Health Services
LOS ANGELES COUNTY

POLICIES AND PROCEDURES

SUBJECT: DHS ERYTHROPOIESIS-STIMULATING AGENTS (ESAs) USAGE POLICY

POLICY NO: 329.009

PURPOSE:

The purpose of this policy is to describe the requirements, which include treatment guidelines, to ensure the safe use of erythropoiesis-stimulating agents (ESAs) in chronic kidney disease (CKD) and cancer patients.

BACKGROUND:

ESAs, which are similar to the naturally occurring protein erythropoietin, stimulate red blood cell production. Due to the risks for serious adverse events, the Food and Drug Administration (FDA) states that healthcare professionals must weigh the benefits of ESA usage with the potential risks.

The FDA released several MedWatch alerts regarding the usage of ESAs in cancer and CKD patients. The boxed warnings and labels for ESAs have been revised to include new dosing recommendations and safety communications. Patients should receive individualized therapies which utilize the lowest therapeutic doses to reduce the need for transfusions.

This policy and procedure document will provide recommendations and guidelines to ensure the healthcare professionals in the Los Angeles County Department of Health Services (DHS) are adequately minimizing the risk to ESA-receiving patients.

POLICY:

A. Erythropoiesis-stimulating agents Use in Chronic Kidney Disease (CKD) Patients

1. ESA medication guides should be given to patients or to a representative of the patient.
2. The lowest therapeutic ESA dose sufficient to reduce the need for red blood cell transfusions should be used. It is inappropriate to target a hemoglobin level greater than 11 g/dL because there is an increased incident of serious cardiovascular events without additional therapeutic benefit.

3. When initiating or adjusting therapy, monitor hemoglobin levels weekly until stable; then monitor hemoglobin monthly. Pharmacy will not refill ESA prescription unless monthly hemoglobin levels are evaluated.
4. For patients with CKD **NOT on dialysis**:
   a. Consider initiating ESA treatment ONLY when the Hgb is less than10 g/dL
      AND
      i. The rate of hemoglobin decline indicates the likelihood of requiring a red blood cell transfusion
      AND
      ii. Minimizing the risk of alloimmunization and/or other red blood cell transfusion-related risks is a goal.
   b. If the hemoglobin level exceeds 10 g/dL, reduce or interrupt the dose of ESA and use the lowest dose of ESA sufficient to reduce the need for red blood cell transfusions.
5. For patients with CKD **on dialysis**:
   a. Initiate ESA treatment only if Hgb is less than10 g/dL.
   b. Once the hemoglobin level approaches or exceeds 11 g/dL, reduce or interrupt the dose of ESA.
6. Pharmacy will not refill prescriptions unless monthly hemoglobin values are evaluated.
7. For patients who do not respond adequately over a 12-week escalation period, increasing the ESA dose further is unlikely to improve response and may increase risks.

B. Erythropoiesis-stimulating Agents Use in Chemotherapy-Induced Anemia (CIA) Patients

FDA Mandated REMS (Risk Evaluation and Mitigation Strategies) Program - APPRISE

Amgen and Centocor Ortho Biotech Products has set up the APPRISE (Assisting Providers and Cancer Patients with Risk Information for the safe use of ESAs) Oncology Program, which is located online at esa-apprise.com, as a part of the REMS (Risk Evaluation and Mitigation Strategy) mandated by the FDA. All hospitals and healthcare providers who dispense ESAs to cancer patients must enroll in the APPRISE program. Patient registration is not required.

1. **Prescribing**
    a. Training and enrollment of healthcare providers and hospital designees, as well as documentation of the counseling and education of patients with cancer on the risks of ESAs prior to ESA administration, are key requirements of the ESA APPRISE Oncology Program.
    b. Healthcare providers are required to be enrolled in the ESA APPRISE Oncology Program for Los Angeles County Department of Health Services to prescribe for or dispense to an ESA for cancer patients.
    c. Failure to comply with the ESA APPRISE Oncology Program requirements will result in suspension of facility's/prescriber's access to ESAs.
    d. The preprinted "Adult Darbepoetin Physician's Order" must be used when prescribing darbepoetin (Aranesp®) for inpatients, if applicable.
    e. Prior to dispensing ESA to patients with cancer, all of the following key requirements of ESA APPRISE must be met:
        i. The Healthcare Provider (HCP) has completed the ESA APPRISE Oncology Program training, which includes a review of the risk of ESA therapy and appropriate use of ESAs in patients with cancer.
        ii. The HCP has enrolled in the ESA APPRISE Oncology program by completing the ESA APPRISE Oncology Program Enrollment Form for Healthcare Providers.
        iii. Prior to each new course of ESA therapy, the HCP has provided and reviewed the appropriate Medication Guide and counseled each patient on the risks and benefits of ESA. The HCP has also reviewed ESA risk:benefit information with his/her patient and answered any questions he/she may have.
        iv. The HCP has documented that the ESA risk:benefit discussion occurred using the ESA APPRISE Oncology Program Patient and Healthcare Professional (HCP) Acknowledgment Form. Ensured the HCP's ESA APPRISE enrollment ID number has been filled in, and both the HCP and the patient have signed the form.
        v. The HCP has provided the form to the Hospital Designee for the ESA APPRISE Oncology Program at our facility.
    f. If treatment has elapsed for more than 30 days, a new Acknowledgment Form is required.
    g. Pharmacy will not refill prescriptions unless monthly hemoglobin values are evaluated.

2. **Erythropoiesis-stimulating Agents Indication for Chemotherapy-Induced Anemia (CIA)**
   a. Treatment of anemia due to concomitant myelosuppresive chemotherapy, which have been shown to reduce RBC transfusions in patients with metastatic, non-myeloid malignancies.
      i. Discontinue ESA upon completion of chemotherapy course.
3. **Erythropoiesis-stimulating Agents Exclusion Criteria for Chemotherapy-Induced Anemia**
   a. The following patient population should NOT receive ESAs for chemotherapy induced anemia:
      i. ESAs are not indicated for use in patients receiving hormonal agents, therapeutic biologic products, or radiotherapy, unless receiving concomitant myelosuppressive chemotherapy.
      ii. ESAs are not indicated for patients receiving concomitant myelosuppressive therapy when the anticipated outcome is curative.
      iii. ESA therapy should not be initiated at hemoglobin levels greater than or equal to10 g/dL and dosing should be adjusted to maintain the lowest hemoglobin level sufficient to avoid RBC transfusion.

C. Recommended FDA Treatment Guidelines

Parameter	Chronic Kidney Disease	Chemotherapy-Induced Anemia
Indication	Hemoglobin less than10 g/dL	Anemia in patients with non-myeloid malignancies, where anemia is due to chemotherapy
Exclusion Criteria	• Uncontrolled hypertension • Hypersensitivity to active substance or the excipients	• Uncontrolled hypertension • Hypersensitivity to active substance or the excipients
Initial Dosing	***CKD dosing for darbepoetin:*** 0.45mcg/kg SubQ or IV every 4 weeks ***CKD on Dialysis dosing for darbepoetin :*** 0.45mcg/Kg SubQ or IV every week OR	***CIA dosing for darbepoetin:*** 2.25mcg/Kg SubQ every week **OR** 500mcg SubQ every 3 weeks **OR** 300mcg SubQ every 2 weeks

Parameter	Chronic Kidney Disease		Chemotherapy-Induced Anemia
	0.75mcg/Kg SubQ or IV every 2 week		
Monitoring Parameters	• Blood Pressure prior to each dose • CBC(Hg) every week until stable, then every month • Ferritin, transferrin at baseline • Renal function tests		• Blood Pressure prior to each dose • CBC(Hg) Every week until stable, then every month • Ferritin, transferrin at baseline
Upper Limit of Hemoglobin	***CKD***: 10g/dL	***CKD on Dialysis:*** 11g/dL	Lowest possible dose to prevent RBC transfusion
Comments	• For patients who do not respond adequately over a 12-week escalation period, increasing the ESA dose further is unlikely to improve response and may increase risks.		• Prescribers need to enroll in the APPRISE program

REFERENCES:

ESA APPRISE Oncology Program (https://www.esa-apprise.com)
FDA Drug Safety Communication (http://www.fda.gov/Drugs/DrugSafety/ucm259639.htm)
MICROMEDEX Healthcare Drug Resources
Aranesp ® Package Insert, Amgen. 2011.
Epogen ® Package Insert, Amgen. 2011.