European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

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QUESTIONS AND ANSWERS ON THE SAFETY OF ACOMPLIA (RIMONABANT)

As part of its continuous monitoring of medicines, the European Medicines Agency (EMEA) has reviewed the available information on the safety of ACOMPLIA (rimonabant), particularly on the medicine's psychiatric safety. It has concluded that ACOMPLIA's benefits continue to outweigh its risks, but that patients with ongoing major depression or who are receiving antidepressant treatment should not be prescribed ACOMPLIA and that some of the warnings in the medicine's prescribing information should be strengthened.

What is ACOMPLIA?

ACOMPLIA is a medicine containing the active substance rimonabant. It is used together with diet and exercise to reduce weight in adult patients who are:

- obese (very overweight) with a body mass index (BMI) greater or equal to 30 kg/m^2, or,
- overweight (BMI greater or equal to 27 kg/m^2) and also have other risk factors, such as type 2 diabetes or dyslipidaemia (abnormal levels of fat in their blood).

The active substance in ACOMPLIA, rimonabant, is a cannabinoid receptor antagonist. It acts by blocking a specific type of receptor called cannabinoid type 1 (CB1) receptors. These receptors are found in the nervous system and are part of the system that the body uses to control food intake. By blocking the receptors, rimonabant can help patients to reduce food intake and to lose weight. The receptors are also found in peripheral tissues including adipocytes (fat cells).

ACOMPLIA is authorised in the European Union/European Economic Area, and is marketed in 13 European countries. Rimonabant is also authorised as ZIMULTI, but this product is not marketed in the European Union.

Why has the EMEA reviewed the medicine?

ACOMPLIA received a positive opinion from the EMEA's Committee for Medicinal Products for Human Use (CHMP) on 27 April 2006, and a marketing authorisation from the European Commission on 19 June 2006. During the approval procedure, the main safety issue identified with the medicine was psychiatric side effects, especially depression. The company that makes ACOMPLIA was requested to monitor these side effects.

In June 2007, as part of its continuous monitoring of the safety of this medicine, the CHMP requested all available information on the psychiatric safety of ACOMPLIA from sanofi-aventis. The review of this information was finalised at the CHMP meeting of 16-19 July 2007.

Which data has the CHMP reviewed?

The review included information on the psychiatric safety of ACOMPLIA, focusing on cases of depression in patients taking the medicine, including suicidal ideation (thoughts about committing suicide) and suicide attempts. This information came both from the company's monitoring of the use of the medicine from its launch until 18 June 2007, and from five studies involving 781 patients taking ACOMPLIA, which have been completed since ACOMPLIA was granted marketing authorisation.

What were the conclusions of the CHMP?

The CHMP concluded that the benefits of ACOMPLIA continue to outweigh its risks, except in patients with ongoing major depression and/or taking antidepressants.

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It concluded that the risk of depression is approximately doubled in patients taking ACOMPLIA, compared to obese or overweight patients not taking the medicine. In a small minority of cases, this could lead to suicidal ideation or even suicide attempts. This doubling of the risk of depression occurs in all types of patients; however, this risk may be increased in patients with a past history of depression. Although this pattern of side effects is similar to what was seen during the approval procedure of the medicine, the CHMP concluded that this increased risk is of concern, since ACOMPLIA is now being used in patients with a history of psychiatric events. This could result in patients with depression being at risk of their disease getting worse.

The CHMP also noted that too many patients are taking ACOMPLIA at the same time as antidepressants, even though ACOMPLIA is not recommended for use in patients also taking antidepressants.

Therefore, the CHMP recommended the following changes to the medicine's prescribing information:

- upgrading to a contraindication the warning on the use of ACOMPLIA in patients with ongoing major depression or taking antidepressants. This means that ACOMPLIA must no longer be used in these patients,
- adding a warning that treatment with ACOMPLIA should be stopped if a patient develops depression,
- including additional information on the psychiatric safety of ACOMPLIA.

The Committee also requested that the company provides a letter to be sent to healthcare providers explaining the changes in recommendations of use for ACOMPLIA.

What is the advice to patients and prescribers?

- Doctors should only prescribe ACOMPLIA according to the updated prescribing information.
- Patients and their family should be aware of the risk of depression in patients taking ACOMPLIA, and that patients should not take ACOMPLIA if they are taking an antidepressant.
- Patients who start to experience symptoms of depression while taking ACOMPLIA should consult their doctor.
- Patients who are taking ACOMPLIA and have questions or concerns should talk to their doctor or pharmacist.

For further information, see the updated Product Information adopted by the CHMP on 19 July 2007.

A European Commission Decision on this opinion will be issued in due course.