18th December 2011

Circular No. P19 /2011

Dear Healthcare Professional,

Re: European Medicines Agency updates on safety of Pradaxa

The Medicines Authority would like to inform you that the European Medicines Agency (EMA) has made an update on the safety of the anticoagulant medicine Pradaxa (dabigatran etexilate).

Pradaxa is authorised and marketed in Europe including Malta for primary prevention of venous thromboembolic events in adults who have had elective total hip replacement surgery or total knee replacement surgery. Since August 2011, it is also authorised for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation. The efficacy of Pradaxa was demonstrated in clinical trials and this remains unchanged.

The EMA became aware of recent media interest regarding fatal cases of bleeding in patients treated with Pradaxa. The risk of bleeding with all anticoagulant medicines is well-known. For Pradaxa, this has been reflected since its initial marketing authorisation in the approved EU product information, which recommends that doctors check for signs of bleeding and discontinue treatment in patients with severe bleeding. Pradaxa is contraindicated in a number of conditions, including in patients who are bleeding and patients with severe renal impairment, and it should be used with caution and at lower doses in elderly patients and patients with moderate renal impairment (depending on indication and circumstances).

The issue of renal problems has been kept under close review and in October 2011 the Agency's Committee of Medicinal Products for Human Use (CHMP) recommended further changes to the product information. The recommended updated product information includes the following advice:

- Renal function to be assessed in all patients before starting Pradaxa treatment
- While on treatment, renal function should be assessed at least once a year in patients over 75 years of age

Medicines Authority
203 Level 3, Rue D'Argens, Gzira, GZR 1368 – Malta.
Tel. (+356) 23439000 Fax. (+356) 23439161 www.medicinesauthority.gov.mt

- Renal function should be assessed whenever a decline in renal function is suspected in patients of any age.

On the 25th of October 2011 these recommendations were relayed in a letter sent by the marketing authorisation holder Boehringer-Ingelheim, to all Maltese General Practitioners, Cardiologists, Haematologists, Stroke Physicians, Clinical Neurophysiologists, Geriatricians, Orthopaedic Surgeons and Hospital Pharmacists.

On 6 November 2011 the number of worldwide spontaneous case reports of serious bleeding resulting in death associated with the use of dabigatran, the active substance of Pradaxa totalled 256 within the EudraVigilance database. 21 out of these 256 cases were reported in the EU. The number of reports of bleedings in patients treated with Pradaxa has to be seen in the context of the rapidly increasing use of Pradaxa world-wide as a result of approval of a new indication (prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation) in several regions of the world and also the increased awareness about the drug, a factor that is known to lead to higher than usual reporting of side effects.

The CHMP is of the opinion that the recommended changes to the use of Pradaxa can adequately manage the risk of bleeding. The overall safety profile of Pradaxa will continue to be monitored to confirm that the frequency of occurrence of fatal bleedings does not increase and that the recommended changes in product information is appropriate to manage the risk.

Healthcare professionals are encouraged to maintain vigilance on Pradaxa. Suspected Adverse Drug Reactions may be reported using the Medicines Authority yellow card scheme or online at http://www.medicinesauthority.gov.mt/pub/adr.doc or to the marketing authorisation holder or their local representatives.

The full **press release** on Pradaxa issued by the EMA is attached here for your perusal.

Healthcare professionals are encouraged to check the Medicines Authority website regularly for product safety updates as these are issued on an ongoing basis.

Medicines Authority
203 Level 3, Rue D'Argens, Gzira, GZR 1368 – Malta.
Tel. (+356) 23439000 Fax. (+356) 23439161 www.medicinesauthority.gov.mt