EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Renin-angiotensin-system (RAS)-acting agents

Combined use of medicines affecting the renin-angiotensin system (RAS) to be restricted – CHMP endorses PRAC recommendation

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has endorsed restrictions on combining different classes of medicines that act on the renin-angiotensin system (RAS), a hormone system that controls blood pressure and the volume of fluids in the body.

These medicines (called RAS-acting agents) belong to three main classes: angiotensin-receptor blockers (ARBs, sometimes known as sartans), angiotensin-converting enzyme inhibitors (ACE-inhibitors) and direct renin inhibitors such as aliskiren. Combination of medicines from any two of these classes is not recommended and, in particular, patients with diabetes-related kidney problems (diabetic nephropathy) should not be given an ARB with an ACE-inhibitor.

Where combination of these medicines (dual blockade) is considered absolutely necessary, it must be carried out under specialist supervision with close monitoring of kidney function, fluid and salt balance and blood pressure. This would include the licensed use of the ARBs candesartan or valsartan as add-on therapy to ACE-inhibitors in patients with heart failure who require such a combination. The combination of aliskiren with an ARB or ACE-inhibitor is strictly contraindicated in those with kidney impairment or diabetes.

The CHMP opinion confirms recommendations made by the Agency's Pharmacovigilance Risk Assessment Committee (PRAC) in April 2014, following assessment of evidence from several large studies in patients with various pre-existing heart and circulatory disorders, or with type 2 diabetes. These studies found that combination of an ARB with an ACE-inhibitor was associated with an increased risk of hyperkalaemia (increased potassium in the blood), kidney damage or low blood pressure compared with using either medicine alone. Furthermore, no significant benefits from dual blockade were seen in patients without heart failure and benefits were thought to outweigh risk only in a selected group of patients with heart failure in whom other treatments were unsuitable. This broad review of evidence relating to all RAS-acting agents supported the conclusions of a previous EMA review relating specifically to medicines containing aliskiren.[1]

The CHMP opinion will now be forwarded to the European Commission, which will issue a final decision valid throughout the EU in due course.

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[1] European Medicines Agency recommends new contraindications and warnings for aliskiren-containing medicines.