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Boehringer Ingelheim Limited
Medical Division

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Direct Healthcare Professional Communication on the importance of assessing renal function in patients treated with Pradaxa® (dabigatran etexilate)

Our Reference
DHPC/Pradaxa/IE

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Dear Healthcare Professional,

This letter is to inform you of new recommendations to assess renal function in patients being considered for, or already being treated with Pradaxa. These recommendations follow an evaluation of reports of cases of fatal bleeding in Japan. Some of these cases occurred in elderly patients with severe renal impairment, which constitutes a contraindication for Pradaxa treatment.

Summary:

- **Renal function should be assessed in all patients prior to initiating Pradaxa® therapy.**
- **Pradaxa® is contraindicated in patients with severe renal impairment.**
- **While on treatment renal function should be assessed in clinical situations where a decline in renal function is suspected.**
- **In elderly patients (> 75 years) or in patients with renal impairment the renal function should be assessed at least once a year.**

The communication of this information has been agreed with the European Medicines Agency (EMA) and the Irish Medicines Board (IMB).

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Further information on the safety concern:

Pradaxa® is authorized in the European Union for the following indications:

(1) primary prevention of venous thromboembolic events in adult patients who have undergone elective total hip replacement surgery or total knee replacement surgery,

(2) prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation with one or more risk factors as outlined in the SmPC.

Most patients that experienced fatal bleeding in Japan were elderly with severe renal impairment. In the current EU SmPC for Pradaxa it is stated that factors such as high age, moderate renal impairment (30-50 ml/min CrCL), low body weight, use of acetylsalicylic acid, clopidogrel or NSAID, and presence of esophagitis/gastritis/gastroesophageal reflux requiring treatment increase the risk of bleeding associated with Pradaxa treatment. Furthermore, patients at increased risk of bleeding should be closely clinically monitored looking for signs of bleeding and anaemia.

The following new instructions will be added to the Summary of Product Characteristics (SmPC) as well as in updated educational materials:

Recommendations:

- ✓ Prior to initiation of treatment with Pradaxa® the renal function should be assessed by calculating the creatinine clearance (CrCl) to exclude patients for treatment with severe renal impairment (i.e. CrCl < 30 ml/min).

- ✓ While on treatment renal function should be assessed in certain clinical situations when it is suspected that the renal function could decline or deteriorate (e.g. hypovolemia, dehydration, and with certain comedications).

- ✓ In patients above 75 years of age or in patients with renal impairment renal function should be evaluated at least yearly.

As serum creatinine values alone are often not sufficient to accurately evaluate renal function it should be evaluated via an estimation of creatinine clearance to ensure such patients do not have renal impairment that precludes the safe and effective use of Pradaxa® (i.e., creatinine clearance less than 30 mL/min). Provision of sex, age and body weight on a laboratory

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requisition will usually result in a creatinine clearance value, which should be used for an assessment of renal function.

In patients at high risk of bleeding a reduction in dabigatran dose may be necessary. A diluted Thrombin Time test (dTT) is commercially available and can be used to identify patients at increased risk because of excessive exposure to dabigatran, e.g. when renal function could be impaired.

Healthcare professionals should report any adverse events suspected to be associated with the use of Pradaxa® (dabigatran etexilate) to the Irish Medicines Board using the online reporting system or using the yellow card system.

Any adverse events suspected to be associated with the use of Pradaxa® (dabigatran etexilate) may also be reported to Boehringer Ingelheim on 01 291 3960 or +44 1344 741346 or fax +44 1344 742661 or email DSCQ.BRA@boehringer-ingelheim.com.

Communication information

The product information (SmPC) and prescriber guide will be revised to include this new information.

For further medical information on Pradaxa®, please contact Boehringer Ingelheim on 1850 946100 or +44 1344 742578.

Yours faithfully

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