Indian Health Service

IHS National Pharmacy and Therapeutics Committee
Erythropoiesis Stimulating Agents November 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 CKD related medications. 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. In the southwest region, rates of CKD are 6.5 times greater in the AI/AN population as compared to the Caucasian population. Anemia is a common complication seen in patients with CKD.

Discussion:

Erythropoiesis Stimulating Agents (ESAs) have traditionally been used in patients with CKD related anemia. As the name implies, they stimulate the division and differentiation of progenitor cells to induce reticulocyte release from the bone marrow, thereby helping correct the anemia. Historically, they have also been used in the treatment of cancer related anemia. However, in February 2010, the FDA approved a risk evaluation and mitigation strategy (REMS) to ensure safe use of the erythropoiesis stimulating agent (ESA) class of medications. This was in response to data that showed increase risk of tumor growth and a decrease in survival for patients with cancer who used ESAs. Additionally, data show the ESAs can increase the risk of MI, HF, stroke or blood clots. These products now contain a black box warning discussing these risks. The goals for the ESA REMS are:[8]

- To support informed decisions between patients and their healthcare professionals who are considering treatment with an ESA by educating them on the risks of ESAs.
- To mitigate the risk of decreased survival and/or poorer tumor outcomes in patients with cancer by implementing the part of the REMS called the ESA APPRISE (Assisting Providers and Cancer Patients with Risk Information for the Safe use of ESAs) Oncology Program.

As part of the REMS, a medication guide should be dispensed <u>each time</u> an ESA is dispensed to a patient or their representative, <u>regardless of indication</u>. For healthcare providers who use ESAs to treat non-cancer related anemia, enrollment in the APPRISE program is not required. For facilities and providers using ESAs for cancer related anemia, the requirements include:[8]

- Healthcare providers who prescribe ESAs for patients with <u>cancer</u> must complete a training module over ESAs before being eligible for the APPRISE program (Note: “Healthcare providers not enrolled in the ESA APPRISE Oncology program will not be able to prescribe ESAs for use in patients with cancer.”)
- Healthcare providers must attest to their understanding of the risks of using ESAs in cancer patients.
- Hospitals must be enrolled in the ESA APPRISE Oncology program to dispense ESAs.
- Hospitals must have a system in place to ensure that providers who prescribe ESAs for cancer patients have enrolled in the APPRISE program and comply with the program.
- Failure to comply with the APPRISE program could lead to suspension of access to ESA agents.

In light of this information, it appears that the ESA place in therapy is more in question and clinicians should employ a benefit versus risk assessment before using ESAs for CKD related anemia.

Findings:

Because of the findings listed within the FDA data, as well as data from the relevant literature, the NPTC did not add ESAs to the IHS National Core Formulary. It was felt that the decision should be made at the local level on a case-by-case basis. Providers should carefully assess the potential benefit for use versus the potential risk and follow the FDA guidance for ESA use for this class. If ESAs are used for cancer related anemia, each facility

and provider should enroll and follow the guidance from the APPRISE program. If ESAs are dispensed to patients, a medication guide should be dispensed at each visit regardless of indication.

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.

4. 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.

5. 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. Information on Erythropoiesis-Stumulating Agents (ESA) Epoetin alfa (marketed as Procrit, Epogen) Darbepoetin alfa (marketed as Aranesp).

http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM109375; Accessed August 31, 2010.