Health Canada Endorsed Important Safety Information on Pradax® (dabigatran etexilate)

March 16, 2012

Dear Health Care Professional:

Subject: Updated new recommendations for Pradax® (dabigatran etexilate) regarding renal function assessment, and use in patients with severe valvular disease or prosthetic heart valves.

Boehringer Ingelheim (Canada) Ltd., in consultation with Health Canada, would like to inform you of important new recommendations which have been added to the Product Monograph for Pradax® (dabigatran etexilate).

Pradax® (dabigatran etexilate), an oral anticoagulant, is authorized in Canada for the prevention of stroke and systemic embolism in patients with atrial fibrillation, in whom anticoagulation is appropriate, or for the prevention of venous thromboembolic events in patients following hip or knee replacement surgery.[1]

The new recommendations for Pradax® are as follows:

- Given that renal impairment is a risk factor for bleeding with Pradax®:
  - Prior to initiation of treatment, renal function should be assessed in all patients to exclude patients with severe renal impairment.
  - While on treatment, renal function should be assessed routinely in clinical situations when a decline in renal function may be suspected.
  - In elderly patients (older than 75 years) or in patients with moderate renal impairment, renal function should be assessed at least once a year.
- Use of Pradax® in patients with hemodynamically significant rheumatic valvular heart disease, especially mitral stenosis, or in patients with prosthetic heart valves is not recommended.

Risk of bleeding and renal function assessment:

Based on post-marketing reports of serious bleeding and the use of Pradax® in the elderly and patients at high risk of bleeding or patients with renal impairment, the Product Monograph (PM) has been updated. The updates now include new recommendations to assess renal function in patients being considered for, or already being treated with Pradax® and are as follows:

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

- While on treatment with Pradax®, renal function should be assessed in clinical situations when it is suspected that renal function could decline or deteriorate rapidly, such as hypovolemia, dehydration, and with certain co-medications. These clinical situations may result in an increase of dabigatran exposure.

- In the elderly (> 75 years), or in patients with moderate renal impairment (CrCl 30-50 ml/min), renal function should be assessed routinely by calculating the creatinine clearance at least once a year.

Health Care Professionals are also reminded that:

- Pradax® is contraindicated in patients with severe renal impairment (i.e. CrCl < 30 ml/min).

- Patients at high risk of bleeding should not be prescribed Pradax®.

- Patients should be monitored clinically for signs of bleeding or anaemia.

- Treatment with Pradax® should be discontinued should severe bleeding occur and the source of bleeding investigated.

Patients with Valvular Disease:

Safety and efficacy of Pradax® have not been studied in patients with hemodynamically significant rheumatic valvular heart disease, especially mitral stenosis, or patients with prosthetic heart valves. There are no data to support that Pradax® provides adequate anticoagulation in patients with prosthetic heart valves, with or without atrial fibrillation. Therefore, the use of Pradax® is not recommended in patients with hemodynamically significant rheumatic valvular heart disease or in patients with prosthetic heart valves.

The full text of the updated Product Monograph[1] can be found at:
http://www.boehringer-ingelheim.ca/en/human_health/our_products.html

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of serious or unexpected adverse reactions in patients receiving Pradax® should be reported to Boehringer Ingelheim (Canada) Ltd, or to Health Canada:

Boehringer Ingelheim (Canada) Ltd.,
5180 South Service Rd.
Burlington, ON, L7L 5H4
Tel: 1 (800) 263-5103 Ext. 84603.
http://www.boehringer-ingelheim.ca/en/contact.html

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario K1A 0K9

The Reporting Forms, postage paid labels, and Guidelines can be found on the MedEffect™ Canada Web site in the Adverse Reaction Reporting section (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php). The Reporting Form is also in the *Canadian Compendium of Pharmaceuticals and Specialties.*

For other health product inquiries related to this communication, please contact Health Canada at:
Marketed Health Products Directorate
E-mail: mhpd_dpsc@hc-sc.gc.ca
Telephone: 613-954-6522 Fax: 613-952-7738

The Pradax® Product Monograph[1] as well as a copy of this letter can be found on the Boehringer Ingelheim (Canada) Ltd., website at: http://www.boehringer-ingelheim.ca/en/human_health/our_products.html

Sincerely,

original signed by

Mathias Knecht, M.D.
Vice President, Medical and Regulatory Affairs
Boehringer Ingelheim (Canada) Ltd.

References:

1. Pradax® Product Monograph, dated January 27, 2012
http://webprod3.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp