**NHS LINCOLNSHIRE in association with**
**UNITED LINCOLNSHIRE HOSPITALS TRUST**

# SHARED CARE GUIDELINE:
# Erythropoiesis Stimulating Agents in the treatment of Anaemia of Chronic Kidney Disease

**Epoetin Beta (NeoRecormon®), Darbepoetin alfa (Aranesp®), Epoetin Alfa (Eprex®)**

**This guideline only applies to the use of these drugs via subcutaneous injection. All intravenous use is the responsibility of the renal service.**

## General Principles

Shared Care Responsibilities:
In its guidelines on responsibility for prescribing (circular EL (91) 127) between hospitals and general practitioners, the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription. (*BNF* 56, September 2008, pg.4)

Aims:
(1) The aim of shared care guidelines is to provide information and/or guidance to GPs and hospital staff relating to the potentially complex implications of sharing patient care for a specific drug between primary and secondary/tertiary care.

(2) Specific shared care guidance should be available for any high cost drug, high-risk drug therapy or device that may be prescribed for a patient following specialist referral. Such guidance will only be produced where shared care is considered an appropriate option.

(3) Each guideline will include a clear statement of the responsibilities of both the GP and the specialist unit within the overall provision of the treatment to the patient.

(4) Shared care guidelines will ensure that the GP has sufficient information available to undertake to prescribe a specialist treatment if s/he so wishes. It is not the intention of these guidelines to insist that GPs prescribe such treatment and any doctor who does not wish to accept clinical or legal responsibility to prescribe such a drug is under no obligation to do so. Nonetheless the development of a shared care guideline will only be undertaken within the context of a broad acceptance between the Lincolnshire Prescribing and Clinical Effectiveness Forum (PACEF) and secondary/tertiary care that GP prescribing of such a treatment is appropriate within the constraints of formal shared care. Any drug approved for the development of a shared care guideline will automatically be classified as amber on the Lincolnshire Traffic Lights List and, if high-cost, will be supported financially through the High Cost Drugs Reserve. Thus there should be no financial reason why a GP should be deterred from prescribing a high cost drug under a shared care guideline.

## Further copies

Further copies of any guidelines in this series are available from NHS Lincolnshire Prescribing Advisers.

**Date of Issue: November 2008**
**Review Date: November 2010**

**Drug Details**

Approved Names: Epoetin alfa, Epoetin beta, Darbepoetin alfa
Brand Names: Eprex, NeoRecormon, Aranesp
Form: Prefilled syringes

In line with the MHRA recommendations for Erythropoiesis Stimulating Agents (ESAs) (December 2007), this SCA complies with the recommendations on target haemoglobins, and should only be used for the anaemia of renal disease. ESAs should only be used for patients with renal disease if symptoms of anaemia are present.

**Specialist Responsibilities**

The specialist secondary/tertiary care service will:

1. Send a letter to the GP suggesting that shared care is agreed for this patient. The first one to two months of the ESA will be supplied from secondary care.
2. Carry out baseline measurements of haemoglobin, serum ferritin, transferrin saturation rate, Full Blood Count, vitamin B12, folate and CRP, and before commencing therapy will communicate these to the GP.
3. Initiate treatment with the ESA and ensure patient is stabilised on treatment before transferring the prescribing responsibility to the GP.
4. Provide patient with information leaflet and patient held record card for blood pressure and date of next haemoglobin check.
5. Provide the patient with training in administration of the ESA, in conjunction with company training, or arrange administration in Primary Care.
6. Ensure that blood pressure is stable and well controlled, and any anti-hypertensive therapy is maximised before initiating the ESA.
7. Blood pressure should be checked at the practice. BP does need to be monitored on an ongoing basis (every 2 weeks initially, increasing to once weekly if concerns, and decreasing to monthly if stable and within target (<130/80 for all renal patients and lower in some). Each patient has an individualised care plan for BP on their BP cards.
8. Anti-hypertensive therapy should be adjusted by the GP to achieve target BP.
9. Provide the GP with clear instructions as to the initial dose of ESA including details of any dose titration that might be required and when the patient will next be reviewed in clinic.
10. Periodically (at one- to six-monthly intervals in clinic) review the patient's clinical condition.
11. Prescribe and arrange for administration of IV iron when necessary.
12. Communicate promptly any changes in biochemistry monitoring and modification of ESA dose to the GP.
13. Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.
14. Follow up any adverse drug reactions reported by the GP and report back to the GP.
15. Advise the GP in stopping treatment.

**GP Responsibilities**

The GP Will:

1. Notify the consultant in writing, within two weeks, if they agree to share care.
2. Prescribe the ESA in accordance to written instructions received from the specialist service.
3. Monitor the Hb monthly for the first 3 months then every 2-3 months depending on stability.
4. Haemoglobin levels should be monitored one month after each dose change.
5. Monitor ferritin every 3 months with transferrin saturations and alert the secondary care team of the Hb or ferritin fall outside the target limits (Hb 10.5 – 12g/dl; ferritin less than 200 micrograms/litre or transferrin saturation rate less than 20%).
6. Provide repeat prescriptions according to recommendations on dosage by the renal unit, Lincoln County Hospital.
7. Monitor the patients overall health and wellbeing.
8. Monitor the patient for adverse drug reactions and remain vigilant to the risk of potential drug interaction.
9. Carry out any investigations that are communicated and deemed appropriate.

**Referral Criteria**

1. Pre-existing uncontrolled hypertension must be treated.
2. The current iron status of patients is established by measuring serum ferritin and transferrin saturation rate. If serum ferritin is less than 200micrograms per litre and the transferrin saturation rate is less than 20% a course of intravenous iron will be prescribed.
3. Baseline measurements of haemoglobin , folate (range 2.3-17.6ng/ml), vitamin B12 ( range 179- 1162mg/l) and CRP( less than 8mg/l) are established

**Licensed Indications**

Epoetin alfa (Eprex®) Epoetin beta (NeoRecormon®), Darbepoetin alfa(Aranesp®) are all licensed for treatment of symptomatic anaemia associated with chronic renal failure in patients on dialysis and for symptomatic anaemia associated with chronic renal failure in patients not yet on dialysis.

**Recommended Dosage and Administration**

**Starting Dose:** The starting dose is determined according to body weight and is also dependent upon whether the patient is established on dialysis or pre-dialysis. Erythropoiesis stimulating drugs should be initiated when the haemoglobin has been lower than 11g/dl on at least two recordings more than two weeks apart. Other causes of anaemia should be excluded and iron stores should be adequate prior to initiation of therapy. The target haemoglobin is 10.5-12g/dl. However, this is individualised for each patient according to the existence of other co-morbidities.

**Pre-dialysis, peritoneal dialysis or home haemodialysis patients:**

Epoetin beta (NeoRecormon®), Epoetin alfa(Eprex®): 25-30units per kg twice per week by subcutaneous injection

Darbepoetin (Aranesp®): up to 0.45micrograms per kg once a week by subcutaneous injection

Dose is titrated at monthly intervals according to response

Although epoetin alfa and beta are clinically indistinguishable the prescriber must specify which is required.

**Background Pharmacology**

Human erythropoietin is an endogenous glycoprotein hormone that is the primary regulator of erythropoiesis through specific interaction with the erythropoietin receptor on the erythroid progenitor cells in the bone marrow. The production of erythropoietin primarily occurs in and is regulated by the kidney in response to changes in tissue oxygenation. Production of endogenous erythropoietin is impaired in patients with chronic renal failure and the primary cause of their anaemia is due to erythropoietin deficiency.

Darbepoetin alfa stimulates erythropoiesis by the same mechanism as the endogenous hormone. Darbepoetin alfa has five N-linked carbohydrate chains whereas the endogenous hormone and recombinant human erythropoietins (r-HuEPO) have three. The additional sugar residues are molecularly indistinct from those on the endogenous hormone. Due to its increased carbohydrate content darbepoetin alfa has a longer terminal half-life than r-HuEPO and consequently a greater *in vivo* activity. Despite these molecular changes, darbepoetin alfa retains a very narrow specificity for the erythropoietin receptor.

**Preparations Available**

**All preparations should be stored in a refrigerator at 2 – 8$^{o}$ C**

*Prefilled syringes containing 1000, 2000, 3000, 4000, 5000, 6000, 8000 and 10 000 units (Eprex and NeoRecormon)*

*Prefilled syringes containing 10, 15, 20, 30, 40, 50, 60, 80, 100, 130 and 150 micrograms darbepoetin (Aranesp)*

**Adverse 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.
Dose dependent increase in platelet count during initiation of treatment.
Other side effects include influenza-like symptoms at the initiation of treatment, clotting of arteriovenous fistulae, hyperkalaemia and skin reactions.
The CSM advise: There have been very rare reports of pure red cell aplasia in patients treated with epoetin alfa. If a diagnosis of pure red cell aplasia is made, treatment with epoetin alfa must be discontinued and testing for erythropoetin antibodies considered. Patients who develop pure red cell aplasia should not be switched to another form of erythropoetin.

**Drug Interactions**

ACE inhibitors and Angiotensin II receptor antagonists: antagonism of hypotensive effect and increased risk of hyperkalaemia

**Precautions and Contraindications**

Precautions

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.

Contraindications

Severe uncontrolled hypertension.
Pure red cell aplasia following erythropoietin.
Patients unable to receive thromboprophylaxis.
Darbepoetin is contraindicated in breastfeeding mothers.

**Monitoring**

**Prior to commencement of therapy.**
Pre-existing uncontrolled hypertension must be treated.
Blood Pressure should be checked at the practice. BP should be monitored on an ongoing basis (every 2 weeks initially, increasing to once weekly if concerns, and decreasing to monthly if stable and within target (<130/80 for all renal patients and lower in some.) Each patient has an individualised care plan for BP on their BP cards.

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.
Baseline measurements of haemoglobin, reticulocyte count, folate, vitamin B12 and CRP are established.

**After initiation of therapy**

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 (10.5-12g/dl) the dose should be reduced by 50% and haemoglobin monitored every 4-6 weeks with titrated dose adjustments to maintain within target limits. (maintenance phase)
Haemoglobin levels should be monitored one month after each dose change.

**Treatment should be reviewed and secondary care team alerted if haemoglobin falls outside target range of 10.5-12g/dl, urgent specialist advice should be sought if Hb > 13g/dl or <8.5g/dl**

**Indication of Likely Cost of Therapy in Primary Care**

NHS Cost of treatment (April 2008):

Epoetin Beta (NeoRecormon®): 2000units twice weekly for 4 weeks = £124.72

Epoetin Alfa (Eprex®): 2000units twice weekly for 4 weeks = £100.56

Darbepoetin alfa (Aranesp®): 20microgram once weekly for 4 weeks=£124.68

**Information Given to the Patient**

Patient information leaflet available with each container of ESA
Hand held blood pressure measurement card

## Contact Details

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## References


1. BNF Volume 56, September 2008 .
2. Leicestershire Medicines Strategy Group Shared Care Agreement April 2008
3. SPC Epoetin Beta (Neo-Recormon®), Darbepoetin alfa (Aranesp®) Epoetin Alfa (Eprex®)



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