

BCCA Protocol Summary Guidelines for Selecting and Monitoring Oncology Patients using Erythropoiesis-Stimulating Agents (ESAs) (Epoetin and Darbepoetin)

Protocol Code	SCESA
Tumour Group	Supportive Care
Physician Contact	Dr. Barb Melosky
Pharmacist Contact	Dr. Anne Dar Santos

Drug Acquisition:

- Erythropoiesis-stimulating agents are not BC Cancer Agency benefit drugs and are not covered by any BCCA program including Class I, Class II, Compassionate Access Program / Undesignated Indications Request or Emergency Aid Program.
- Patients being treated with these agents should have prescriptions filled at a community pharmacy and must arrange their own payment for the drug.
- Some financial assistance may be available through the Spectrum Support Program for Eprex[®] (epoetin) at 1-877-793-7739 or the Victory Program (darbepoetin) at 1-888-706-4717.
- Patients who are eligible for an ESA under renal/dialysis or other program should access financial assistance through those programs

Eligibility:

- Anemia secondary to concomitant, myelosuppressive chemotherapy.
 - a. Low baseline hemoglobin levels (lesser or equal to 100 g/L) at the start of cancer chemotherapy, OR
 - b. A decrease in baseline hemoglobin to lesser or equal to 100 g/L during chemotherapy.
- If appropriate, red blood cell transfusion is preferred to manage anemia in patients with a “reasonably long life expectancy”.
- Anemia must be related to the cancer treatment and not to blood loss, hemolysis, or iron, folate or B₁₂ deficiency, or to the malignancy itself.
- The benefits of treatment must be weighed against the possible risks for individual patients.

Exclusion:

Absolute

- Anemia secondary to malignancy in the absence of treatment with chemotherapy
- Patients for whom the anticipated outcome of chemotherapy is cure
- Patients who have previously developed pure red cell aplasia (PRCA) following treatment with an ESA

Relative

- Past history of thromboembolism, hypercoagulability, or heart disease
- Platelet count below $10 \times 10^9/L$ (physician discretion regarding potential hematoma formation)
- Severe liver disease
- Past history of seizures or convulsions
- Past history of porphyria
- Pregnancy, lactation or unreliable contraception
- Acute infection

Tests:

- Baseline: CBC, differential, reticulocyte count, serum iron, ferritin, transferrin saturation, blood pressure
- If clinically indicated: RBC folate and B₁₂ should be assessed, as a deficiency can blunt response to ESAs
- During treatment: weekly CBC, differential, blood pressure

Pre-Therapy Patient Selection:

- Patients must be iron replete at the start of therapy (ideally ferritin at least 100 ng/ml, and transferrin saturation at least 20%), otherwise treat with iron (ferrous sulfate 300 mg po TID or equivalent). Ongoing daily supplemental iron should be used (unless medically contraindicated) to maintain serum ferritin levels that support erythropoiesis.
- The decision to use ESAs should be based on discussions with the patient involving a benefit vs. risk assessment. This should take into account the specific clinical context, including the type of cancer and the disease stage, the degree of anemia, life expectancy, the environment in which the patient is being treated and known risks of transfusions and ESAs.

Treatment:

- Epoetin alfa 40,000 U once weekly or 150 U/kg three times/week
- Darbepoetin 2.25 µg/kg once weekly or 500 µg every three weeks

Monitoring and Dose Modifications:**Early Predictors of Response**

- Hemoglobin increase of greater than or equal to 10 g/L from baseline to week 4.
- Reticulocyte increase of greater than or equal to 40,000/µL from baseline to week 4.

Continuation of Therapy Beyond 4th Week

1. ESAs should be only be given while patients are receiving concomitant, myelosuppressive chemotherapy.

2. Target hemoglobin level recommended for patients with cancer treated with ESAs is 120 g/L.
3. If hemoglobin exceeds 120 g/L, the dose should be held:
 - a. Dose held until hemoglobin falls below 120 g/L
 - b. Reinitiated at 25% below previous dose (epoetin)
 - c. Reinitiated at 40% below previous dose (darbepoetin)
4. If hemoglobin increases by more than 10 g/L in a 2 week period, the dose should be reduced:
 - a. by 25% (epoetin)
 - b. by 40% (darbepoetin)
5. If hemoglobin does not rise by 10 g/L and reticulocytes do not increase $\geq 40,000/\mu\text{L}$ from baseline after 4 weeks, increase the ESA dosage:
 - a. Epoetin alfa may be increased to 60,000 U once weekly or 300 U/kg three times/week
 - b. Darbepoetin may be increased to 4.5 $\mu\text{g}/\text{kg}$ once weekly
6. If there is no further response to the increased dose in the next 4-week period, discontinue ESA therapy. In most circumstances, no therapeutic trial should go beyond 2 months.
7. ESAs should be discontinued after completion of chemotherapy.

Precautions:

- **Thromboembolism:** Treatment with ESA should be discontinued. The lowest dose of ESAs needed to avoid transfusion should be used to lower the risk of serious cardiovascular and thrombovascular events.
- **Hypertension:** If hypertension develops, the dose should be decreased or treatment discontinued. The hypertension should be managed in the interim.
- **Survival:** Treatment with ESA has not been shown to increase survival, and increasing hemoglobin beyond 120 g/L may adversely affect survival, tumour progression, or recurrence.

Call Dr. Barb Melosky or tumour group delegate @ (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment protocol.

Date activated: 1 Jun 2010

Dated revised:

References

1. EPREX Sterile Solution Monograph Janssen-Ortho Inc January 21, 2009
2. Abels R, Larholt K, Nelson R, Young D. Risk of transfusion in small cell lung cancer patients receiving chemotherapy. Blood 1994; 84(10) Suppl. 1:664a-664a. Abstract.
3. Bohlius J, Brillant C, Clark M, et al. Recombinant Human Erythropoiesis Stimulating Agents in Cancer Patients: Individual Patient Data Meta-Analysis on Behalf of the EPO IPD metaanalysis Collaborative Group. ASH 2008 abstract LBA-6
4. Henry D, Abels R, Larholt K. Prediction of response to recombinant human erythropoietin (r-huepo/epoetin-alpha) therapy in cancer patients (3). Blood 1995; 85:1676-1678.

5. Ludwig H, Fritz E, Leitgeb C, Pecherstorfer M, Samonigg H, Schuster J. Prediction of response to erythropoietin treatment in chronic anemia of cancer. *Blood* 1994; 84:1056-1063.
6. Glaspy J, Bukowski R, Steinberg D, Taylor C, Tchekmedyian S, Vadhan-Raj S. Impact of therapy with epoetin alfa on clinical outcomes in patients with nonmyeloid malignancies during cancer chemotherapy in community oncology practice. *J.Clin.Oncol.*1997; 15:1218-1234.
7. Gabrilove JL, Einhorn LH, Livingston RB, et al. Once-weekly dosing of epoetin alfa is similar to three-times-weekly dosing in increasing hemoglobin and quality of life. *Proceedings of ASCO*; Atlanta, GA 1999.
8. Couture F, Turner AR, Melosky B, Xiu L, Plante RK, Lau CY, Quirt I. Prior red blood cell transfusions in cancer patients increase the risk of subsequent transfusions with or without recombinant human erythropoietin management. *Oncologist*. 2005; 10(1):63-71.