Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Angiotensin Converting Enzyme Inhibitors***
-August 2014-

Background:
The IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed the angiotensin converting enzyme inhibitor (ACEI) class of medications at the August 2014 meeting. The discussion included clinical, utilization and procurement data. There were no recommendations to modify the current formulary; however, the committee felt a formulary brief should be developed with an emphasis on avoiding use during pregnancy and cautioning use in women of childbearing age.

Discussion:
Benazepril, captopril, enalapril maleate, fosinopril sodium, lisinopril, moexipril, perindopril, quinapril, ramipril and trandolapril were the primary ACEIs discussed. A Cochrane review in 2008 used ninety-two trials and evaluated the dose-related trough blood pressure lowering efficacy of 14 different ACEIs in 13,000 patients. The data suggested that no particular ACEI was any better or worse at lowering blood pressure and therefore the authors concluded there was no clinically meaningful blood pressure lowering differences between different ACEIs.[1]

ACEIs are considered Category D drugs for pregnancy and carry a black box warning to discontinue as soon as possible when pregnancy is detected, as drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.[2] Also noted was an epidemiologic study demonstrating infants exposed to ACEIs during the first trimester had an increased risk of major congenital malformation (risk ratio (RR): 2.71; 95% CI, 1.72 to 4.27) when compared with those who had no exposure to antihypertensive medications (n=29,096). Infants exposed to other antihypertensive medications only during the first trimester (n=202) did not have an increased risk of major congenital malformation (RR: 0.66; 95% CI, 0.25 to 1.75). Further, the 209 infants exposed to ACEIs were at increased risk for cardiovascular malformations (RR: 3.72; 95% CI, 1.89 to 7.3) and central nervous system malformations (RR: 4.39; 95% CI, 1.73 to 14.02).[2,3] Conversely, a 2011 population based, retrospective cohort study (465,754 mother-infant pairs) examined the association between the use of ACEIs during the first trimester and risk of malformations in offspring and concluded that neither use of ACEI or of other antihypertensive agents in the first trimester was associated with an increased congenital heart defects risk (odds ratios; 1.14 [0.65 to 1.98] and 1.12 [0.76 to 1.64], respectively).[4] Furthermore, an additional 2011 study of 91 pregnancies in women taking ACEIs or ARBs in early pregnancy found no convincing excess of congenital anomalies.[5]

Findings:
Although some differences exist among ACEIs relating to potency and clearance, they are generally interchangeable when appropriately dosed.[1,6-8] Consensus among hypertensive guidelines support the use of ACEIs as first-line treatments in hypertension but do not recognize clear advantages to any specific class agent.[7-10] Although results are conflicting regarding congenital malformations in infants of mothers taking ACEIs in early pregnancy (first trimester), providers should adhere to FDA recommendations and discontinue ACEIs in all pregnant patients as soon as possible. Women of childbearing potential taking ACEIs should be encouraged to use adequate contraception or have their ACEI replaced with an alternate antihypertensive agent.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

References:

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