

**SHARED CARE POLICY**

**FOR**

**ANAEMIA MANAGEMENT**

**IN RENAL PATIENTS**

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**On Behalf of**

**Cambridgeshire, Northamptonshire, Leicestershire and Lincolnshire  
Primary Care Trusts**

**University Hospitals of Leicester NHS Trust**

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## **Introduction and Purpose**

The nature and continuing care of patients with renal disease requires a collaborative approach between general practitioners and the Renal Unit. A system of shared care; encompassing primary and specialist care optimises care delivery and continuing management. This protocol outlines the principles of therapy with erythropoiesis stimulating drugs and gives guidelines for the continuing management of patients undergoing treatment.

## **Disease Background**

The kidney produces endogenous erythropoietin, a hormone that stimulates the production of red blood cells within the bone marrow in response to hypoxia. Renal disease can result in a deficiency of erythropoietin production and secretion (due to a decrease in functional renal tissue). A persistent uraemic state can also cause a shortened red cell lifespan. Many symptoms of chronic renal failure are produced or exacerbated by anaemia due to its multi-system impact. Patients may experience symptoms such as lethargy, reduced exercise tolerance, altered sleep patterns, reduced cognition and disturbed sexual function. Clinical studies have illustrated that renal patients with persistent chronic anaemia (Hb<10g/dl) develop irreversible left ventricular hypertrophy. Treatment with exogenous erythropoietin (epoetin or darbepoetin) can halt further development of left ventricular hypertrophy and correct anaemia with resolution of patient symptoms.

## **Drugs covered by the policy and its place in treatment**

Currently three erythropoiesis stimulating drugs are available:-

- Epoetin beta (Neorecormon®)
- Darbepoetin (Aranesp®)
- Epoetin alfa (Eprex®)

Epoetin beta (Neorecormon®) and darbepoetin (Aranesp®) can be administered subcutaneously and are included in this policy. Epoetin alfa is only licensed for intravenous administration in renal patients and is not included in this policy.

## **Hospital Clinician Responsibilities**

1. Identification of patients who need treatment.
2. Initiation of therapy and provide two months supply of drug
3. Request to GP to participate in shared care
4. Provide to GP appropriate information and protocols, in the form of a letter giving details of the drug and dose (Appendix 1), a copy of the shared care policy, and the standard monitoring policy (Appendix 2).
5. Provide written notification of changes to therapy
6. Monitor haemoglobin, ferritin, B12, folate, blood pressure, CRP
7. Arrange administration of intravenous iron if indicated by haematinics
8. Provide back up advice as required by the GP
9. Provision of patient/carer support will be through the renal home care team

**Contact details:**

Renal Home Care Team	0116 2584273
Dr K.Harris, Clinical Director	0116 2584195
Gill Hartley, Renal Pharmacist	0116 2588177

**GP Responsibilities**

1. Reply to request from hospital to participate in shared care
2. Continue prescribing of epoetin beta or darbepoetin
3. Make changes to prescription in line with any recommendations made by the hospital
4. By mutual agreement participate in monitoring of haematological indices in the maintenance phase to ensure haemoglobin remains within the range required. Monitoring will be performed in line with agreed protocols and the results discussed with the hospital as required (See Appendix 2). The GP will liaise with hospital staff with regard to any alterations that are made to prescriptions following the monitoring to ensure patient records are updated. If preferred by the GP monitoring of haematological indices during the maintenance phase can be undertaken by the hospital.
5. Reporting of any adverse events
6. Management of hypertension

**Prescribing Guidelines-**

**Licensed Indications:** Epoetin beta (Neorecormon®) is licensed for treatment of anaemia associated with chronic renal failure in dialysis patients and for symptomatic anaemia of renal origin in patients not yet on dialysis. Darbepoetin alfa (Aranesp®) is licensed for anaemia associated with chronic renal failure.

**Dose:** The starting dose is determined according to body weight and is also dependent upon whether the patient is dialysing.

Erythropoiesis stimulating drugs should be initiated when the Hb is less than 10g/dl. It is essential to ensure iron stores are adequate prior to initiation of therapy. The target haemoglobin is 10-12g/dl, however this is individualised for each patient according to the existence of other co-morbidities.

**Pre-dialysis patients:**

Weight <50kg:	Epoetin beta 2000international units weekly Darbepoetin alfa 10micrograms once weekly
Weight > 50kg	Epoetin beta 4000internatinal units weekly Darbepoetin alfa 20micrograms once weekly

**Patients established on dialysis**

Weight<50kg	Epoetin beta 4000 international units weekly Darbepoetin alfa 20micrograms once weekly
Weight >50kg	Epoetin beta 6000 international units weekly Darbepoetin 30micrograms once weekly.

The total weekly dose of epoetin beta can be given in divided doses if required.

Typical maintenance doses are of the order of:

Epoetin beta	4000-8000units weekly
Darbepoetin Alfa	20-40micrograms once weekly

In most cases patients will have been taught to self-administer doses sub-cutaneously. Administration by a District Nurse may be required in those patients who are unable to self inject for any reason.

### **Pharmacology**

Epoetin beta is recombinant human erythropoietin. Darbepoetin is a hyperglycosolated derivative of epoetin with a longer half-life.

### **Contraindications**

Epoetin and darbepoetin are contra-indicated in severe uncontrolled hypertension

### **Cautions for use**

Inadequately treated or poorly controlled hypertension (monitor blood pressure and haemoglobin)

Exclude other causes of anaemia; give iron supplements if necessary.

Ischaemic vascular disease, thrombocytosis (monitor platelet count for first eight weeks), epilepsy, malignant disease, chronic liver failure, avoid in cardiovascular disease including recent myocardial infarction and cerebrovascular accident, pregnancy and breastfeeding

### **Side effects**

The most important side effect is hypertension which occurs in about 35% of patients and is dose dependent. Hypertension should be treated with conventional therapies. Severe resistant and uncontrolled hypertension requires suspension of therapy until blood pressure is controlled. Hypertensive encephalopathy and seizures are rare but recognised complications of uncontrolled hypertension associated with the use of erythropoiesis stimulating drugs. Other side effects include influenza-like symptoms at the initiation of treatment, clotting of arteriovenous fistulae, hyperkalaemia and skin reactions. Pure red cell aplasia is a very rare side effect and results in a sudden loss of response. However this was principally associated with sub-cutaneous use of epoetin alfa (Eprex®) in chronic renal failure.

### **Monitoring**

#### **Prior to commencement of therapy**

Pre-existing uncontrolled hypertension must be treated. Maximising iron stores will optimise the response to erythropoiesis stimulating therapy. The current iron status of patients is established by measuring serum ferritin and transferrin saturation rate. If serum ferritin is less than 150micrograms per litre and the transferrin saturation rate is less than 20% a course of intravenous iron will be prescribed. Baseline measurements of haemoglobin, reticulocyte count, folate, vitamin B12 and CRP are established.

The dose is titrated at intervals of 3-4 weeks to achieve a maximum rise in haemoglobin of 1g/dl per month (correction phase). When the target haemoglobin is achieved (usually 10-12g/dl) the dose should be reduced by 50% and serum indices

monitored every 4-6 weeks with titrated dose adjustments to maintain within target limits. (maintenance phase)

### **Drug Interactions**

Erythropoiesis stimulating drugs may antagonise the effects of antihypertensive medication, including ACE inhibitors and angiotensin II antagonists with which there is also an increased risk of hyperkalaemia

### **Current NHS Cost**

Epoetin beta for 1 month 2000units twice weekly = £134.08

Darbepoetin alfa 20micrograms once weekly = £134.08

### **Further Information**

Poor or non-response should be investigated in conjunction with the Renal Unit. The cause is most commonly iron or other haematinic deficiency. Other causes of non-response are:

Faulty administration/compliance issues

Chronic infection/inflammation

GI blood loss (consider FOB, endoscopy)

Bone marrow failure (hypo-responsive bone marrow)

Malignancy

Excess aluminium or hyperparathyroidism