DRUGS USED IN RENAL ANAEMIAS
EPOETIN BETA (NEORECORMON®)

This shared care guideline sets out details for the sharing of care of patients with **RENAL ANAEMIA** prescribed **EPOETIN BETA**. These guidelines provide additional limited information necessary to aid in the treatment of patients with **RENAL ANAEMIA**. As with all shared care guidelines they highlight significant prescribing issues but should be used in conjunction with the ABPI summary of product characteristics (SPC/Data sheet) and ***do not*** replace them.

ARCHIVED

INTRODUCTION/BACKGROUND INFORMATION

Anaemia is an almost invariable consequence of chronic renal failure (CRF). It causes many debilitating symptoms, e.g. tiredness, lethargy, muscle fatigue, poor exercise capacity. Anaemia is also a major factor contributing to the high prevalence of cardiovascular disease in renal patients, and the consequent increased morbidity and mortality.

The main cause of renal anaemia is loss of peritubular cells in the kidney responsible for synthesis and secretion of erythropoietin (EPO). Supplementation with recombinant human erythropoietin (rHuEPO) is currently the standard treatment for anaemia in CRF patients.

This Shared Care Guideline refers specifically to epoetin beta based on licensed indications.

INDICATIONS FOR THE PURPOSES OF THIS GUIDELINE

'Treatment of anaemia associated with chronic renal failure in adults and paediatric patients ≥ 11 years of age'. Therapy should be initiated by a physician experienced in this area.

DOSAGE AND ADMINISTRATION

Epoetin dosage schedules are split into a correction and a maintenance phase.

Correction phase: The initial dose of epoetin beta is 3 x 20 units per kg weekly administered by subcutaneous injection (SC) The dosage may be increased every 4 weeks by 3 x 20 IU/kg per week if the increase in haemoglobin (< 0.5 % per week).

By intravenous injection (IV) the initial dosage is 3 x 40 IU/kg per week. The dosage may be raised after 4 weeks to 80 IU/kg - three times per week - and by further increments of 20 IU/kg if needed, three times per week, at monthly intervals.

For both routes of administration, the maximum dose should not exceed 720 IU/kg per week.

Maintenance phase: To maintain a haemoglobin of 11-12 g/dl, the dosage is initially reduced to half of the previously administered amount. Subsequently, the dose is adjusted at intervals of one or two weeks individually for the patient (maintenance dose).

In the case of subcutaneous administration, the weekly dose can be given as one injection per week or in divided doses three to seven times per week. Patients who are stable on a once weekly dosing regimen may be switched to once every two weeks administration. In this case dose increases may be necessary.

Treatment with epoetin beta is normally a long-term therapy.
It can, however, be interrupted, if necessary, at any time.

If the rise in haemoglobin is greater than 2.5 g/dl in four weeks reduce the dose by between 25 and 50%, depending on the rate of increase. If the haemoglobin exceeds 13 g/dl, discontinue therapy until it falls below 12 g/dl and then restart the treatment at approximately 25% below the previous dose. The haemoglobin should be measured every one or two weeks until it is stable. Thereafter the haemoglobin can be measured periodically.

CONTRAINDICATIONS:

Patients who develop anti-erythropoietin antibodies and Pure Red Cell Aplasia (PRCA) following treatment with any erythropoietin should not receive any further epoetin or darbepoetin.

- Epoetin is contraindicated in patients with hypersensitivity to darbepoetin, epoetin, or any of the excipients. N.B. Contains phenylalanine, thus not suitable for patients with phenylketonuria.
- Poorly controlled hypertension
- Cardiovascular disease including recent myocardial infarction, cerebrovascular accident, unstable angina or history of thromboembolic disease.
- Epoetin beta should be used with caution in the presence of refractory anaemia with excess blasts in transformation, epilepsy, thrombocytosis, and chronic liver failure. Folic acid and vitamin B12 deficiencies should be ruled out as they reduce the effectiveness of epoetin.

PRECAUTIONS

- Epilepsy
- Chronic liver disease
- Sickle cell anaemia
- Patients with thrombocytosis
- Malignancy
- Pregnancy or breast feeding

SIDE EFFECTS

Very common > [1 in 10] > Common > [1 in 100] > Uncommon > [1 in 1000] > Rare > [1 in 10000] > Very rare

Very common/common:

- Hypertension, headache (stabbing migraine-like pain can be warning of hypertensive crisis).

Uncommon/rare/very rare:

- Hypertensive crisis, shunt thrombosis, thrombocytosis, rash, pruritus, urticaria, influenza-like symptoms, PRCA and anaphylaxis.

MONITORING

The following parameters should be monitored in patients receiving epoetin therapy.

Initial monitoring – undertaken in hospital.

In *chronic renal failure* patients there may be a moderate dose-dependent rise in the platelet count within the normal range during treatment with epoetin beta, especially after intravenous administration. This regresses during the course of continued therapy. It is recommended that the platelet count be monitored regularly during the first 8 weeks of therapy.

Monitoring	Guidance
Haemoglobin Every one or two weeks (until levels are stabilised).	During the correction phase. During the maintenance phase after any dose adjustment. If route of administration is changed. If darbepoetin is substituted for Epoetin.
Ferritin	Baseline level to be taken prior to treatment

Subsequent monitoring

Haemoglobin level and blood pressure should be monitored both in general practice and the hospital settings.

Monitoring	Guidance
Blood pressure monitor every 2 weeks. Aim to keep BP <140/80 with anti-hypertensive medication	If blood pressure is >180/100 omit epoetin and control BP. **Inform renal department.** Blood pressure medication should generally be: 1. ACE inhibitor or Angiotensin receptor blockers (ARB) - use in glomerular disease but not with renovascular disease. 2. Calcium Channel Blocker. 3. Beta blocker. 4. Diuretic. 5. Others.
Haemoglobin monitor monthly	Mark them "Copy results to Sue Hussain – Specialist Anaemia nurse RD&E".
If Haemoglobin (Hb) > 12 g/dL and platelets > 500,000.	Advice obtained from anaemia nurse on dose alterations. Normally: 'Suspend the epoetin dose until Hb drops below 12g/dL and then restart the darbepoetin with a dose 25% below the dose prior to stopping.'
If Hb <10 g/dL and falling or patient is symptomatic.	Advice obtained from anaemia nurse on dose alterations. Normally: 'Double the epoetin dose'. If failure to respond to an increased dose of epoetin then contact the renal department
Potassium. Monitor monthly	Maintain within normal levels. Patients with hyperkalaemia should be referred

Other monitoring will take place during patient visits to the renal clinic:

- Test Ferritin level every 2 or 3 months during treatment. Where possible the blood test for Ferritin should be taken by the GP practice **a week before** the patient's next visit to the hospital. This allows action on the results at the next appointment. Bloods sent should be marked for copying to the renal department.
- Monitoring of folic acid and vitamin B12 levels every 6 months in the renal clinic.

REFER TO THE SPECIALIST TEAM IF

- Hypertension (>180/100) Omit epoetin and inform renal department. **URGENT REFERRAL**.
- Haemoglobin outside of ranges recommended in monitoring or an increase of >2.5g/dL in a month.

COMMON/SIGNIFICANT DRUG INTERACTIONS

Data available so far do not indicate any significant interaction of epoetin or darbepoetin with other substances. There is some evidence to suggest that hyperkalaemia and antagonism of hypotensive effect of **ACE inhibitors and angiotensin receptor blockers (ARB)** may occur.

As ciclosporin and tacrolimus are bound to red blood cells there is a potential for a drug interaction. If epoetin and ciclosporin/tacrolimus are administered concurrently, monitoring of immunosuppressant level is advised, with dose adjustment as Hb rises.

NOTES

Supplementary iron therapy is recommended for all patients with serum ferritin values <150mcg/l or whose transferrin saturation is below 20%, to ensure effective erythropoiesis.

Non-response to treatment with epoetin should be investigated. Factors that may compromise an erythropoietic response include: deficiencies in folic acid, iron, or vitamin B12; intercurrent infections; occult blood loss; severe aluminium toxicity; haemolysis; underlying haematological disease; bone marrow fibrosis; and inflammatory or traumatic episodes.

- **NICE Clinical Guideline 39: Anaemia management in people with chronic kidney disease issued September 2006.**

  http://www.nice.org.uk/Guidance/CG39

PRODUCT INFORMATION

Store at +2°C to +8°C (in a refrigerator) in outer carton to protect from light.

Epoetin beta (NeoRecormon®) - Available in:

- Multidose vials. Doses 50000, 100000 unit vials cost £0.838 per 100 units).
- Vial for reconstitution (Reco-Pen®). Doses 10000, 20000, 60000 unit cartridge (cost £0.779 per 100 units).
- Pre-filled syringes. Doses 500,1000,2000, 3000, 4000, 5000, 6000, 10000, 20000, 30000 units (cost £0.779 per 100units).

ARCHIVED

REFERENCES:

- Summary of Product Characteristics: Neorecormon® Accessed January 2008.
- BNF 55 March 2008.
- NICE guidance CG039 accessed 15/11/2006 http://www.nice.org.uk/guidance/cg39
- European Best Practice Guidelines: http://ndt.oupjournals.org/content/vol14/suppl_5/
- accessed 09/01/04
- Renal Association guidelines: http://www.renal.org/Standards/RenalStandards_2002b.pdf accessed 09/01/04
- NSF for renal diseases. http://www.dh.gov.uk http://www.dh.gov.uk/en/Healthcare/NationalServiceFrameworks/Renal/RenalInformation/DH_4102636

AUTHORS:

- Dr R D'Souza – Consultant, renal medicine.
- Dr C Bingham – Consultant, renal medicine.
- Dr. H. Clarke – Consultant, renal medicine.
- Dr.M.Bello-Villalba – Consultant, renal medicine.
- Dr. L. Smyth – Consultant, renal medicine.
- Dr C Mulgrew – Consultant, renal medicine.
- Mr C Richman – Prescribing Support Pharmacist.
- North and East Devon Health Community Shared Care Guidelines Group.
- Alice Foster – HTA Support Pharmacist Devon PCT.

Date Endorsed by the Effective Practice Committee: March 2008
Review Date: March 2010

ARCHIVED

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

These are suggested ways in which the responsibilities for the management of patients with **RENAL ANAEMIA** who are prescribed **EPOETIN BETA** can be shared between the specialist and the general practitioner. GPs are **invited** to participate. If the GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist**. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical.**

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Specialist responsibilities:

- ❑ Initiation of **epoetin beta** and stabilisation of patient's condition for a minimum of 3 months.
- ❑ Provide the patient or patient's parents/guardians/carers with suitable written and verbal information about the drug prior to starting medication and discuss the benefits and side effects of treatment.
- ❑ Ensure that training in the administration of the drug is provided to the patient or patient's carer.
- ❑ Monitoring of haemoglobin, blood pressure, ferritin, potassium, folic acid, and vitamin B12 as described in the Shared Care Guideline.
- ❑ Prompt verbal communication followed up in writing to the GP of any changes in treatment, results of monitoring undertaken and assessment of adverse events.
- ❑ As appropriate, liaison with other members of the multidisciplinary team e.g. anaemia nurse, renal specialist nurse, renal pharmacist.
- ❑ Ask the GP whether they are willing to participate in shared care.
- ❑ Prescribing the drug until the patient's condition/dose is stabilised and the GP agrees to take over responsibility for prescribing.
- ❑ Specify review dates at clinically relevant time intervals for both the GP and the consultant.
- ❑ Advice to GPs on change in dose, monitoring requirements or when to stop treatment.
- ❑ Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this drug.
- ❑ Reporting adverse events to the CSM.

General Practitioner responsibilities:

- ❑ Reply to the request for shared care as soon as practical.
- ❑ Prescribing of **epoetin beta** after communication with specialists regarding the need for treatment and stabilisation of the condition.
- ❑ Arrange for monitoring of blood pressure and haemoglobin and (where possible) ferritin blood levels as outlined in the shared care guideline. **Ensure that blood monitoring forms include the note "Copy to Sue Hussain – Specialist Anaemia Nurse RD&E"**
- ❑ Responding to advice from secondary care on dose changes and frequency of monitoring.
- ❑ Prompt referral to a specialist if there is a change in the patient's status.
- ❑ Reporting to and seeking advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- ❑ Reporting adverse events to the specialist and CSM.
- ❑ Stopping treatment in the case of a severe adverse event or as per shared care guideline.

Patient responsibilities:

- ❑ Report any adverse effects to their GP and/or specialist regarding their treatment.
- ❑ Ensure that they have a clear understanding of their treatment
- ❑ Ensure they attend for monitoring requirements as per shared care guideline, including making appointment for monitoring of ferritin levels in general practice one week prior to attendance at renal clinic.
- ❑ Liaise with secondary care over dosage changes
- ❑ Aware that treatment will be affected if patient does not attend for monitoring.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No:	E-mail address
Dr R D'Souza	(01392) 402587	Richard.DSouza@rdeft.nhs.uk
Dr C Bingham	(01392) 406366	Coralie.Bingham@rdeft.nhs.uk
Dr. H. Clarke	(01392) 406367	Helen.Clarke@rdeft.nhs.uk
Dr.M.Bello-Villalba	(01392) 402191	Maria.Bello@rdeft.nhs.uk
Dr. L. Smyth	(01392)406366	Lucy.Smyth@rdeft.nhs.uk
Dr. C Mulgrew	(01392) 403535	Chris.Mulgrew@rdeft.nhs.uk
Sue Hussain	(01392) 402532	Suzan.Hussain@rdeft.nhs.uk

ARCHIVED

Shared Care Agreement Letter - Consultant Request

To: Dr.....

Practice Address: .....

.....

.....

Patient Name:	
Hospital number:	
Date of birth:	
Address:	

DIAGNOSED CONDITION: **.....**

I recommend treatment with the following drug: **.....**

I am requesting your agreement to sharing the care of this patient according to the Devon Primary Care Trust North and East Devon Health Community Shared Care Prescribing Guidelines for this drug.

Signed:	
Consultant name:	
Department:	
Contact telephone number:	
Date:	

GP RESPONSE

I agree/ do not agree* to share the care of this patient in accordance with the Shared Care Guideline.

Signed: ..... Date: .....

GP name: ..... *Delete as appropriate

ARCHIVED