

WYOMING DRUG UTILIZATION REVIEW

July 2006



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Hypertension Diagnosis and Treatment

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A recent review of patient data from Wyoming Medicaid from October 2004 to October 2005 found 3534 patients with a hypertension diagnosis (ICD-9 401 or 642). However, only 2520 of these patients filled any sort of antihypertensive medication.²

JNC 7 states “the relationship between blood pressure and risk of CVD events is “continuous, consistent and independent of other risk factors. The higher the blood pressure, the greater the chance of heart attack, heart failure, stroke and kidney disease.”¹ Antihypertensive therapy has been associated in clinical trials with a reduction in stroke incidence averaging 35–40%; myocardial infarction, 20–25%; and heart failure more than 50%.¹ In patients with stage 1 hypertension and additional cardiovascular risk factors, it is estimated that a sustained 12 mmHg decrease over 10 years will prevent 1 death for every 11 patients treated.¹ This number drops to 1 for every 9 treated patients with CVD or target organ damage.¹

In the US, only 34% of patients with hypertension (defined as systolic blood pressure \geq 140 mmHg or diastolic blood pressure \geq 90 mmHg) are controlled (defined as systolic blood pres-

sure $<$ 140 mmHg and diastolic blood pressure $<$ 90 mmHg)¹ and only 59% are being treated with an antihypertensive medication.¹ Effective blood pressure control is achievable in most patients with prescriptions for lifestyle modification and adequate antihypertensive drug doses.¹ Sometimes, two or more antihypertensive medications are required.¹

Of course, not every patient with a hypertension diagnosis on their profile is a candidate for hypertensive therapy. A copy of the Quick Reference Card from JNC 7 with guidelines for appropriate treatment regimens for patients at each diagnostic level is available at <http://www.nhlbi.nih.gov/guidelines/hypertension/jnc7card.htm>. The full guidelines are available online free of charge at <http://www.nhlbi.nih.gov/guidelines/hypertension>.

References

1. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. National Heart, Lung, and Blood Institute; national high blood pressure education program coordinating committee. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension. 2003 Dec;42(6):1206-52. Epub 2003 Dec 1.
2. Internal Wyoming drug utilization review data. Accessed January 2006 by Grande, K.

Use of ACE Inhibitors in Pregnancy

Kendra Grande, RPh

A new study in the New England Journal of Medicine suggests there may be a link between angiotensin-converting enzyme inhibitors (ACEI) and an increased risk of birth defects when used in the first trimester of pregnancy.¹ The observational study looked at a cohort of 29,507 infants in the Tennessee Medicaid program from 1985 and 2000. Infants whose mothers had maternal diabetes were excluded. The study defined maternal diabetes as:

1. Two or more prescriptions for insulin or an oral hypoglycemic
2. An outpatient diabetes diagnosis and one related prescription or
3. A hospital diagnosis of diabetes.

Other infant exclusions were made for maternal use of angiotensin-receptor antagonist (2 infants), exposure to an ACEI beyond the first trimester (1001 infants) and exposure to other teratogens (2239 infants). The study attempted to identify those

infants with a major congenital malformation not related to a chromosomal defect or a clinical genetic syndrome.¹

In the first trimester alone, 411 infants were exposed to antihypertensive medications.¹ Table 1 on page 2 presents a brief summary of the major findings.

Exposure to ACE inhibitors during the first trimester of pregnancy was previously thought to be safe.² This study showed a potential risk of increased congenital malformation with ACEI usage in the first trimester.¹ Based on this study, FDA has issued a Public Health Advisory with the following recommendations:

1. Healthcare 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 during the second and third trimesters.

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2. Pregnant women should only be prescribed ACE inhibitors if the expected benefit clearly exceeds the potential risk.
3. Women who become pregnant should have their ACE inhibitor changed to a different medication as soon as possible.
4. Women who are taking ACE inhibitors to treat high blood pressure should tell their healthcare professionals if they are planning a pregnancy or think they might be pregnant.³

At this time, FDA is not changing the pregnancy category for ACEI. It will remain a D for the 2nd and 3rd trimesters and a C for the 1st trimester. However, FDA and the Agency for

Healthcare Quality and Research are attempting to identify additional sources of data to study this further.³

Page 3 of this newsletter is a patient information sheet on this advisory that may be freely distributed to patients.

References

1. Cooper WO, Hernandez-Diaz, S, Arbogast PG, Dudley JA et al. Major congenital malformations after first-trimester exposure to ACE inhibitors. N Engl J Med 2006;35:2443-51.
2. Lip GY, Churchill D, Beevers M, Auckett A, Beevers DG. Angiotensin-converting-enzyme inhibitors in early pregnancy. Lancet 1997 Nov 15;350(9089):1446-7.
3. FDA Public Health Advisory: Angiotensin-converting enzyme inhibitor (ACE inhibitor) drugs and pregnancy. US Food and Drug Administration. 2006 June 7. Available online at: <http://www.fda.gov/cder/drug/advisory/ACEI.htm>.

Table 1: Maternal ACE Inhibitor Usage and Major Congenital Malformations in Infants¹

	ACE Inhibitor	Other Antihypertensive Medication	No Antihypertensive
Total infants (N)	209	202	29,096
Infants with any congenital malformation	18	4	834
Risk Ratio	2.71	0.66	1
95% Confidence Interval	1.72-4.27	0.25-1.75	Reference

Efficacy and Safety of High-Dose Narcotics

Addendum

Scott L Johnston, MD

Several recent studies of high dose narcotics revealed an increasing risk of respiratory depression, central sleep apnea, and sleep disordered breathing^{1,2,3,4}. Although in the past this was thought to happen only after raising the dose and last a short period of time, more recent data suggests that it happens with chronic use. This appears to begin at 200 mg per day of morphine or morphine equivalent. This respiratory depression is not responsive to conventional treatment including CPAP⁵. The recommended therapy is to decrease or stop the narcotics. (The original article appeared in the April 2006 issue.)

References

1. Teichtahl H, Wang D, Cunningham D, Quinnell T, Tran H, Kronborg I, Drummer OH. Ventilatory responses to hypoxia and hypercapnia in stable methadone maintenance treatment patients. Chest. 2005 Sep;128(3):1339-47.
2. Farney R., Walker J., Cloward t., Rhondeau S. Sleep-disordered breathing associated with long-term opioid therapy. Chest 2003;123:632-639
3. Wang D, Teichtahl H, Drummer O, Goodman C, Cherry G, Cunningham D, Kronborg I. Central sleep apnea in stable methadone maintenance treatment patients. Chest. 2005 Sep;128(3):1348-56.
4. Teichtahl H, Prodromidis A, Miller B, Cherry G, Kronborg I. Sleep-disordered breathing in stable methadone programme patients: a pilot study. Addiction. 2001 Mar;96(3):395-403.
5. Unpublished data. Personal communication with Dr Farney 22 May 2006. Email rjfund@msn.com

Partnership for Prescription Assistance

Partnership for Prescription Assistance (PPA) helps qualifying patients who lack prescription coverage get the medicines they need through a public or private program. PPA offers a single point of access to more than 475 public and private patient assistance programs, including more than 150 programs offered by pharmaceutical companies. To find out more about PPA visit the PPA website at www.pparx.org or call toll free 1-888-4777-2669.

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Patient Information Sheet

Angiotensin-Converting Enzyme Inhibitor Drugs (ACE Inhibitors)

This is a summary of the most important information about prescription ACE inhibitors. For more information, talk to your healthcare professional.

FDA ALERT [06/2006]: Blood pressure medicines called angiotensin-converting enzyme inhibitors (ACE inhibitors) may be associated with increased risk of birth defects if taken during early pregnancy (first three months, or first trimester).

On June 8, 2006, the *New England Journal of Medicine* published an article reporting a study that showed babies whose mothers had taken an ACE inhibitor during the first three months of pregnancy had an increased risk of birth defects. The number of birth defects was small, and the study has not been repeated.

Before this study, it was known that ACE inhibitors can harm an unborn baby when taken during the last six months of pregnancy (second and third trimester).

If you are pregnant or planning to become pregnant and take a blood pressure medicine, talk with your healthcare professional. High blood pressure is a condition that needs treatment. Your healthcare professional can advise you on the blood pressure medicine that is best for you and your baby during pregnancy.

This information reflects FDA's preliminary analysis of data concerning these drugs. FDA is considering, but has not reached a final conclusion about, this information. FDA intends to update this sheet when additional information or analyses become available.

What Are ACE inhibitors?

- ACE inhibitors are used alone or with other medicines to treat high blood pressure in adults.

ACE inhibitors include: Benazepril (Lotensin), Captopril (Capoten), Enalapril/Enalaprilat (Vasotec oral and injectable), Fosinopril (Monopril), Lisinopril (Zestril and Prinivil), Moexipril (Univasc), Perindopril (Aceon), Quinapril (Accupril), Ramipril (Altace), and Trandolapril (Mavik).

There is a list of prescription ACE inhibitors available at: http://www.fda.gov/cder/drug/infopage/ace_inhibitors/default.htm

Who Should Not Take ACE Inhibitors?

If you are pregnant or planning to become pregnant and take a blood pressure medicine, talk with your healthcare professional. ACE inhibitors can harm or even cause death to

an unborn baby (fetus) if taken during the last six months of pregnancy.

What Are The Risks?

The following are the major potential risks and side effects of ACE inhibitor therapy. However, this list is not complete.

- **Birth defects or death of an unborn baby.**
- **Kidney problems** that include worsening of kidney problems that you already have. Symptoms include a sudden weight gain and swelling of your arms, hands, legs, and feet.

The most common side effects with ACE inhibitors are:

- Dizziness
- Dry cough
- Sore throat

What Should I Tell My Healthcare Professional?

Before you start taking an ACE inhibitor, tell your healthcare professional if you:

- have had hives or allergic-type reactions after taking another ACE inhibitor
- have kidney problems
- are trying to become pregnant, are already pregnant, or are breast-feeding

If you are already taking an ACE inhibitor, tell your healthcare professional if you

- become pregnant.
- notice swelling of your face, mouth or throat, or have difficulty swallowing or breathing – this could be serious and you should get medical help right away.

Can Other Medicines or Food Affect ACE Inhibitors?

ACE inhibitors and certain other medicines can interact with each other. Tell your healthcare professional about all the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of them with you to show your healthcare professional.



Questions? Call Drug Information, 1-888-INFO-FDA (automated) or 301-827-4570
Druginfo@fda.hhs.gov

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Wyoming Preferred Drug List: www.uwyo.edu/PDL