Boehringer Ingelheim Limited · Ellesfield Avenue, Bracknell, Berkshire RG12 8YS

Boehringer Ingelheim Limited

4 January 2013

Pradaxa® (dabigatran etexilate) is now contraindicated in patients with prosthetic heart valve requiring anticoagulant treatment

Our reference
DHPC/Pradaxa/II 44/ROI

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Dear Healthcare Professional,

Boehringer Ingelheim would like to inform you that the use of Pradaxa® is now contraindicated in patients with prosthetic heart valves requiring anticoagulant treatment. The existing warning in section 4.4 not to use Pradaxa® in patients with prosthetic heart valves is strengthened to a contraindication based on the availability of new data from clinical trials.

Summary

- **Pradaxa® is now contraindicated in patients with prosthetic heart valves requiring anticoagulant treatment.**

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

Please see current clinical guidelines for appropriate choice of an antithrombotic agent for the prevention of thromboembolic complications in patients with prosthetic heart valves.

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Further information on the safety concern and recommendations

Pradaxa® is authorised 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 and one or more additional risk factors (see attached SmPC).

Pradaxa® is now contraindicated in patients with prosthetic heart valves requiring anticoagulant treatment. The basis for this SmPC change is data from one investigational phase II trial and its extension trial in a total of 252 patients examining dabigatran etexilate and warfarin use in patients with recent mechanical heart valve replacement surgery (i.e. within the current hospital stay) and in patients who received a mechanical heart valve replacement more than three months ago. This patient population is different from those covered by the labelled indications. The study investigated a dose range from 150 mg twice daily to 300 mg twice daily with the majority of patients treated with a dabigatran etexilate dose that is higher than the approved dosages More thromboembolic events and more bleeding events were observed with dabigatran etexilate than with warfarin. In the early post-operative patients, major bleeding manifested predominantly as post-operative haemorrhagic pericardial effusion.

A summary of the clinical trial results in patients with prosthetic heart valves will be included in section 5.1 of Summary of Product Characteristics, as follows:

> *A phase II study examined dabigatran etexilate and warfarin in a total of 252 patients with recent mechanical heart valve replacement surgery (i.e. within the current hospital stay) and in patients who received a mechanical heart valve replacement more than three months ago. More thromboembolic events (mainly strokes and symptomatic/asymptomatic prosthetic valve thrombosis) and more bleeding events were observed with dabigatran etexilate than with warfarin. In the early post-operative patients, major bleeding manifested predominantly as*

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haemorrhagic pericardial effusions, specifically in patients who started dabigatran etexilate early (i.e. on Day 3) after heart valve replacement surgery.

Health care providers are reminded to strictly follow the indications of Pradaxa®.

Call for reporting

Healthcare professionals should report any adverse events suspected to be associated with the use of Pradaxa® (dabigatran etexilate) to the IMB using a Yellow Card obtained either from the IMB, or electronically via the website at www.imb.ie.

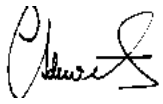
Any adverse events suspected to be associated with the use of Pradaxa® (dabigatran etexilate) may also be reported to Boehringer Ingelheim on 01 291 3960 or +44 1344 741346 or fax +44 1344 742661 or email PV_local_UK_Ireland@boehringer-ingelheim.com.

Communication information

The product information text (SmPC) and prescriber guides 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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