Boehringer Ingelheim

Direct Healthcare Professional Communication on the incidence of gastrointestinal bleeding which may be associated with the use of all oral anticoagulants including Pradaxa® (Dabigatran etexilate) and the importance of renal function assessment with these agents as per the recent guidelines recommendations.

Boehringer Ingelheim
Scientific Office - Egypt

18 June 2015

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Egypt.

Dear Healthcare Professional,

Boehringer Ingelheim would like to remind you about the following:

- The incidence of gastrointestinal bleeding which is an expected side effect associated with all oral anticoagulants including Pradaxa®,
- In accordance with the approved local Pradaxa® label, dose selection should be based on patient's characteristics (e.g. age, renal impairment, co-medication) as defined in the local label

Boehringer Ingelheim would like to emphasize that the risk/benefit profile remains unchanged, and that this communication is not triggered by any new safety concerns.

Recommendations in case of bleeding

In the event of hemorrhagic complications, Pradaxa® treatment must be discontinued and the source of bleeding investigated. Since dabigatran is excreted predominantly by the renal route, adequate diuresis must be maintained. Depending on the clinical situation appropriate standard treatment, e.g. surgical hemostasis as indicated and blood volume replacement should be undertaken.

Consideration may be given to the use of fresh whole blood or fresh frozen plasma. Coagulation factor concentration (activated or non-activated) or recombinant Factor VIIa may be taken into account. There is some experimental evidence to support the role of these agents in reversing the anticoagulant effect of dabigatran but their usefulness in clinical settings has not yet been systematically demonstrated.

Consideration should also be given to administration of platelet concentrates in cases where thrombocytopenia is present or long acting antiplatelet drugs have been used. All symptomatic treatment has to be given according to the physician's judgment. As protein binding is low, dabigatran is dialysable, however there is limited clinical experience in using dialysis in this setting.

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Recommendations for the renal function assessment

- Renal function should be assessed in all patients prior to initiating Pradaxa® therapy using the Cockcroft-Gault method. This method is recommended when assessing patients' CrCL prior to and during Pradaxa treatment.

  - For creatinine in μ mol/L:
    $$\frac{1.23 \times (140 - \text{age [years]}) \times \text{weight [kg]} \ (\times 0.85 \text{ if female})}{\text{serum creatinine [μmol/L]}}$$

  - For creatinine in mg/dL:
    $$\frac{(140 - \text{age [years]}) \times \text{Weight [kg]} \ (\times 0.85 \text{ if female})}{72 \times \text{serum creatinine [mg/dL]}}$$

- Pradaxa® is contraindicated in patients with severe renal impairment (CrCL < 30 mL/min). Before starting Pradaxa and while on treatment, renal function should be assessed in clinical situations where a decline in renal function is suspected (e.g. hypovolaemia, dehydration, and in case of concomitant use of certain medicinal products).

- In elderly patients (> 75 years) or in patients with moderate renal impairment (CrCL 30-50mL/min) the renal function should be assessed at least once a year.

The information in this letter has been approved by the Saudi Food and Drug Authority.

Call for reporting
Any adverse reactions should be reported in accordance with the Saudi Vigilance spontaneous reporting system to
The National Pharmacovigilance and Drug Safety Centre NPC
Email: npc.drug@sfda.gov.sa
Fax: +966112057662
Phone: +966-11-2038222 Ext: 2317-2356- 2353-2354- 2334-2340
Toll free phone: 8002490000

In addition, suspected adverse reactions related Boehringer Ingelheim products may be reported to Boehringer Ingelheim Pharmacovigilance department:
Email: PV_local_Saudi_Arabia@boehringer-ingelheim.com
Phone: +966-11-207 8275

Sincerely,

Marian Amin
MENA Medical Director