27th December 2011

Circular No. P21/2011

Dear Healthcare Professional,

Re: European Medicines Agency starts review of aliskiren-containing medicines following termination of ALTITUDE study

The European Medicines Agency is reviewing aliskiren-containing medicines, to assess the impact of data coming from the ALTITUDE study on the balance of benefits and risks of these medicines in their approved indication. Aliskiren-containing medicines are approved for the treatment of essential hypertension. There are currently 2 products containing aliskiren which are authorised in Malta and these are marketed as Rasilez and Rasilez HCT film coated tablets.

The Agency's Committee for Medicinal Products for Human Use (CHMP) started the review after it was informed on 19 December 2011 by the marketing authorisation holder of the decision to terminate the ALTITUDE study* early. This clinical trial included patients with type 2 diabetes and renal impairment and/or cardiovascular disease. In most patients arterial blood pressure was adequately controlled. The patients included in the trial received aliskiren in addition to either an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB). Termination of the placebo-controlled phase III trial was recommended by the independent Data Monitoring Committee overseeing the study, because the results showed that there was no benefit with aliskiren and that there were more cases of stroke, renal complications, hyperkalemia and hypotension in patients who received aliskiren compared with patients who received placebo.

The information available at present is limited. The Committee has asked the company to provide additional analyses to allow the CHMP to assess the impact of the results of the ALTITUDE trial on the overall benefit-risk profile of aliskiren-containing medicines and to determine the need for regulatory action.

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

Interim advice for doctors and patients

While the review is ongoing the CHMP recommends, as a precautionary measure, that doctors should not prescribe aliskiren-containing medicines to diabetic patients in combination with ACE inhibitors or ARBs.

Doctors should therefore review the treatment of patients taking aliskiren at a routine (non-urgent) appointment, and if patients are diabetic and are also taking ACE inhibitors or ARBs, aliskiren should be stopped and alternative treatments considered.

Patients should not stop any of their treatment before speaking to their doctor, because stopping anti-hypertensive medication without medical supervision can put them at risk. They are advised to discuss their treatment with their doctor at their next scheduled (non-urgent) appointment.

Further information on the review of aliskiren-containing medicines will be provided when available.

The Medicines Authority is in agreement with the full **press release** issued by the EMA, attached here for your perusal. Healthcare professionals are encouraged to maintain vigilance on aliskiren containing products. 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.

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* The ALTITUDE study was designed to determine whether aliskiren, on top of conventional treatment including an ACE inhibitor or ARB, reduces the risk of disease and death from heart and circulatory or kidney problems in patients with type 2 diabetes and renal impairment and /or cardiovascular disease.

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

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