22 December 2011
EMA/990270/2011

# Questions and answers on ongoing review of aliskiren-containing medicines

Interim advice while review is ongoing

The European Medicines Agency is currently reviewing[1] aliskiren-containing medicines, following the early termination of a study investigating aliskiren. The Agency's Committee for Medicinal Products for Human Use (CHMP) is assessing the impact of data from the study on the benefit-risk balance of these medicines. While the review is ongoing, as a precautionary measure, the CHMP recommends that doctors should not prescribe aliskiren-containing medicines to diabetic patients in combination with an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB). Treatment of patients already taking aliskiren should be reviewed at their next scheduled (non-urgent) appointment.

## What are aliskiren-containing medicines?

Aliskiren-containing medicines are used to treat essential hypertension (high blood pressure) in adults. 'Essential' means that the hypertension has no obvious cause.

Aliskiren is a renin inhibitor. It blocks the activity of a human enzyme called renin, which is involved in the production of a substance called angiotensin I in the body. Angiotensin I is converted into the hormone angiotensin II, which is a powerful vasoconstrictor (a substance that narrows blood vessels). By blocking the production of angiotensin I, levels of both angiotensin I and angiotensin II fall. This causes vasodilation (widening of the blood vessels), so that the blood pressure drops.

Eight aliskiren-containing medicines are authorised in the European Union (EU) since 2007: Rasilamlo, Rasilez, Rasilez HCT, Rasitrio, Riprazo, Riprazo HCT, Sprimeo, Sprimeo HCT. Some of these medicines (Rasilamlo, Rasilez HCT, Rasitrio, Riprazo HCT and Sprimeo HCT) are combinations of aliskiren with other antihypertensive medicines. Aliskiren-containing medicines are available as tablets and marketed in all EU Member States, except Estonia, Latvia, Lithuania and Romania.[2]

## Why are these medicines being reviewed?

On 19 December 2011, the marketing authorisation holder for aliskiren-containing medicines, Novartis Europharm Ltd., informed the Agency of its decision to terminate the ALTITUDE study early. The study

[1] The CHMP assessment is being conducted in the context of a formal review under Article 20 of Regulation (EC) No 726/2004, started at the request of the European Commission on 20 December 2011.
[2] More information on aliskiren-containing medicines can be found in the relevant European public assessment reports (EPARs) for each medicine: www.ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.

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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. In most patients arterial blood pressure was adequately controlled.

Termination of the study was recommended by the independent Data Monitoring Committee overseeing it, because the results showed that there was no benefit from aliskiren, and patients treated with it experienced a significantly higher number of cardiovascular and renal problems than patients given placebo. This particularly involved stroke, renal complications, hyperkalaemia (high blood potassium levels) and hypotension (low blood pressure).

## What is the current status of discussions at the CHMP?

The CHMP is currently assessing the available data from the ALTITUDE study, which are however limited, and has asked the company to provide additional information from this and other ongoing studies with aliskiren. While the review is ongoing, the CHMP, as a precautionary measure, has given advice to patients and healthcare professionals.

## What is the advice for patients and healthcare professionals?

- Doctors should not prescribe aliskiren-containing medicines to diabetic patients in combination with ACE inhibitors or ARBs. Alternative treatment options should be considered if needed.
- Doctors should 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.
- Patients in clinical trials with aliskiren should contact their study site for guidance on their medication.
- Patients who have any questions or concerns about their treatment should speak to their doctor or pharmacist at a routine appointment.

## What will happen next?

These recommendations are issued in order to protect public health while the review is being finalised. The European Medicines Agency will issue further advice as necessary.