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Questions and answers on the review of angiotensin II receptor antagonists and the risk of cancer

Outcome of a procedure under Article 5(3) of Regulation (EC) 726/2004[1]

The European Medicines Agency has completed a review of the risk of new cancers with the use of angiotensin II receptor antagonists (ARBs). The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that there is no increased risk of cancer in patients using these medicines and that therefore the benefits continue to outweigh the risks.

What are angiotensin II receptor antagonists?

Angiotensin II receptor antagonists (ARBs) have been authorised in the European Union since the mid-1990s for the treatment of hypertension (high blood pressure). They are also used in the treatment of conditions such as heart failure and kidney disease in type 2 diabetes and for the prevention of strokes and heart disease.

Several ARBs are authorised in the EU[2], three of them (irbesartan, telmisartan, and valsartan) centrally. ARBs are available in medicines alone or in combination with other active substances or as generics.

ARBs are medicines that block receptors for a hormone called angiotensin II which is a powerful vasoconstrictor (a substance that narrows blood vessels). By blocking the receptors, they stop the hormone having its narrowing effect on the blood vessels, allowing the blood vessels to widen and causing blood pressure to fall.

Why were these medicines reviewed?

The review of ARBs was initiated to investigate a possible link between the use of these medicines and the occurrence of new cancers. This followed the publication of a meta-analysis[3] (an analysis of several clinical trials together) which showed a small increased risk of new cancers (particularly lung cancer)

[1] Article 5(3) of Regulation (EC) 726/2004, opinion on any scientific matter concerning the evaluation of medicinal products for human use.
[2] candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan and valsartan
[3] Sipahi I, Debanne SM, Rowland DY, Simon DI, Fang JC. Angiotensin-receptor blockade and risk of cancer: meta-analysis of randomised controlled trials. Lancet Oncol. 2010 Jul;11(7):627-36.

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with ARBs compared with placebo and other heart medicines (7.2 % versus 6 %). The meta-analysis included data from nine trials involving almost 95,000 patients.

The CHMP decided to carry out the review, which was formally requested by the Italian medicines agency, to examine the strength of the evidence from the meta-analysis and to review all available evidence on the risk of cancer with ARBs.

Which data has the CHMP reviewed?

The CHMP looked at all publicly available data on the risk of cancer of ARBs. These included the results from the meta-analysis as well as other clinical data (including data from clinical trials and epidemiological studies) and non-clinical data on ARBs.

What are the conclusions of the CHMP?

The CHMP was of the view that the evidence from the meta-analysis was weak and noted several problems with the analysis: the patients in the trials were not followed up long enough to clearly establish a link between ARBs and cancer, information on the risk of cancer before start of treatment was lacking, and there was a possibility of publication bias, whereby studies that showed a link with cancer were more likely to have been included in the analysis.

When the CHMP looked at all other available data, which included data from large population-based studies and more complete meta-analyses that did not have the same methodological problems as the original meta-analysis by Sipahi et al.[3], the results did not show an increased risk of cancer with ARBs.

The CHMP therefore concluded that the existing evidence did not support a link between the use of ARBs and the occurrence of new cancers and that the benefits of ARBs continue to outweigh their risks. The CHMP did not recommend any changes to the prescribing information for these medicines.

What will happen next?

As with all medicines the safety of ARBs will be continuously monitored by EU regulatory authorities.