

## **Erythropoietin Stimulating Agents**

### **Indications for use: (4)**

- Hb <100 g/L
- No other identifiable causes

### **Target Hb: (5)**

- 100 to 120 g/L
  - Check monthly when in range

### **Dosage: (3)**

- Epoetin
  - Initial dose: 80 – 120 IU/kg/week in divided doses
  - Maximum dose: 900 IU/kg/week
- Darbepoetin alfa
  - Initial dose: 0.45ug/kg/week in a single dose

### **Route of administration: (3, 16)**

- Haemodialysis patients:
  - Given as either sub-cut or intravenous injection
- Predialysis and PD patients:
  - Given as a sub-cut injection, with rotation of site

### **Response to ESA therapy: (1, 2)**

- **Prior to commencing treatment:**
  - Check FBC
  - Iron studies
  - B12 and folate levels
  - Check CRP (indication of infection and/or inflammation)
- **Once treatment has been commenced: (1, 2)**
  - Monitor BP
  - Check Hb 2<sup>nd</sup> weekly until Hb within range
  - Monitor iron studies monthly until Hb has stabilized.

### **INADEQUATE RESPONSE TO EPO THERAPY:**

- In patients with inadequate response to EPO, possible causes should be investigated (12, 14)
- **Possible causes:**
  1. Absolute or Functional Iron Deficiency
  2. Insufficient levels of B12 and folate
  3. Infection/inflammation (i) p 368
    - a. Including access infection and auto-immune diseases

## St George Hospital Renal Department: INTERNAL ONLY

- b. Up to 53% of patients can have elevated levels of serum CRP
- 4. Chronic blood losses
  - a. Retention of blood in lines and dialyser
  - b. Blood sampling for laboratory testing
  - c. Accidental bleeding from access and surgical blood losses
  - d. Occult gastrointestinal bleeding
- 5. Inadequate dialysis
- 6. Malnutrition, low albumin and poor absorption of oral iron
- 7. Elevated PTH and hyperphosphatemia
  - a. Associated with bone marrow fibrosis
- 7. Aluminium toxicity
- 8. Haemoglobinopathies
- 9. Multiple myeloma or other malignancies
- 10. Hemolysis
- 11. Alcohol consumption

### COMPLICATIONS OF EPO THERAPY: (12, 16)

1. Worsening of hypertension:
  - 33% of patients will need to increase antihypertensive medication
  - Not found in anaemic patients without renal disease who are treated with EPO
  - Risk factors
    - pre-existing hypertension
    - rapid increase in haematocrit
  - Possible causes:
    - reversal of hypoxic vasodilatation as haematocrit rises
    - increased blood viscosity
    - increased cardiac output
2. Seizures:
  - Small risk associated with periods of rapidly rising haematocrit
3. Fistula/graft thrombosis:
  - No conclusive evidence
  - Risk associated with increased blood viscosity
4. Underdialysis and decreased Kt/V:
  - Associated with increased clotting of dialyser
  - Reduced proportion of plasma to red cell volume
5. Phosphorus balance:
  - Associated with an improvement in appetite and dietary intake in combination with reduced dialyser clearance
6. Flu-like symptoms immediately following injections
  - Can last up to a few hours to weeks after injection

**References:**

1. McMahon L. Haemoglobin. *Nephrology*. 2008; 13:s44-s47
2. CARI: Caring for Australasians with renal impairment: Guideline summary; 2009 [cited 2010 July 14]. Available from: [http://www.cari.org.au/DIALYSIS\\_bht\\_published/Iron.pdf](http://www.cari.org.au/DIALYSIS_bht_published/Iron.pdf)
3. MacDougall I, Eckardt K. Chapter 72: Anaemia in chronic kidney disease. In Feehally J, Floege J, Johnson R J. *Comprehensive clinical nephrology*. 3<sup>rd</sup> ed. Philadelphia: Mosby, 2007. p. 853-860
4. Singh A K, Hertello P. The benefits of IV iron therapy in treating anemia in patients with renal disease and co morbid cardiovascular disease. *Nephrol Nurs J*. 2005; 32(2):199-206
5. Goldsmith D, Covic A. Time to reconsider evidence for anaemia treatment (TREAT) = Essential safety arguments (ESA). *Nephrol Dial Transplant*. 2010; 25:1734-1737
6. FDA Information for Healthcare Professionals: Erythropoiesis Stimulating Agents (ESA): FDA ALERT [11/16/2006, Updated 2/16/2007 and 3/09/2007]. Available: <http://www.fda.gov.au>
7. Unger E F, Thompson A M, Blank M J, Temple R. Erythropoiesis-stimulating agents – Time for a reevaluation; 2010 [cited 2010 January 1]. Available from: [www.nejm.org](http://www.nejm.org)
8. Anker S D, Toto R. Future perspectives on treatment with erythropoiesis-stimulating agents in high-risk patients. *NDT Plus*. 2009; 2(Suppl 1):i3-i8
9. Eason A. Correcting iron-restricted erythropoiesis and improving anemia in patients on hemodialysis: practical tips that can make a difference. *Nephrol Nurs J*. 2009; 36(5):529-534
10. De Francisco A L M, Stenvinkel P, Vaulont S. Inflammation and its impact on anaemia in chronic kidney disease: from haemoglobin variability to hyporesponsiveness. *NDT Plus*. 2009; 2(Suppl 1):i18-i26
11. Burrows LaV, Muller R. Chronic kidney disease and cardiovascular disease: pathophysiologic links. *Nephrol Nurs J*. 2007; 34(1):55-63
12. Daugirdas J T, Blake P G, Ing T S. *Handbook of dialysis*. 3<sup>rd</sup> ed. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 159-162, 477-489
13. KDOQI (Kidney Disease Outcomes Quality Initiative). Clinical practice recommendation for anaemia in chronic kidney disease in adults. 2006 [cited 2009 September 15]. Available from: <file:///F:/Anaemia%20identifying%20patients.htm>
14. Enders H M. Evaluating iron status in hemodialysis patients. *Nephrol Nurs J*. 2002; 29(4):366–369

## St George Hospital Renal Department: INTERNAL ONLY

15. Strippoli G F M, Navaneethan S D, Craig J C, Palmer S C. Haemoglobin and haematocrit targets for the anaemia of chronic kidney disease. Cochrane database of systematic reviews. 2006, Issue 4 [cited 2010 May 5]. Available from: <http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles>
16. Hayat A, Haria D, Salifu M. Erythropoietin stimulating agents in the management of anemia of chronic kidney disease. Patient Prefer Adherence. 2008; 2:195-200
17. Locatelli F, Covic A, Eckardt E-U, Wiecek A, Vanholder R. Anaemia management in patients in chronic kidney disease: a position statement by the Anaemia Working Group of European Renal Best Practice (ERBP). Nephrol Dial Transplant. 2009; 24:348-354