Boehringer Ingelheim is pleased to provide you with this Educational Pack, which has been developed to give practical and relevant information on the appropriate use of Pradaxa®. The pack includes:

- Pradaxa® 110mg – Summary of Product Characteristics
- Pradaxa® 75mg – Summary of Product Characteristics
- Prescriber Guide – this addresses recommendations for the use of Pradaxa® in order to minimise the risk of bleeding
- Patient Alert Card

To order additional copies of the Patient Alert Card please go to: www.pradaxa.co.uk/pVTEducationalpack

You can also order or download this Educational Pack.

References:

1. Boehringer Ingelheim. Pradaxa® 110mg hard capsules Summary of Product Characteristics.
2. Boehringer Ingelheim. Pradaxa® 75mg hard capsules Summary of Product Characteristics.

Prescribing Information (pVTEp UK) – PRADAXA® (dabigatran etexilate)

Capsules containing 75 mg or 110 mg dabigatran etexilate (as mesilate) **Action:** Direct thrombin inhibitor **Indication:** Primary prevention of venous thromboembolic events in adult patients who have undergone elective total hip or knee replacement surgery. **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 dose is 220 mg once daily orally taken as 2 capsules of 110 mg. Initiate treatment within 1-4 hours of completed surgery with a single capsule 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. In patients with moderate renal impairment (CrCL 30-50 mL/min); the elderly (age > 75 years); concomitant amiodarone, quinidine or verapamil (take at the same time as Pradaxa) the recommended dose is 150 mg once daily taken as 2 capsules of 75 mg. Moderate renal impairment and concomitant verapamil consider 75 mg daily. Pradaxa is contraindicated in severe renal impairment (CrCL < 30 mL/min). Assess renal function 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 anticoagulants to Pradaxa then Pradaxa should be given 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. No relevant use of Pradaxa in the paediatric population in the indication. Pradaxa should be swallowed whole with water, with or without food. 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 at significant risk of major bleeding such as 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 the circumstances of switching therapy to or from Pradaxa 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 ketoconazole, cyclosporine, itraconazole, tacrolimus, dronedarone; 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); 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 gastroesophageal reflux. 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. 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. 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. No data on the use of Pradaxa in patients undergoing hip fracture surgery, therefore treatment not recommended. Contains Sunset Yellow (E110) which may cause allergic reactions. **Interactions:** Anticoagulants and antiplatelet aggregation medicinal products; strong P-gp inhibitors co-administration (close clinical surveillance): amiodarone, quinidine, verapamil reduce Pradaxa dose to 150mg (see above); consider dose reduction to 75 mg daily in patients with both moderate renal impairment and on verapamil; close monitoring with clarithromycin; 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; 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 14% of patients treated short-term for elective hip or knee replacement surgery; major bleeds, including wound site bleedings < 2%. Common (≥ 1/100 to <1/10): anaemia; haemoglobin decreased; epistaxis; gastrointestinal haemorrhage; abdominal pain; diarrhoea; dyspepsia; nausea; hepatic function abnormal/liver function test abnormal; genitourological haemorrhage. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** *75 mg* 10 capsules £10.98; 60 capsules £65.90 *110 mg* 10 capsules £10.98; 60 capsules £65.90 **Legal category** POM **MA numbers:** *75 mg* EU/1/08/442/001 (10 capsules); EU/1/08/442/003 (60 capsules) *110 mg* EU/1/08/442/005 (10 capsules); EU/1/08/442/007 (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** February 2013.

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).

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PRADAXA® (DABIGATRAN ETEXILATE)

EDUCATIONAL PACK

For primary prevention of venous thromboembolic events in adult patients who have undergone elective total hip replacement surgery or total knee replacement surgery[1,2]