

Angiotensin-Converting Enzyme Inhibitors and Pregnancy

FDA Public Health Advisory

THE ISSUE

On June 7, 2006, the FDA issued a Public Health Advisory warning health care providers and patients about the risk of congenital malformations with the use of angiotensin-converting enzyme (ACE) inhibitors in the first trimester of pregnancy.

THE DRUG

ACE inhibitors are a broad class of drugs used to treat hypertension alone or with other agents. They work by inhibiting the production of angiotensin II, a potent vasoconstrictor. Some ACE inhibitors include benazepril (Lotensin[®]), captopril (Capoten[®]), lisinopril (Zestril[®] and Prinivil[®]) and ramipril (Altace[®]).

THE WARNING

The FDA advisory states that the use of ACE inhibitors in the first trimester of pregnancy may lead to an increased risk of birth defects. An observational study published in the *New England Journal of Medicine* showed that exposure to ACE inhibitors during the first trimester of pregnancy may place the infant at increased risk for major congenital malformations. There is already a black box warning on the labeling of all ACE inhibitors that warns of fetal harm in the second and third trimesters.

WHAT YOU NEED TO KNOW

Currently, ACE inhibitors are pregnancy category C in the first trimester and category D in the second and third trimesters. Most malformations identified were various cardiac septal defects. The results of this study do not establish a causal relationship. There are at present no plans to change the prescribing information for ACE inhibitors to reflect the findings of this study. If the fetal abnormalities are related to the angiotensin II receptor, then angiotensin receptor antagonists such as candesartan (Atacand[®]), losartan (Cozaar[®]), and valsartan (Diovan[®]) may also be dangerous in the first trimester. Currently, the angiotensin receptor antagonists are pregnancy category C in the first trimester and category D in the second and third trimesters. Health care providers who care for women of reproductive age should counsel those who are treated with an ACE inhibitor about the potential risks of these drugs throughout pregnancy, especially in the second and third trimesters.

WHAT TO TELL YOUR PATIENTS

Pregnant women should be prescribed ACE inhibitors only if the expected benefit clearly exceeds the potential risk. Women who become pregnant should have their ACE inhibitors changed to a different medication as soon as possible. Women who are taking ACE inhibitors to treat high blood pressure should tell their health care professionals if they are planning a pregnancy or think they might be pregnant.

RESOURCES

FDA Public Health Advisory: <http://www.fda.gov/cder/drug/advisory/ACEI.htm>

New England Journal of Medicine article (subscription required): <http://content.nejm.org/cgi/content/full/354/23/2443>

Pregnancy Risk Categories: http://www.fda.gov/fdac/features/2001/301_preg.html#categories

DISCLAIMER

This publication is intended to provide key practical information regarding this drug product in a brief format. It does not contain sufficient information upon which to base formulary or other medication use policy decisions.

