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Press Release

Warnings and Alerting

Severe haemorrhages in patients treated with an anticoagulant "*Prazaxa (dabigatran etexilate) capsules"

*PRAZAXA® in Japan, PRADAXA® in the USA, EU countries

August 12, 2011

MHLW has required the Marketing Authorization Holder (MAH) of "Prazaxa capsules" to add BOXED WARNING and to revise "PRECAUTIONS" of the package insert to call attention, and to immediately provide healthcare professionals with necessary information. Several fatal cases resulted from haemorrhagic adverse effects including gastrointestinal haemorrhages have been reported in patients who received an anticoagulant "Prazaxa capsules".

- "Prazaxa capsules" (See Annex 1) is an anticoagulant drug to prevent blood clots forming that can cause a stroke and a systemic embolism in patients experienced atrial fibrillation and other conditions. Haemorrhage that lasts a long time is known as an adverse effect.

- As of 13 June 2011, one fatal case caused by serious haemorrhagic adverse effect has been reported in patient with renal failure who received this drug. The MAH has immediately provided information to healthcare professionals. By 11 August 2011, MHLW has received 4 fatal cases caused by hemorrhagic adverse events for which a causality of the drug can not be ruled out.

- The 5 fatal cases involved 1 man and 4 women. One of them is in 70's, and four of them are in 80's.

- Following measures are important for ensuring patient safety:
  1. To perform renal function tests before and during the treatment.
  2. To monitor patients for any signs including haemorrhage and anemia, and to take appropriate measures if haemorrhage occurs.
  3. To educate patients to call their doctors immediately if any signs of heamorrage occur.
     MHLW has required the MAH to add BOXED WARNING, to revise the "Precautions" and to provide healthcare professionals with information on this issue immediately.

- It should be noted that patients taking Prazaxa should pay attention to any symptoms including epistaxis, gingival haemorrhages, subcutaneous haemorrhages, haematuria and haematochezia, and immediately communicate with their doctors in case of haemorrhages.

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Annex 1

Prazaxa Capsules

Summary of the product

- Nonproprietary name: Dabigatran Etexilate Methanesulfonate
- Brand name: Prazaxa Capsules 75mg, 110mg
- MAH (Marketing Authorisation Holder): Nippon Boehringer Ingelheim Co., Ltd.
- Indications: Prazaxa is indicated to reduce the risk of ischaemic stroke and systemic embolism in patients with non-valvular atrial fibrillation
- Launched into Japan: March 2011
- Number of patients treated with this drug: approximately 64,000
- Prazaxa has an anticoagulant effect through direct thrombin inhibition. Prazaxa is contraindicated in patients with severe renal disorder, because this drug is mainly renally excreted. Blood levels of dabigatran may be elevated leading to an increased risk of haemorrhage in patients with moderate renal disorder. Patients aged 70 and older or with history of gastrointestinal haemorrhages also have an increased risk of haemorrhage. Therefore, Prazaxa should be administered to these patients cautiously with monitoring the condition of patients. Dose reduction should be considered in these patients as necessary.