Boehringer Ingelheim

IMPORTANT MEDICINE SAFETY INFORMATION

23 July 2019

Dear Healthcare Professional

Notification of an important new warning with treatment of patients with anti phospholipid syndrome (APS) and the use Pradaxa: Increased risk of thrombo-embolic events

Ingelheim Pharmaceuticals (Pty) Ltd, in agreement with the South African Health Products Regulatory Authority (SAHPRA) would like to inform you of the following:

Patients with antiphospholipid syndrome (especially if triple-positive for antiphospholipid antibodies) are at an increased risk for thromboembolic events. While the efficacy of Pradaxa is established for the treatment and prevention of venous thromboembolism it has not been studied in patients with APS, including patients with triple antibody positive APS.
Careful consideration of all treatment options is recommended before use of Pradaxa is considered in patients with antiphospholipid syndrome as efficacy and safety of Pradaxa have not been established in patients with APS.

Background on the safety concern
Currently, there is not enough evidence that Pradaxa offers sufficient protection in patients with established APS, particularly in those at highest risk for thromboembolic events.

In an investigator sponsored randomised open-label multicentre study (TRAPS, (registered at www.clinicaltrials.gov as #NCT02157272; Blood. 2018 Sep 27;132 (13):1365-1371) with blinded endpoint adjudication, rivaroxaban was compared to warfarin in patients with a history of thrombosis, diagnosed with APS and at high risk for thromboembolic events (persistently tested positive for all 3 antiphospholipid tests). The trial was terminated prematurely after the enrolment of 120 patients due to an excess of thromboembolic events among patients in the rivaroxaban arm. Mean follow-up was 569 days. 59 patients were randomised to rivaroxaban 20 mg (15 mg for patients with creatinine clearance <50 mL/min) and 61 to warfarin (INR 2.0-3.0). Thromboembolic events occurred in 12% of patients randomised to rivaroxaban (4 ischaemic stroke and 3 myocardial infarctions). No thromboembolic events were reported in patients randomised to warfarin. Major bleeding occurred in 4 patients (7%) of the rivaroxaban group and 2 patients (3%) of the warfarin group.

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Further information
The Professional Information of Pradaxa will be amended to include a new warning regarding its use in patients with APS.

Healthcare professionals should report all suspected adverse events associated with the use of Pradaxa (dabigatran etexilate) to Ingelheim Pharmaceuticals (Pty) Ltd by email: PV_local_South_Africa@boehringer-ingelheim.com, fax: + 27 86 407 1026 or tel: + 27 11 348 2542 or to the SAHPRA Pretoria Office, email: adr@sahpra.org.za or tel: + 27 12 842 7609/10 or alternatively to the National Adverse Drug Event Monitoring Centre (NADEMC), tel: +21 447 1618 or fax +21 448 6181

S4 Pradaxa® 75 mg. Each capsule contains 75 mg of dabigatran etexilate base (as mesilate salt). Reg. No. 42/8.2/0130

S4 Pradaxa® 110 mg. Each capsule contains 110 mg of dabigatran etexilate base (as mesilate salt). Reg. No. 42/8.2/0131

S4 Pradaxa® 150 mg. Each capsule contains 150 mg of dabigatran etexilate base (as mesilate salt). Reg. No. 45/8.2/0162

For full prescribing information refer to the package insert approved by the Medicines Regulatory Authority.

Applicant details: Ingelheim Pharmaceuticals (Pty) Ltd, 407 Pine Ave, Randburg. Tel: +27 (011) 348-2400. Cpy. Reg. No. 1966/008618/07.

Yours sincerely,

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