European Medicines Agency

London, 24 April 2008
Doc. Ref. EMEA/218318/2008

QUESTIONS AND ANSWERS ON THE USE OF ANGIOTENSIN II RECEPTOR ANTAGONISTS DURING PREGNANCY

As part of its continuous monitoring of medicines, the European Medicines Agency (EMEA) has reviewed the available information on the safety of angiotensin II receptor antagonists, in particular their effects on the unborn child when they are taken by pregnant women.

The EMEA's Committee for Medicinal Products for Human Use (CHMP) has recommended that the prescribing information for the medicines in this class be made consistent, stating that their use should be avoided during the first trimester (the first three months) of pregnancy. The CHMP also recommended that the prescribing information for the medicines in this class should continue to include a contraindication stating that they must not be used during the second and third trimesters (the last six months) of pregnancy.

What are angiotensin II receptor antagonists?

Angiotensin II receptor antagonists (AIIRAs) are a group of medicines that are used in patients with essential hypertension (high blood pressure that has no identifiable cause). AIIRAs work by blocking the receptors for the hormone angiotensin II. Angiotensin II is a powerful vasoconstrictor, which means that it causes the blood vessels to narrow. By blocking the receptors to which angiotensin II normally fixes itself, AIIRAs stop the hormone's effects. This allows the blood vessels to widen, lowering the blood pressure.

AIIRAs have been available in the European Union since the mid-1990s. Three are available in medicines that are 'centrally authorised' (authorised by the European Commission): irbesartan[1], telmisartan[2] and valsartan[3]. The other AIIRAs are authorised by regulatory authorities in Member States, and not by the European Commission.

What is the issue with AIIRAs?

Prior to this review, the CHMP noted that the product information for irbesartan- and telmisartan-containing medicines included information stating that their use should be avoided during the first trimester. However, the prescribing information for valsartan-containing medicines contained a contraindication stating that they must not be used during this stage of pregnancy. The CHMP wished to determine whether the same information should be included in the prescribing information for all centrally authorised medicines in this class.

The prescribing information for all centrally authorised AIIRAs already included a contraindication stating that they must not be used during the second and third trimesters of pregnancy.

[1] The centrally authorised medicines containing irbesartan are Aprovel, Karvea, Irbesartan BMS and Irbesartan Winthrop. Irbesartan is also available in combination with hydrochlorothiazide in the following centrally authorised medicines: Coaprovel, Karvezide, Irbesartan Hydrochlorothiazide BMS and Irbesartan Hydrochlorothiazide Winthrop.

[2] The centrally authorised medicines containing telmisartan are Micardis, Pritor and Kinzalmono. Telmisartan is also available in combination with hydrochlorothiazide in the following centrally authorised medicines: MicardisPlus, PritorPlus and Kinzalkomb.

[3] Valsartan is available in combination with amlodipine in the following centrally authorised medicines: Exforge, Copalia, Dafiro and Imprida.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 86 68
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

What are the conclusions of the CHMP?

Following a review of the safety of the use of AIIRAs during pregnancy, the CHMP confirmed that the benefits of these medicines do not outweigh their risks in the second and third trimesters of pregnancy. It therefore recommended that the product information for all medicines in this class should continue to include a contraindication stating that they must not be used during these stages of pregnancy.

The CHMP also concluded that there is insufficient evidence to determine whether there is a risk of harm to the unborn child when AIIRAs are taken during the first trimester of pregnancy. CHMP advised that women who were planning to become pregnant should switch to alternative treatments unless continued treatment with AIIRAs is essential. This may include some women who have high blood pressure and additional risk factors, such as diabetes or kidney disease, who may gain a greater benefit from treatment with AIIRAs than from some other treatments. Therefore, in these women, the benefits of treatment with AIIRAs could outweigh the potential risks of exposure during early pregnancy. These women should be switched to suitable alternative treatments when pregnancy is confirmed.

On the basis of these conclusions, the CHMP recommended that the prescribing information for AIIRAs should be made consistent, stating that their use during the first trimester of pregnancy should be avoided and that they must not be used during the second and third trimesters.

What is the advice to patients and prescribers?

- Women who are taking AIIRAs should tell their doctor if they think they are or might become pregnant.
- Doctors should prescribe AIIRAs according to the updated product information:
    - they should switch women who are planning to become pregnant to alternative treatments unless continued treatment with AIIRAs is essential;
    - they should not prescribe AIIRAs to women who are pregnant;
    - they should stop treatment with AIIRAs in women who become pregnant. These women should be switched to alternative treatments for high blood pressure if necessary.
- Patients who have any questions or concerns should talk to their doctor or pharmacist.

European Commission decisions on these opinions will be issued in due course.