Indian Health Service

IHS National Pharmacy and Therapeutics Committee
Vitamin D Analogs used in CKD October 2010

Background:[1-7]

In September 2010, the IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed the agents used in the treatment of chronic kidney disease (CKD). The NPTC felt it would be important to discuss the general findings from its review of the medications used in the treatment of CKD. CKD is a multi-factorial condition affecting approximately 26 million American adults. Common risk factors for developing CKD include diabetes and hypertension, which are commonly seen in the American Indian/Alaska Native (AI/AN) population as there is a 3.5 times higher risk of diabetes related kidney failure compared to the general population. In the southwest region, rates of CKD are 6.5 times greater in the AI/AN population as compared to the Caucasian population.

CKD is generally a progressive and irreversible condition that can eventually lead to "deterioration in mineral homeostasis, with a disruption of normal serum and tissue concentrations of phosphorus and calcium, and changes in circulating levels of hormones."[4] At CKD stage 3, the kidneys ability to excrete phosphorus becomes reduced, leading to hyperphosphatemia and elevated parathyroid hormone (PTH). Additionally, 1, 25hydroxyvitamin D (1, 25 $(OH)_2D$) is reduced, thereby reducing intestinal calcium absorption. Many patients with stage 4-5 CKD have high levels of phosphorus, which is linked to the development of CKD-Metabolic Bone Disease (MBD). This can include the development of secondary hyperparathyroidism (HPT) and reduced levels of serum calcitriol, which may necessitate supplementation with vitamin D or a vitamin D analog.

Available products within this class include: Ergocalciferol (D2), cholecalciferol (D3), calcitriol, doxercalciferol and paricalcitol.

Discussion:

Because of the effects of CKD-MBD described above, supplementation with vitamin D or one of its analogs may be considered. These products may reduce PTH levels, but increase calcium and phosphorus levels. Vitamin D analogs may have similar effect on PTH levels, with less effect on calcium and phosphorus. It remains important to monitor calcium levels while using vitamin D supplementation. If patients have persistent or recurrent hypercalcemia, vitamin D or vitamin D analogs should be discontinued. If serum PTH is rising and remains elevated "despite correction of modifiable factors," the KDIGO guidelines suggest (expert opinion) treatment with calcitriol or vitamin D analogs. These guidelines note a lack of randomized clinical trial data showing a correlation of patient level clinical outcomes (mortality, fracture, quality of life, hospital admission, cardiovascular) and improved PTH levels treated with vitamin D or vitamin D analogs.[4] A separate, independent meta-analysis of clinical data found no clear benefits of using vitamin D analogs over vitamin D agents.[8]

Findings:

The IHS National Core Formulary (NCF) has formulary status for "vitamin D, any product."[9] The NCF does not have a vitamin D analog on formulary. During the clinical review of agents used in CKD, the NPTC did not modify the NCF to include vitamin D analogs as there did not appear to be superiority over existing NCF products.

If you have any questions regarding this document, please contact the NPTC at nptc1@ihs.gov.

References:

1 The Facts About Chronic Kidney Disease. National Kidney Foundation Website. http://www.kidney.org/kidneydisease/ckd/index.cfm#facts. Accessed August 19, 2010. .

2 Bailie GR JC, Mason NA and St.Peter WL. Chronic Kidney Disease 2006: A Guide to Select NKF-KDOQI Guidelines and Recommendations. *National Kidney Foundation.* 2006.

3. Diabetes in American Indians and Alaska Natives: Facts At-a-Glance. Deptartment of Health and Human Services. Indian Health Services Division of Diabetes Treatment and Prevention. http://www.ihs.gov/MedicalPrograms/Diabetes/HomeDocs/Resources/FactSheets/AIANs08.pdf. Accessed August 19, 2010.

1 KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl.* Aug 2009(113):S1-130.

2 K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis.* Oct 2003;42(4 Suppl 3):S1-201.

6. Indian Health Service Division of Diabetes Treatment and Prevention. Indian Health Diabetes Best Practice Chronic Kidney Disease. http://www.ihs.gov/MedicalPrograms/Diabetes/HomeDocs/Tools/BestPractices/2009_BP_Chronic_Kidney_Disease.pdf Accessed August 19, 2010. 2009.

7. Narva AS, Sequist TD. Reducing health disparities in American Indians with chronic kidney disease. *Semin Nephrol.* Jan 2010;30(1):19-25.

8. Palmer SC, McGregor DO, Macaskill P, Craig JC, Elder GJ, Strippoli GF. Meta-analysis: vitamin D compounds in chronic kidney disease. *Ann Intern Med.* Dec 18 2007;147(12):840853.

9. IHS National Core Formulary:

http://www.ihs.gov/MedicalPrograms/NPTC/index.cfm?module=formulary&option=core; accessed December 3, 2010.