/min/1.73m^2 in paediatric patients; 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 (UFH), low molecular weight heparins (enoxaparin, dalteparin etc), heparin derivatives (fondaparinux etc), oral anticoagulants (warfarin, rivaroxaban, apixaban etc) except under specific circumstances. These are switching anticoagulant therapy, when UFH is given at doses necessary to maintain an open central venous or arterial catheter or when UFH is given during catheter ablation for atrial fibrillation; hepatic impairment or liver disease expected to have any impact on survival; concomitant treatment with the following strong P-glycoprotein (P-gp) inhibitors: systemic ketoconazole, cyclosporine, itraconazole, dronedarone and the fixed-dose combination glecaprevir/pibrentasvir; prosthetic heart valves requiring anticoagulant treatment. **Warnings and Precautions:** Not recommended if liver enzymes > 2 upper limit of normal (ULN). Haemorrhagic risk: Close clinical surveillance (signs of bleeding or anaemia) is recommended throughout the treatment period, especially if haemorrhagic risk is increased or risk factors combined. Factors which may increase haemorrhagic risk: The concomitant use of dabigatran etexilate with P-gp inhibitors has not been studied in paediatric patients but may increase the risk of bleeding; acetylsalicylic acid (aspirin) and other platelet aggregation inhibitors such as clopidogrel; NSAIDs; selective serotonin re-uptake inhibitors (SSRIs) or selective serotonin norepinephrine re-uptake inhibitors (SNRIs); other medicinal products 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. Limited clinical data are available for paediatric patients with risk factors, including patients with active meningitis, encephalitis and intracranial abscess. In these patients, dabigatran etexilate should only be given if the expected benefit outweighs bleeding risks. The measurement of dabigatran related anticoagulation may be helpful to detect excessive high exposure to dabigatran in the presence of additional risk factors. Patients who develop acute renal failure must discontinue dabigatran etexilate. When severe bleeding occurs, discontinue treatment and investigate the source of bleeding. Haemodialysis can remove dabigatran. The efficacy and safety of idarucizumab, a specific rapid reversal agent that reverses the anticoagulant effect of dabigatran, has not been established in paediatric patients. 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 ischemic 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 therefore surgical interventions may require the temporary discontinuation of dabigatran etexilate. Prescribers should consult the Summary of Product Characteristics for further information relating to surgery and interventions. 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. Direct acting Oral Anticoagulants (DOACs) including dabigatran etexilate are not recommended for patients with a history of thrombosis who are diagnosed with antiphospholipid syndrome. There is limited data on efficacy and safety for paediatric patients with active cancer. For some very specific paediatric patients, e.g. patients with small bowel disease where absorption may be affected, use of an anticoagulant with parenteral route of administration should be considered. **Interactions:** Interaction studies have only been performed in adults. Prescribers should consult the Summary of Product Characteristics for further information on interactions. **Fertility, pregnancy and lactation:** Avoid pregnancy during treatment. Do not use in pregnancy unless clearly necessary. Discontinue breast-feeding during treatment. **Undesirable effects:** A total of 26% of paediatric patients treated with dabigatran etexilate for VTE and for prevention of recurrent VTE experienced adverse reactions. Adverse reactions identified from the studies in paediatric patients are listed with frequency using the following convention: common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), not known (cannot be estimated from the available data). Common: anaemia; thrombocytopenia; rash; urticaria; haematoma; epistaxis; diarrhoea; dyspepsia; nausea; gastroesophageal reflux disease; vomiting; hepatic enzyme increased; alopecia. Uncommon: haemoglobin decreased; haematocrit decreased; neutropenia; drug hypersensitivity; pruritus; intracranial haemorrhage; haemoptysis; gastrointestinal haemorrhage; abdominal pain; rectal haemorrhage; gastroesophagitis; dysphagia; alanine aminotransferase increased; aspartate aminotransferase increased; hyperbilirubinaemia; skin haemorrhage; genitourological haemorrhage, including haematuria; traumatic haemorrhage. Not known: agranulocytosis; anaphylactic reaction; angioedema; bronchospasm; haemorrhage; haemorrhoidal haemorrhage; gastrointestinal ulcer, including oesophageal ulcer; hepatic function abnormal/liver function test abnormal; haemarthrosis; injection site haemorrhage; catheter site haemorrhage; incision site haemorrhage. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** *75 mg* 10 capsules £8.50; 60 capsules £51.00 *110 mg* 10 capsules £8.50; 60 capsules £51.00 *150 mg* 60 capsules £51.00 **Legal category:** POM **MA numbers:** *75 mg* PLGB 14598/0219; *110 mg* PLGB 14598/0217; *150 mg* PLGB 14598/0218 **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, Binger Str. 173, 55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in** April 2022.

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