20th February 2012

Circular No. P03/2012

Dear Healthcare Professional,

Re: European Medicines Agency recommends new contraindications and warnings for aliskiren-containing medicines.

The Medicines Authority would like to inform healthcare professionals that the European Medicines Agency (EMA) has concluded its review of aliskiren-containing medicines, recommending that these medicines should be contraindicated in patients with diabetes or moderate to severe renal impairment who take angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs). In addition, the Agency recommended the inclusion of a warning that the combination of aliskiren and ACE inhibitor or ARB is not recommended in all other patients because adverse outcomes cannot be excluded.

There are currently 2 products containing aliskiren which are authorised in Malta and these are marketed as Rasilez and Rasilez HCT film coated tablets. Aliskiren containing medicines are approved for the treatment of essential hypertension. As the Medicines Authority had informed you in circular P21/2011, a review of aliskiren containing products was started in December 2011 by the EMA's Committee for Medicinal Products for Human Use (CHMP). The review was started after the Agency was informed by the marketing authorisation holder of the decision to terminate the ALTITUDE* study early. This placebo-controlled phase III 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 ACE inhibitor or an ARB.

Since then further data and analyses from the ALTITUDE study, alongside all data from other studies and spontaneous reports of suspected adverse drug reactions, have become available and were

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

reviewed by the CHMP. The data suggest a risk of adverse outcomes (hypotension, syncope, stroke, hyperkalaemia and changes in renal function, including acute renal failure) when aliskiren is combined with ACE inhibitors or ARBs, especially in diabetic patients and those with impaired renal function. Although less evidence is available for other patient groups, adverse outcomes cannot be excluded and therefore the CHMP no longer recommends the use of this combination.

Advice for doctors and patients

Doctors should stop prescribing aliskiren-containing medicines to patients with type 1 or type 2 diabetes or with moderate to severe kidney impairment who are also taking an ACE inhibitor or ARB, and should consider alternative antihypertensive treatment as necessary.

For all other patients receiving aliskiren-containing medicines in combination with an ACE inhibitor or an ARB, the balance of benefits and risks of continuing treatment should be considered carefully.

Pharmacists should inform patients that they should discuss their treatment with their doctor at their next scheduled (non-urgent) appointment. They 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.

The Medicines Authority is in agreement with the full **press release** issued by the EMA. 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.

---

* 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.

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