Guidelines for the use of haemopoietic growth factors (Erythropoietin) in ADULTS

Erythropoietin (epoietin or EPO) in the management of cancer related anaemia

Chronic anaemia resulting from cancer, or its treatment, is an important clinical problem. Blood transfusions are the traditional and fastest method of alleviating symptoms however studies have shown that erythropoietin can increase haemoglobin (Hb) levels and reduce the need for transfusion. Erythropoietin is a haematological growth factor that regulates proliferation, maturation and differentiation of red blood cells.

Symptoms of anaemia can include fatigue, drowsiness, light-headedness, inability to concentrate, lassitude, dyspnoea and tachycardia.

NICE: Erythropoietin analogues with iron injections are recommended as a possible treatment for anaemia caused by cancer treatment only in:

- women receiving platinum-based chemotherapy for cancer of the ovaries who have a blood haemoglobin level of 8 g/100 ml or lower
- people who have very severe anaemia and cannot receive blood transfusions.

Definition of response rate:

Absolute increase in haemoglobin (Hb) ≥ 2g/dl and/or elimination of transfusion requirements

Predicting which patients will respond is not always possible, though patients with high erythropoietin levels (>100mIU/ml) prior to treatment are unlikely to benefit.

Patients showing a rise in Hb of > 0.5g/dl after 2 weeks usually respond well to long-term treatment. (After 4 weeks a rise in Hb of >1g/dl)

A smaller rise in Hb indicates a poorer long-term response and epoetin should be discontinued.

Patient selection

All patients with a solid tumour, malignant lymphoma, chronic lymphocytic leukaemia or myeloma (but NOT those with acute leukaemia or MDS) undergoing chemotherapy who meet the following criteria may be considered:

- Cannot be given RBC e.g. Jehovah’s witnesses, compatible blood unavailable.
- Are anaemic (Hb < 10g/dl) before starting chemotherapy or become anaemic during therapy with at least 3 cycles of chemotherapy remaining.

Contraindications: poorly controlled hypertension.

Cautions: epilepsy, thrombocytosis, and chronic liver failure.

Before starting

- The following tests may be done and the results obtained, before erythropoietin can be initiated by a Consultant.
- Ensure the patient has adequate iron stores, additional supplementation may be required.
- Check all other causes of anaemia have been excluded and correct any haemodynamic deficiency.
- Check folate and vitamin B12 levels, additional supplementation may be required.
- It must be made clear to the patient, at initiation, that therapy will be stopped after 4-8 weeks of treatment if there is no response (response being defined as a Hb increase > 1g/dl at 4-8 weeks).
Dosage and administration (according to local preferences)
Epoetin alfa (Eprex®) 150u/kg 3 x week (or 450u/kg 1 x week), increase to 300u/kg 3 x week SC.
Epoetin beta (NeoRecormon®) 450u/kg weekly in 3–7 divided doses increase, to 900u/kg 3–7 divided doses (in haematological malignancies the entire lower weekly dose may be given once weekly, the higher weekly dose in 2–7 divided doses) SC.
Darbepoietin (Aranesp®) 6.75mcg/kg every 3 weeks if ineffective stop (or 2.75mcg/kg once weekly increasing to 4.5mcg/kg once weekly) SC.

Assess at 4 weeks:
- If Hb increases > 1g/dl, continue at the same dose reviewing the patient monthly.
- If Hb decreases ≥1g/dl then further therapy may not be effective therapy and so stop erythropoietin.
- If Hb increase is not > 1g/dl, increase dose as above and review after 4 weeks. If after 4 weeks at increased dose the Hb increase is not > 1g/dl, then stop erythropoietin.
- If Hb increases >2g/dl in 4 weeks, reduce erythropoietin dose by 25-50%.
- If Hb >14g/dl, discontinue therapy until it falls below 12g/dl then re-start with a dose reduction of 50%

Failure to respond at 4 weeks should lead to a careful assessment of other causes of anaemia / poor response to erythropoietin – haematinic deficiency, GI blood loss, haemolysis, splenomegaly.

Monitoring - monthly
- Blood pressure
- Ferritin and/or % hypochromic RBCs, free erythrocyte protoporphyrin
- FBC, reticulocytes, blood film, platelets

Duration of treatment
- Initially prescribe for 4 weeks then review patient, if the patient has not responded increase dose as above for 4 weeks and review. If patient has not responded to 4 weeks of increased dose then stop.
- If patient has responded continue erythropoietin, monitoring and reviewing the patient monthly, until 3 weeks (solid tumours) or 4 weeks (haematological malignancies) after the last cycle of chemotherapy then stop erythropoietin.

Transfusion policy whilst on EPO
- RBC transfusion when Hb < 8g/dl or symptoms of anaemia
  - during the first 4 weeks, this does NOT constitute failure of erythropoietin therapy as it may take this time to start to see a response.