

**Pharmacist led decision support protocol for the management of anaemia utilising erythrocyte stimulating agents in patients undergoing haemodialysis.**

**(Pharmacist Lead Anaemia Management), PLAM trial.**

WHO - U1111-1202-8264

ANZCTR - 373722

HREC Reference Number - HREC/17/QTHS/224

**Investigators/affiliations –**

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**Proposal summary** – This research project is a pre-post comparative cohort study of a pharmacist led decision support protocol in anaemia management vs. the current physician based treatment system. The cohort will include dialysis dependent stage 5 chronic kidney disease patients within 3 dialysis units of Fraser Coast renal service (FCRS), within Wide Bay Hospital and Health Service South (WBBHS South). The intervention group will be based in Hervey Bay Hospital (HBH), Maryborough Hospital (MBH) and the Fraser Coast home haemodialysis unit. The current patients being treated in the Fraser Coast renal service will act as their own control. Post hoc data will be collected for four previous months of standard physician based treatment. FCRS mostly use Darbepoetin alfa and Iron polymaltose as part of the current anaemia treatment plan. A t-test will be used to statistically compare the clinical parameters in the two arms of treatment. The main outcomes will be the impact of the pharmacist involvement in optimising anaemia management. This will be summarised by looking at the target haemoglobin and iron stores for the patients. Patients are best stabilised with a haemoglobin between 95-115mg/L (9.5-11.5g/DL). Ferritin targets should maintain between 200-500μg/L and transferrin saturation between 20-40%9,10,11,12,17. A t-test will examine the null hypothesis (H0) comparing the 2 treatment arms.

Primary outcome will investigate if a pharmacist led decision support protocol in anaemia management will adequately maintain the haemoglobin within the target range.

Secondary outcome will measure stability in Ferritin, TSAT%, the appropriate and safe use of iron and erythropoietin stimulating agents (ESA), and the efficiency of medication use.

**Background**

**The situation** - Of the 1.4 million hospitalisations in Australia in 2011-12, 86% of admissions were for regular dialysis treatment. This makes dialysis treatment the most common reason for hospitalisation in Australia. Over the course of a decade the hospitalisations for dialysis patients has almost doubled. Chronic Kidney Disease (CKD), admissions that excluded dialysis have risen from an age standardised rate of 125 to 156 per 100000 people from the period of 2000-01 to 2011-121,2.

The numbers of patients in the Wide Bay South with CKD and ESRF is growing at an extensive rate and is adding pressure into the current system. As of 30/06/2016 there were 103,291 people who live in the catchment zone of the local Nephrologist7. On a national average, 9.6% to 11% of the population will fit into the stage 3a,3b, 4 and 5 CKD6. The populous ages 65 years and above in Wide Bay South account for 24.5% of the population. This is above the national average. Subjects aged 65 years and over account for 15.7% of Australians population6. With these numbers in mind, it is safe to assume there are approximately 9900 to 11000 people within Wide Bay south who have stage 3a or above CKD. The current wait times as of August 2017, to see a Nephrologist in the clinics in WBHHS are within 30 days for a Category 1 (urgent), Category 2’s wait time are up to 90 days and Category 3 (non-urgent) wait times are up to 9 months.

Chronic kidney failure is a disease state of progressive nature. There are three main ways in which kidneys are damaged including pre-renal, post-renal and renal-chronic renal failure (CRF). The most common cause of irreversible damage to the kidney occur primarily due to renal CRF caused by diabetic nephropathy, hypertensive nephrosclerosis, vasculitis, interstitial nephritis and polycystic kidney disease3. Most of the Wide Bay south patients fall into this majority as there is a high population of elderly patients with age related progressive disease states. There are two patients who identify as either Aboriginal or Torres Strait Islander within WBHHS South dialysis units.

Prevalence of anaemia is a common and significant ailment associated with chronic kidney disease. A previous land mark study25 found that 68% of pre-dialysis patients in USA had a haematocrit of less than 30mg/dL. Another study26 completed in Korea found that 96% non-dialysis depended stage 5 CKD patients had or were treated for anaemia. In Fraser Coast renal service (FCRS), a snap shot study found to date nearly all patients current being dialysed are also currently being treated for or have been treated for anaemia in the past 4 months. Currently, 75% of all dialysis patients in Fraser Coast renal service are actively being treated for anaemia. Additionally, 7 more patients were treated in the past 4 months for anaemia, making to a grand total of 84% of all current patients have been treated for anaemia.

**Mechanism of Anaemia in renal disease**

The pathogenesis of anaemia in renal disease is very complicated and involves a multifactorial progression of renal disease. The discovery of anaemia in chronic kidney disease (CKD) was first identified in the 1830’s12. Today, we understand the decreasing production in normal human erythropoietin (EPO) occurs in conjunction with the declining renal mass27. The reduction in EPO may be the main etiologic factor, however, there have been many other contributing factors involved. Typically, renal based anaemia has been identified as a normocytic, normochromic, hypoperliferative red cell disease12. Many studies have shown a higher concentration of urea in the blood have a uremic-induced inhibitory effects on EPO12. Radioisotopes have also identified that red cells have a shorter life in renal disease28. Due to an increased loss of iron in dialysis patients, they tend to need iron supplementation. Normally there is a loss of about 1-2mg of iron a day in homeostasis. However, dialysis patients suffer increased bleeds due to platelet dysfunction, frequent phlebotomy and poor oral iron absorption. This leads to the typical iron loss of around 1000-3000mg per year29,30,31.

**Previous studies in this area**

A similar study to this one was conducted by Aspinall S, et al in 2012 in the USA9. Using non-dialysis dependant end stage CKD patients in 16 veteran affairs units across Illinois state, pharmacist prescribed ESA’s and iron, and monitored their outcomes. The primary outcomes measured were quality of ESA prescribing, which is defined as the proportion of haemoglobin values between their target of 10-12g/DL, (100-120mg/L)9. This target Hb has been re-evaluated since that time of the study and adjusted to the lower target range of 95-115mg/L13. The mean age and other biological brackets were simular compared to the cohort at WBHHS South. The study however had two major differences between WBHHS South and the cohort in Illinois. In Illinois most of the subjects were male, and there was a much larger cohort concentration of African American and Hispanic ethnicity9. In WBHHS South there is an even split of males and females, and there is no current African American and or Hispanic subjects in the cohort. The pharmacist managed anaemia clinics collected the data and used a t-test for the continuous variables. The results showed the pharmacist had more results within the target Hb range compared to the standard care (71.1% vs 56.9%) P<0.001.

**Evidence Gap’s**

Currently to my knowledge, there has been no studies conducted within Australia for the management of chronic anaemia in end stage renal disease by a pharmacist. There have been numerous studies conducted by pharmacist for pharmacist led warfarin clinics around the world32. Several studies have showed pharmacist from overseas can manage haemoglobin in CKD clinics4,9,10 as well as outreach haemodialysis clinics11. These studies and more have shown that a pharmacist is capable of managing chronic disease medications in various fields of medicine with confidence and safety in mind.

Currently, other renal units within Queensland and Australia have doctor managed iron and haemoglobin programs and or nurse led iron repletion protocols for anaemia management in closed dialysis units. There are simular protocols written in Canada by the Canadian kidney knowledge translation and generation network (CANN-NET) who published nurse or pharmacist led anaemia management protocols4.

**The problem -** One of the major complications for patients and time-consuming tasks for clinicians in ESKD is anaemia management. Constant prescriptions for intravenous iron preparation, ESA's and blood tests with endless results filling the computer screens lead to failures of treatment, over prescribing and patents just getting missed. Previously, the anaemia management plan has been a nurse driven protocol at the Hervey Bay hospital. This process was suspended unfortunately due to lack of nursing confidence and knowledge that had resulted in many adverse events. Currently at the Fraser Coast renal services, the anaemia management plan is led by the very busy nephrologist. This single nephrologist takes care of some 2000 patients on his books and finds himself without sufficient time within the workday.

**Aim**

The aim of this study is to evaluate the impact of a pharmacist led decision support protocol in anaemia management in a regional haemodialysis unit, using an anaemia management protocol, under the supervision of the consultant nephrologist.

* H0 = The implementation of a pharmacist led decision support protocol in anaemia management service will result in no change in optimising clinical parameters related to iron and Hb compared to the current treatment of a physician based anaemia treatment in dialysis dependent stage 5 kidney disease.
* H1 = The implementation of a pharmacist led decision support protocol in anaemia management will show change in optimising clinical parameters related to iron and Hb compared to the current treatment of a physician based anaemia treatment in dialysis dependent stage 5 kidney disease.

The primary outcome will investigate whether a pharmacist led decision support protocol in anaemia management will adequately maintain the haemoglobin within the target range. This will be summarised by looking at the target haemoglobin and iron stores for patients on dialysis. Patients are best stabilised with a haemoglobin between 95-115mg/L (9.5-11.5g/DL)13.

The secondary outcome will measure stability in Ferritin, TSAT%, the appropriate and safe use of iron and erythropoietin stimulating agents (ESA), and the efficiency of medication use. Ferritin targets should maintain between 200-500μg/L and transferrin saturation between 20-40%13,17. Dosing iron and or ESA’s safely and efficiently will help to reduce the potential of adverse effects. There is an increased risk of stroke and cardiovascular effects if ESA’s are dosed above the maximum target Hb range13,14,15. Also, if iron is underutilised, treatment failure of ESA’s will potentially lead to a loss in Hb secondary to renal disease. The secondary outcome will assess the potential for adverse effects of ESA’s. Mean values will be assessed comparing the two sites with the use of random effect Poisson models.

A t-test will examine the null hypothesis (H0) comparing the 2 treatment arms and statistically calculated using SPSS.

**Masters project proposal**

**Methods**

**Pharmacist led decision support protocol for the management of anaemia utilising erythrocyte stimulating agents in patients undergoing haemodialysis.**

Cohort

This research project is a pre-post study of a pharmacist led decision support protocol for the management of anaemia in patients undergoing haemodialysis. The anaemia management protocol will be tested against the current physician based standard care within the Fraser Coast renal service. The pharmacist led decision support protocol will be implemented and compared to post hoc data for patients being treated for dialysis in Fraser Coast renal service. Fraser Coast renal service included patients being treated in Hervey Bay hospital, Maryborough hospital as well as the home haemodialysis patients under the care of the Fraser coast renal service. The size of the cohort will be determined on the day the data collection begins. However, Hervey Bay dialysis unit will roughly have ~40 haemodialysis patients, Maryborough hospital will have roughly ~20 haemodialysis patients and the home haemodialysis patients of Fraser coast will make up roughly ~10 patients. It is likely the study will contain about 70 subjects. All current patients who meet the inclusion/exclusion criteria at the beginning of the study will be given a choice to participate in this study. Post hoc data collection and the intervention will commence once all potential participants have been recruited and consented.

Bias and control.

Considering I am the current renal pharmacist for the renal unit at Hervey Bay Hospital, there is potential for bias. However, I personally have not been involved with the current renal unit’s anaemia management. Currently at FCRS, the anaemia management for patients on dialysis is the standard treatment. Using patients as their own control will help to reduce bias as this study aims to test a change in standard practice to help optimise current therapy. There is currently no direct pharmacist relationship in the delivery of anaemia management in the FCRS. To reduce the risk of bias via the Hawthorne effect, there will be minimal day to day interactions directly between the pharmacist and the patients in relationship to anaemia control. The patients will be informed of the research being conducted in FCRS via the patient information and consent process, although the authors day to day interactions will mostly remain consistent.

A comparison will be studied between the pharmacist led decision support protocol in anaemia management vs. the current system. The current system will be based on post hoc data collection from FCRS over a four-month period of July, August, September and October of 2017 where there was minimal pharmacist intervention for anaemia management.

Data security and retention.

Data collection will be processed via the Queensland health servers locked under their own encryption service. All trial data will be stored in QLD health servers for the minimum of 15 years as per the QLD health’s guidelines for clinical trials. Temporary transfer of unidentified data will only occur with the use of a 128bit USB stick coded with encrypted lock of upper and lower-case password containing a minimum total of 8 characters. Data on this USB stick will be retained for a minimum of 12 months after the completion of the study as per QLD health’s guidelines of short term research projects for assessment purposes only.

Intervention Protocol

Blood from all patients under the study arm will be collected on the first Monday and Tuesday of each month. The bloods will be collected by the dialysis nurses as per their standard practice. The Pharmacist will review the bloods on the Wednesday in the first week of the month for all patients under the study arm. Recommendations will be made for iron and ESA dosing, so the junior doctors may prescribe on the NIMC charts and write PBS18 scripts. These changes will be in effect on the next calendar week. This intervention will be recorded with the *Haemoglobin Management in Patients with End Stage Kidney Disease Form,* and *Iron Management in Patients with End Stage Kidney Disease Form*. These intervention and data collection forms are a part of the guidelines titled, *Haemoglobin Management Protocol in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services* and *Iron Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services,* respectively. Please see appendix for these protocols and forms.

The second Tuesday of each month will be the Nephrologist review for all patients under his care. In this week's process, all recommendations will be checked under the nephrologist’s supervision. If the Nephrologist would like to make alterations to the pharmacist’s recommendations, these alterations will be documented in the terms of a win/loss format. Success of the recommendations will be established and reviewed monthly by the nephrologist to ensure the pharmacist interventions are in the best interest of the patients. The wins and losses will be recorded on the data collection forms of the respective patients and collected and collaborated in the discussion.

The third and fourth weeks of the month, no change will occur to the plan unless the individual patients become medically sick and need to be reviewed by the doctors. Blood forms will be collated by the pharmacist for all patients under the study arm and signed by the medical officer in the last week of the month. All prescriptions will be written and signed by the medical officer under the PBS18. All pathology forms will be signed by the medical officer under Medicare restrictions.

The management protocols will be pre-approved by the director of renal medicine. Further, intervention by the pharmacist will be limited to provision of advice to the medical and nursing staff. At no stage will the pharmacist directly prescribe ESA’s or other measures utilised in the management of anaemia.

The data will be collected once a month for 4 total months of the study period. Post hoc data will be collected for the months of July, August, September and October of 2017. The post hoc data will be collected in the first month of the trial period on the third and forth week of that month. Once the four months has completed, no more data will be collected from the subjects.

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| --- | --- | --- | --- | --- |
| **Monthly plan** | **First Week** | **Second Week** | **Three Week** | **Forth Week** |
| **Pathology collection, Pharmacist intervention** | 🗸 |  |  |  |
| **Nephrologist bloods reviews** |  | 🗸 |  |  |
| **No intervention** |  |  | 🗸 |  |
| **Pathology requests** |  |  |  | 🗸 |

**Selection criteria for subjects**

Inclusion Criteria

Subjects will need to fulfil the following selection criteria.

* Patients must be ≥18 years old
* Must be diagnosed with End Stage Chronic Kidney Disease (Stage 5) by a Nephrologist
	+ Study population – CKD dialysis dependent Stage 5 on haemodialysis or home haemodialysis
* Must be established on dialysis.

Exclusion Criteria

* Non-English-speaking personal and those who have been declared medically incompetent to make health care decisions.
* Pregnant or lactating woman.
* Patient who have a known allergy to any ESA’s or intravenous Iron preparations.
* The nephrologist does not feel that the patient is suitable for the program.
* The patient is currently on an ESA dose greater that the recommended maximum of 150mcg of darbepoetin per week or Mircera dose of 360mcg monthly.
* The patient is currently receiving treatment for malignancy with chemotherapy.

Precautions

* Patients who currently have an active infection, the protocol driven iron preparation administration will be postponed. The Nephrologist must first clear the patient for the continuation of treatment as per protocol with an intravenous iron.
* Patients who are currently in-patients being treated for a non-critical ailment may continue the protocol driven treatment if the nephrologist is happy.
* Patients who are admitted as an in-patient with a life-threatening ailment will be ceased from the protocol and must be deemed medically appropriate to restart the protocol driven treatment plan once again.
* Patients who have a history of stroke must first be approved by the nephrologist to start under this protocol, as the use of EPO does increase the risk of stroke if the haemoglobin raises above 130g/L for ESRD patients.

**Data analysis plan**

**Time frame** – Statistical analysis of the data can show if the intervention had a significant effect. The time frame for collection of data only needs 120 days (the life of a red blood cell RBC) to show stability in Haemoglobin. Previously, Madhan K, et al showed Hb stability after 4 months of treatment with epoetin beta in CKD patients in New Zealand17. Other studies have shown 4-6 months as sufficient time in showing Hb stability once treated with other ESA’s available on the market in end stage kidney disease9,10,11,12,16. Therefore the length of data collection and the intervention time frame will be 4 months.

The data tested will be the full blood count (FBC), and Iron studies as well as c-reactive protein (CRP). CRP is important for the iron tests, as acute inflammation will cause an acute reactive phase in the iron stores, and erythropoietin (EPO) hyperresponsiveness and as a result will distort the Hb and iron studies12. These bloods are part of standard treatment in dialysis and thus will not require additional funding or ethics approval for nonstandard therapy.

The number of patients that will be obtained for this trial will be determined via the use of power analysis. Sample size calculations to determine statistical significance will use a continuous variable tool to determine statistical superiority.



The P-value shall be set at 95% confidence interval with a 1-type 2 error β-value set at 80%. Using a power calculator, with a test sample of 55 subjects, confidence level set at 95%, proportion of 0.5 and an upper value of 0.55000/lower value set at 0.45000. The standard error is set at 0.02551 with a relative standard error of 5.10. The sample size required for statistical power was calculated at 48 subjects16.

Alternatively;

The calculations used n = f(α/2, β) × 2 × σ2 / (μ1 − μ2)

In a previous a study of CKD patients in New Zealand17, 79 patients were treated for renal disease anaemia with a starting Hb of 92.9 and a treatment outcome mean of 118.5 with a standard deviation of 11.7 using these numbers with an alpha of 5% and a power (1-beta) of 90%, sample size required was 10 using a power sample size calculator23,24. It is clear that the subjects needed for statistical power is about 10-48 subjects.

**Statistical analysis**

The comparative nature of the statistical analysis will use a t-test to compare the two arms of the study. The program SPSS will be used to evaluate and statistically analyse the data.

The quantified results will be subject to statistical mathematics with the use of mean, median and Mode. The data will be used to assess changes in haemoglobin, Ferritin and transferrin saturation. A dependent variable t-test will help to identify any statistically significant differences between the 2 arms of data.

Data collection will be collaborated with the use of two documents and laboratory data obtained from AusLab. The *Iron dose recommendation form* will collect the pharmacist intervention for iron dosing and the *EPO dose recommendation form* will collect pharmacist intervention for the use of erythropoietin’s. Those forms will also collect the current Hb, ferritin and TSAT% of the respective patients on that day. Data collection will be processed through a excel data spreadsheet.

Subjects

Fraser Coast renal service includes Hervey Bay Hospital, Maryborough Hospital and the Fraser Coast home haemodialysis unit. Fraser Coast home haemodialysis unit is based in HBH. Maryborough dialysis unit is a satellite dialysis unit of the Fraser coast renal services. All three units fall under the service of Wide Bay Hospital and Health Service South under the care of Dr Madhan, the nephrologist.

The current patient list at HBH includes 42 patients in patient haemodialysis unit and 10 home haemodialysis patients. MBH currently have 20 haemodialysis patients. The total potential sample size of 72 subjects will fit the 48 samples required for statistical power.

**Ethical Approvals**

The Townsville Human Research Ethics and Review (HREA) committee in the Townsville HHS will review this project. HREC Reference Number - HREC/17/QTHS/224. This trial is also being registered with the World Health Organisation under the registration code, WHO - U1111-1202-8264. The Australian New Zealand Clinical Trials Registry code for tracking this trial is ANZCTR - 373722.

Guidelines for Metro South Human Research Ethics Review and Research Governance Submission – is a document developed by Queensland health in order to aid in the submission or research proposals to the research governance office of the national health and medical research council. The form is designed to aid in the submission of ethical approval of medical interventions that are deemed as low-risk studies. The study proposal above requires the author to manage Haemoglobin and Iron levels in Dialysis patients. The primary measurement required blood tests for full blood counts and iron studies. These blood tests occur regardless of the author’s impact and will not include any additional expenses or trauma to the patients other than standard practice. The implementation of a pharmacist led anaemia managed protocol will occur at Fraser Coast renal service. The investigator will collect laboratory data from Hervey Bay Hosptial via the AusLab and prescribing of medications via the dispensing program iPharmacy for all sites involved. Both can be accessed from Hervey Bay over the intranet and will only be accessed with a Queensland Health computer. The Data will be stored on an SPSS spreadsheet for analysis. Retrospective data collection from FCRS will occur over a four-month period as to serve as the control as pre test data. The data collection will be for the months of July, August, September and October of 2017. Ethical approval for post hoc data collection will be obtained for this data collection as part of the HERC applications. As per the NHMRC guidelines, all data collected will be de-identified and given a unique study number that can only be traced through their original Unit Record Number (URN). This trace can only be accessed via the data spreadsheet that will be locked under 128bit encryption and stored in the Queensland health servers. The only people who have access to the identifying data will be the principal investigator, the Director of Renal Medicine and the Director of Pharmacy. Priority will be given to the dignity, rights, safety and well-being of participants at all times. All data collected will be confidential and in undertaking this research, the author will act in a manner so as not to endanger myself or others.

There are patients who identify as Aboriginal and or Torres Strait Islander within WBBHS. These patients are dialysed in the Maryborough unit. The investigator will complete all HREC approvals for the multicentre and Aboriginals and Torres strait Islanders in the Ethic approval process.

**Project planning**

**Budget**

There is no need for additional funding for the pathology tests or medications required to complete this study. This study extends standard protocol, without any extensions to significant change to practice or therapy. The laboratory tests required for this trial will include Full blood count, iron studies, C-reactive protein, Chem20 which includes urea and electrolytes. Included in standard therapy but not required for this trial, bloods to measure parathyroid hormone and only if required, vitamin D levels, B12 levels, Hep B, HIV, inflammatory markers and blood cultures.

All medications required are a part of standard therapy. Iron polymaltose will be the iron of choice as it’s familiar to the nurses, and a part of the standard protocol. Alterations to doses and or the iron preparations due to adverse reactions are stated in the iron protocol, please see attached *Iron Management in patients with end stage kidney disease (Adult) in haemodialysis patients -Fraser Coast renal services.* Erythropoietin stimulating agents used in this trial will be darbepoetin alfa or methoxy polyethylene glycol-epoetin beta. Aranesp™20, will be first line as this medication is also familiar to the nurses and the patients already. For alterations to darbepoetin due to adverse reactions or lack of response, patients will be switched to methoxy polyethylene glycol-epoetin beta under the brand name Mircera™21. For the protocol with detailed explanations of dosages changes to ESA’s, please see attached *Haemoglobin Management in patients with End Stage Kidney Disease (Adult) in Haemodialysis – Fraser Coast Renal Services* in the appendix*.*

All funding to these medications are available on the Pharmaceutical Benefits Scheme18 and Queensland Health List of approved medications. All funding for the laboratory work comes under standard Medicare funding pool8.

Time frame.

**Gantt chart**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Activity** | **Week -3** | **Week -2** | **Week -1** | **Week 1-10** | **Week 10-43** | **Week 44-55** | **Week 55** | **Week 56** |
| **Protocol development**  |   |   |   |   |   |   |   |   |
| **Identification of staff and their roles** |   |   |   |   |   |   |   |   |
| **Preparation of study documents (*e.g.,* protocols)** |   |   |   |   |   |   |   |   |
| **Ethics approval** |   |   |   |   |   |   |   |   |
| **Literature review** |   |   |   |   |   |   |   |   |
| **Data collection** |   |   |   |   | Ongoing for 4 months |   |   |   |
| **Data analysis** |   |   |   |   |   |   |   |   |
| **Study reports** |   |   |   |   |   |   |   |   |
| **Report reviews and revisions** |   |   |   |   |   |   |   |   |
| **Submission of reports for publication** |   |   |   |   |   |   |   |   |

**Support** – The nephrologist is very supportive of this proposal, the nursing staff are constantly requesting a better process, and the director of pharmacy has presented his support to this project and has allowed the author time allocation. The data for all sites can be accessed from Hervey Bay hospital. Therefore, there is no need for extra travel to any other site other than my primary location at work.

**Procedures to be performed or intervention to be implemented**

# Please see attached work unit guideline, Iron Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services

# Please see attached work unit guideline, Haemoglobin Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services

**Abbreviations**

|  |  |
| --- | --- |
| CKD | Chronic Kidney disease |
| ESRD | End stage renal disease |
| ESKD | End stage kidney disease |
| Stage 3a | GFR 59-45 |
| Stage 3b | GFR 44-30 |
| Stage 4 | GFR 29-15 |
| Stage 5 | GFR <15 or on dialysis |
| HBH | Hervey Bay Hospital |
| MBH | Maryborough Hospital |
| FCRS | Fraser Coast Renal Service |
| WBHHS | Wide Bay Hospital and Health Service |
| GFR | Glomerular filtration rate |
| eGFR | Estimated glomerular filtration rate |
| B12 | Vitamin B12 |
| HIV | Human immunodeficiency virus |
| RBC | Red Blood Cell |
| WBC | White Blood cell |
| FBC | Full Blood Count |
| IS | Iron studies |
| CRP | C-Reactive protein |
| EPO | Erythropoietin |
| ESA | Erythropoiesis stimulating agent |

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Daniel Bermingham,

B. pharm. Sci. M.Pharm (Griffith University) Grad Dip Clin Pharm (Queens University).

Senior Pharmacist (Renal) Hervey Bay Hospital.

Appendix.

* [ESA Dose recommendation form](#_Haemoglobin_Management_in)
* [Haemoglobin Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services](#_Haemoglobin_Management_Protocol)
* [Iron dose recommendation form Draft](#_Iron_Management_in)
* [Iron Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services](#_Iron_Management_in_1)
* [Patient Information and Consent Form](#_11.__Appendices)

 WBHHS-PRO-(CGU to assign)

**

## Haemoglobin Management in Patients with End Stage Kidney Disease Form

Patient label

Allergies or ADR’s noted

Iv Erythropoietin: Darbepoetin Alfa / Methoxy polyethylene glycol-epoetin beta

Prescribing guidelines for patients receiving ESA

Pharmacist recommendation:

Give:……………………………………………………Signature………………Date…

# Accompanying documents, Haemoglobin Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services

#

**Any decrease in Hb >15g/L or if Hb drops below 85, Contact the Nephrologist.**

Dose adjustments for darbepoetin alfa

|  |  |  |
| --- | --- | --- |
| **Current Dose** | **Increased dose** | **Decreased dose** |
| **10mcg every 2 weeks** | 10 mcg Weekly | Discontinue – Seek Nephrologist advise |
| **10mcg Weekly** | 20 mcg weekly | 10 mcg every 2 weeks |
| **20mcg Weekly** | 30 mcg Weekly | 10 mcg Weekly |
| **30mcg Weekly** | 40 mcg Weekly | 20 mcg Weekly |
| **40mcg Weekly** | 50 mcg Weekly | 30 mcg Weekly |
| **50mcg Weekly** | 60 mcg Weekly | 40 mcg Weekly |
| **60mcg Weekly** | 80 mcg Weekly | 50 mcg Weekly |
| **80mcg Weekly** | 100 mcg Weekly | 60 mcg Weekly |
| **100mcg Weekly** | 150 mcg Weekly | 80 mcg Weekly |
| **150mcg Weekly** | Seek Nephrologist advise | 100 mcg Weekly |

If Hb increase by <10g/L per month, increase by ~25%, rounded to the nearest convenient formulation.

If Hb target not reached the next month, increase by another 25%, rounded to the nearest convenient formulation.

Dose adjustments for Methoxy polyethylene glycol-epoetin beta

|  |  |  |
| --- | --- | --- |
| **Current Dose** | **Increased dose** | **Decreased dose** |
| **30mcg per Month** | 50mcg per month | Seek Nephrology advise |
| **50mcg per Month** | 75mcg per month | 30mcg per month |
| **75mcg per Month** | 100mcg per month | 50mcg per month |
| **100mcg per Month** | 120mcg per month | 75mcg per month |
| **120mcg per Month** | 150mcg per month | 100mcg per month |
| **150mcg per Month** | 200mcg per month | 120mcg per month |
| **200mcg per Month** | 360mcg per month | 150mcg per month |
| **360mcg per Month** | Seek Nephrology advice | 200mcg per month |

Decrease in dose, if Hb becomes increasing close to or over 120g/L by 25-40%.

If Hb continues to increase, Withhold the next dose and re-test FBC and Iron studies within the next month until Hb starts to decrease then reinitiate decreased dose.

Data collection Hb………….

TSAT%........

Ferritin……..

If Hb increase >10g/L in a 2 week period, decrease dose by 50-25%

 WBHHS-PRO-(CGU to assign)



# Haemoglobin Management Protocol in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services Purpose

**Custodian/Review Officer:**

Clinical Renal Pharmacist

Version no: 1.00

Applicable To: Renal Services Staff

Approval Date:

Effective Date:

Next Review Date:

**Authority:**

Approving Officer

………………………………………

Name:

Dr Krishan Madhan

Daniel Bermingham

Dr Leanne Brown

Supersedes: All other EPO management guidelines

Key Words:Haemoglobin management in end stage renal disease. Erythropoietin, Darbepoetin, Aranesp, Haemodialysis haemoglobin management, Peritoneal Dialysis Iron Management, CKD Iron Management.

Accreditation References:

EQuIP and other criteria and standards

This procedure outlines the safe and appropriate process of administering intravenous and subcutaneous injections of Erythropoietin stimulating agents (ESA), for patients with Chronic Kidney Disease Patient (CKD) in End Stage Renal Failure (ESRF) dialysis dependent (Stage 5 CKD) within the Fraser Coast (WBHHS).

This protocol is in combination with “Iron Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services”. The two specified protocols are a part of the PLAM trial.

## General information

For end stage dialysis dependant renal failure patients, it is recommended that haemoglobin should be kept relatively close between 95 to 115g/L (9.5-11.5g/DL). Erythropoietin’s can be used to treat renal disease related anaemia10.

Erythropoietin formulations used for this purpose

**Aranesp2® (Darbepoetin alfa),** dosages range from 10mcg to 150mcg in prefilled syringes. They can be administered by either subcutaneously of intravenously via the dialysis venous chamber. Alternatively, **Micera1® (methoxy polyethylene glycol-epoetin beta)**, dosages range from 30mcg to 360mcg prefilled syringes. This can also be administered via subcutaneous or intravenous injection.

## Procedure

Early intervention is necessary in avoiding renal disease associated anaemia. Routine iron studies and full blood count are performed for the assessment of Serum Ferritin and Transferritin Saturation levels as well as haemoglobin and red cell count. Markers for Serum Ferritin levels are 200-500 μg/L and Transferritin Saturation (TSAT) at 20 – 40%. Haemoglobin level should be kept steady between 95 – 115g/L as recommended by the KDIGO guidelines and the CARI guidelines5,6. For patients on the transplant waiting list, haemoglobin should be kept on the higher end of the target range. Haemoglobin trends are as important of the absolute level, and often more than one result is required5,6.

The dose of darbepoetin should not exceed 150mcg weekly unless stated by the nephrologist2.

The use of EPO should be avoided in patients who have a history of stroke or malignancy unless started by the nephrologist2,3,5,6.

Before commencing on an EPO, all patients first must have adequate stores of iron.

In the case of EPO hypo-responsiveness, the nephrologist must be informed after 3 consecutive failures to rise within the adequate haemoglobin target range5,6.

For dose modifications, the higher and lower doses must also follow with a statement for extra monitoring within the next rounds of bloods.

All patients must fall under the PBS restrictions for the use of Darbepoetin alfa under s100 HSD public2,3.

[www.PBS.gov.au](http://www.PBS.gov.au) (accessed online 11/07/2017)11

**Authority Required (Streamlined)**

6294 – Anaemia associated with intrinsic renal disease

**Clinical criteria**: Patients must require transfusion, AND Patients must have a haemoglobin level of less than 100g per L, AND Patients must have intrinsic renal disease as assessed by a nephrologist.

**Working protocol for EPO adjustments**



**Any decrease in Hb >15g/L or if Hb drops below 85, Contact the Nephrologist.**

Table 1

**Dose adjustment for Darbepoetin alfa (Aranesp™)2**

|  |  |  |
| --- | --- | --- |
| **Current Dose** | **Increased dose** | **Decreased dose** |
| **10mcg every 2 weeks** | 10 mcg Weekly | Discontinue – Seek Nephrologist advise |
| **10mcg Weekly** | 20 mcg weekly | 10 mcg every 2 weeks |
| **20mcg Weekly** | 30 mcg Weekly | 10 mcg Weekly |
| **30mcg Weekly** | 40 mcg Weekly | 20 mcg Weekly |
| **40mcg Weekly** | 50 mcg Weekly | 30 mcg Weekly |
| **50mcg Weekly** | 60 mcg Weekly | 40 mcg Weekly |
| **60mcg Weekly** | 80 mcg Weekly | 50 mcg Weekly |
| **80mcg Weekly** | 100 mcg Weekly | 60 mcg Weekly |
| **100mcg Weekly** | 150 mcg Weekly | 80 mcg Weekly |
| **150mcg Weekly** | Seek Nephrologist advise | 100 mcg Weekly |

Table 2

**Dose adjustment for methoxy polyethylene glycol-epoetin beta (Mircera™)1**

If Hb increase by <10g/L per month, increase by ~25%, rounded to the nearest convenient formulation.

If Hb target not reached the next month, Increase by another 25%, rounded to the nearest convenient formulation.

|  |  |  |
| --- | --- | --- |
| **Current Dose** | **Increased dose** | **Decreased dose** |
| **30mcg per Month** | 50mcg per month | Seek Nephrology advise |
| **50mcg per Month** | 75mcg per month | 30mcg per month |
| **75mcg per Month** | 100mcg per month | 50mcg per month |
| **100mcg per Month** | 120mcg per month | 75mcg per month |
| **120mcg per Month** | 150mcg per month | 100mcg per month |
| **150mcg per Month** | 200mcg per month | 120mcg per month |
| **200mcg per Month** | 360mcg per month | 150mcg per month |
| **360mcg per Month** | Seek Nephrology advice | 200mcg per month |

Decrease in dose, if Hb becomes increasing close to or over 120g/L by 25-50%.

If Hb continues to increase, Withhold the next dose and retest FBC and Iron studies within the next month until Hb starts to decrease then reinitiate decreased dose.

If Hb increase >10g/L in a 2 week period, decrease dose by 50-25%

**Iron repletion**

Iron replacement in haemodialysis patients, please refer to the sister procedure, *Iron Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services*. Haemodialysis patients receive routine intravenous iron of 100mg ONCE a week if medically indicated as per the table 1 below. The routine schedule is for patients who are prescribed an ESA. Iron prescriptions for patients who are not prescribed a regular ESA may be individualised by the treating doctor.

Table 3: Standard prescription of Iron

|  |  |
| --- | --- |
| If ferritin is <200μg/L or TSAT <20% | Start or recommence iron administration  |
| If ferritin is 200-500μg/L and TSAT is 20-40% | No change, continue current status. |
| If ferritin is >500μg/L or TSAT >40% | Stop iron administration |
| If there is conflict between TSAT % and ferritin levels, consult the CNC or Doctor. |

Iron studies are to be performed monthly. Iron studies cannot be performed more frequently as laboratories will not perform the test more often than monthly. Results are to be reviewed at the next dialysis session. Nurses are to review the result of their allocated patients and results are to be checked by another nurse. Dose adjustments are to be made in accordance with table 3 above.

Iron administration and dose adjustment is discussed in full in the procedure as stated above.

## Risk and Precautions

Very rarely anaphylaxis may occur with intravenous ESA. This generally happens within the first few doses of administration and is characterised by sudden onset of hypotension and or bronchospasm and or upper airway obstruction. Therefore, patients should be established on an EPO prior to being accepted under this procedure under the nephrologist and should be administered within the vicinity of a fully equipped emergency trolley, including Promethazine 25 mg and Hydrocortisone 100 mg (both in intravenous form). Please take note that there are different ESA preparation available and care is required in selecting the correct product for the correct patient.

## Administration

* Wash hands as per Qld Health policy.
* Establish the correct dose of ESA for the current patient and double check the correct dose is prescribed on the medication chart.
* The dose is to be injected intravenously in the last hour of dialysis into the venous port of the dialysis machine.
* Discard the used syringe into the appropriate syringe disposal bin as per QLD health policy.

Monitoring

* The patient should have baseline observations - temperature, heart rate and blood pressure as a minimum.
* Then measure and document the patient’s vital signs (temperature, heart rate and blood pressure) at the end of dialysis on the standard nursing observation chart.

Adverse Reactions1,2

* If there are any adverse reactions, **notify a medical officer immediately.**
* Immediate symptoms of an adverse event:
	+ Hypotension with circulatory collapse
	+ Bronchospasm with dyspnoea
	+ Tachycardia
	+ Facial flushing, faintness, joint and muscle pains
	+ Headache
	+ Nausea and vomiting
* Delayed symptoms of an adverse event:
	+ Flu like symptoms
	+ Chest pain
	+ Oedema, peripheral
	+ Chills and fever
	+ Urticaria and rash
	+ Access haemorrhage or thrombosis
	+ Access infection
	+ Hypertension
	+ Hypotension
	+ Diarrhoea, vomiting, nausea, abdominal pain, constipation
	+ Myalgia arthralgia, limb pain.
	+ Dyspnoea, cough, bronchitis
	+ CVA, TIA
	+ Convulsions
	+ Myocardial infarction

Discussion

Target Hb should be kept close to 95 to 115g/L5,6 in patients who are on end stage haemodialysis depended renal failure. This target is well established by the CREATE, CHOIR and the TREAT trials. All these trials have shown that higher target haemoglobins in ESRD have nil greater benefits and increased risk of harm5,6,7. Therefore, WBHHS have chosen a target Hb of 95-115g/L. The CARI guidelines support these target haemoglobins with a few inclusions5,6.

* Hb concentrations above 130g/L have been associated with increased mortality in CKD patients5,6.
* Patients who are as low risk of atherosclerosis or atheromatous CVD, target haemoglobins between 120-130g/L may be considered under the nephrologist advise5,6.
* Patients who have cardiovascular disease or whom are likely to develop cardiovascular disease should not exceed 120g/L Hb5,6.

Dose should not exceed 150mcg of Darbepoetin alfa per week or 360mcg of methoxy polyethylene glycol-epoetin beta per month1,2. If doses are required above this range, that patient should cease on the protocol and be referred to the nephrologist

Patients who have a history of malignancy and or stroke, ESA’s should be avoided. Erythropoietin is a growth hormone factor and therefore there is a theoretical concern that ESA’s could act as a growth factor for any type of malignancy1,2,4,5.

Initiation of erythropoietin must be referred to the nephrologist. All patients who required an ESA must first be diagnosed and treated by a nephrologist for renal disease based anaemia. Initial doses of erythropoiesis for patients in dialysis should be based on the patient’s dry weights. Darbepoetin alfa’s initial dose is recommended to start at 0.45mcg/kg/week. The starting dose for methoxy polyethylene glycol-epoetin beta is recommended at a dose of 0.6mcg/kg every two weeks and dose adjusted until stabilised or 1.2mcg/kg per month of body weight for patients on not dialysis12. Both darbepoetin alfa and methoxy polyethylene glycol-epoetin beta’s doses should be rounded to the closest whole syringe and initiated in accordance to the PBS restrictions.

## 4. Supporting documents

 Erythropoietin for Anaemia Management – Renal. (2017) Metro South Health

## 5.Definition of terms

|  |  |  |  |
| --- | --- | --- | --- |
| **Term** | **Definition** | **Source**  | **See also** |
| Iron Infusion | Generally have either 1 or both of the following:1. Hb ≤ 100
2. TSAT ≤ 20% Seri, Ferritin ≤ 200µg/L
 | Roger, S., 2005. Haematological Targets-Iron, CARI guidelines, Viewed 11th July 2013Http://www.cari.org.au/DIALYSIS bht published/Iron.pdf. |  |
| Vesicant | A drug capable of causing tissue necrosis when extravasated | Mosby’s medical, Nursing & Allied Health Dictionary (2006). 6th edition. |  |

## References and Suggested Reading

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2, MIMS Online (2017). Aranesp Injection. Retrieved 2th July 2017 from the Queensland Health Electronic Publishing service website <https://www.mimsonline.com.au/Search/AbbrPI.aspx?ModuleName=Product%20Info&searchKeyword=aranesp&PreviousPage=~/Search/QuickSearch.aspx&SearchType=&ID=59100001_2>

3, MIMS Online (2015) Venofer (Iron Sucrose) Product information Retrieved 5th May 2015 from the Queensland Health Electronic Publishing service website, <http://qheps.health.gld.gov.au/>

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6, Drüeke T, Locatelli F, Clyne N, Eckardt K, Macdougall I, Tsakiris D, Burger H, Scherhag A., (2006) Normalization of Hemoglobin Level in Patients with Chronic Kidney Disease and Anemia, *The New England Journal of Medicine* 355:2071-84

7, Singh A, Szczech L, Tang K, Barnhart H, Sapp S, Wolfson M, Reddan D, (2006) Correction of Anemia with Epoetin Alfa in Chronic Kidney Disease. *The New England Journal of Medicine*. 355:2085-98

8, Australian injectable drugs handbook (SHPA) 6th ed. (2015) <http://aidh.hcn.com.au/browse/about_aidh>

9, Erythropoietin for Anaemia Management – Renal. (2017) Metro South Health

10, Madhan K, Chamberlain M, Anderson E., (2017). Anaemia in patients with chronic kidney disease: Management with epoetin beta in primary care setting in New Zealand. *Asian Pacific society of Nephrology*. 13, 428-432

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12, Roger S, Locatelli F, Woitas R, Laville M, Tobe S, Provenzano R, Golper T, Ruangkanchanasetr P, Yung Lee H, Wu K, Nowicki M, Ladanyi A, Martı´nez-Castelao A, Beyer U, Dougherty F., (2011). C.E.R.A. once every 4 weeks corrects anaemia and maintains haemoglobin in patients with chronic kidney disease not on dialysis. Nephrology Dialysis Transplant. Vol 26 3980-3986

* **Consultation**

 Key stakeholders who reviewed this document are:

* Renal clinical Service team
* Nephrologist
* Renal Pharmacist
* Nurse Unit Manager
* Nurse Practitioner (Renal)
* Clinical Facilitator (Renal)
* Renal Anaemia Coordinator
* UQ research coordinators
* Director of Pharmacy WBHHS South

|  |  |
| --- | --- |
| **Version No.** | **Modified by** |
| Level of risk | Low |
| Audit strategy | RISKMAN reviews |
| Audit tool attached | No |
| Audit date | Annual |
| Audit responsibility | Renal Anaemia Coordinator |
| Key elements/ indicators / outcomes | 100% of chronic kidney disease patients ordered iron will have it administered as per this procedure, unless a specific medical order dictates otherwise. |

## 4. Supporting / Relating documents

* Queensland Health List of Approved Medications
* Pharmaceutical Benefits Scheme (PBS)

**Authorising Policy / Standard/s / Legislation:**

*

**Procedures, Guidelines and Protocols:**

*
*

**Forms and templates:**

*

## 5. Definition of Terms

|  |  |
| --- | --- |
| **Term** | **Definition / Explanation / Details** |
| ESA | [Erythropoietin Simulating agent](https://www.amh.net.au/online/view.php?page=chapter7/class2haemopoietics.html#haemopoietics) |
| CKD | Chronic Kidney Disease Patient  |
| ESRF | End Stage Renal Failure  |
| PD | Peritoneal Dialysis |

## 6. Procedure Development / Revision and Approval History

|  |  |  |  |
| --- | --- | --- | --- |
| **Version No.** | **Modified by** | **Amendments authorised by**  | **Approved by** |
| **1.0** |  |  |  |

## 7. Audit Strategy

|  |  |
| --- | --- |
| **Version No.** | **Modified by** |
| Level of risk | Low |
| Audit strategy | Compliance will be assessed through reported medication incidents involving ESA’s and RISKMAN reviews |
| Audit tool attached | No |
| Audit date | Annual |
| Audit responsibility | Renal Pharmacist |
| Key elements / indicators / outcomes | 100% of chronic kidney disease patients ordered ESA’s will have it administered as per this procedure, unless a specific medical order dictates otherwise. |

**8. Communication Plan of Procedure**

|  |  |  |  |
| --- | --- | --- | --- |
| **Audience** | **Facilities** | **Accountable Officer** | **Timeframe** |
|  |  |  |  |

## 9. Approval and Implementation

**Procedure Initiator/Review Officer:** << Daniel Bermingham, Renal Pharmacist>>

**Authority:** <<Dr Krishan Madhan>>

**Approving Officer:** <<Director of Renal Medicine >>

|  |  |
| --- | --- |
| **Date approved by Policy and Procedure Committee** |  |
| **Date published on WBHHS QHEPS page.** |  |
| **Next Review Date:** |  |

|  |  |
| --- | --- |
| **Version No.:** | <<1.0>> |
| **Keywords:** | Erythropoietin, Darbepoetin alfa, methoxy polyethylene glycol-epoetin beta Iron, Ferrosig, Iron Polymaltose, Iron Infusion, Iron carboxymaltose |
| **Accreditation References:** | EQuIP and other criteria and standards* <<insert EQuIP National Standards>>
 |

 WBHHS-PRO-(CGU to assign)

**

## Iron Management in Patients with End Stage Kidney Disease Form

Patient label

Allergies or ADR’s noted

Test dose: Date Reaction: Yes/No – Reaction:

Iv Iron given: Iron Polymaltose / Iron Sucrose / Ferric Carboxymaltose

Target range for adequate Iron stores (CARI guidelines)

Aim to maintain serum Ferritin 200-500µg/L and transferring Saturation (TSAT%) 20-40% for patients receiving ESA’s.

Prescribing guidelines for patients receiving ESA

|  |  |  |  |
| --- | --- | --- | --- |
| Serum Ferritin | TSAT% | Iron Dose | Frequency |
| <200µg/L | <40 | 100mg | Weekly, until next Fe level |
| ≥200-500µg/L | <20 | 100mg | Weekly, until next Fe level |
| ≥200-500µg/L | 20-40 | 100mg | Weekly, until next Fe level |
| >500µg/L | >40 | Cease Iron | Cease until next Fe level |

Pharmacist recommendation:

Give:……………………………………………………Signature………………Date…

# Accompanying documents, Iron Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services

Data collection Hb………….

TSAT%........

Ferritin……..

 WBHHS-PRO-(CGU to assign)



# Iron Management in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services

# Purpose

**Custodian/Review Officer:** insert position

Version no: 1.02

Applicable To Renal Services Staff

Approval Date:

Effective Date:

Next Review Date:

**Authority:**

Approving Officer

………………………………………

Name:

Dr Krishan Madhan

Daniel Bermingham

Dr Leanne Brown

Supersedes: All other iron management guidelines

Key Words:Iron management in end stage renal disease. Iron polymaltose, Iron Sucrose, Ferric Carboxymaltose, Hemodialysis iron management, Peritoneal Dialysis Iron Management, CKD Iron Management.

Accreditation References:

EQuIP and other criteria and standards

This procedure outlines the safe and appropriate process of administering intravenous iron infusions for patients with Chronic Kidney Disease Patient (CKD) in End Stage Renal Failure (ESRF) dialysis dependent (Stage 5 CKD) within the Fraser Coast (WBHHS).

This protocol is in combination with “Haemoglobin Management Protocol in Patients with End Stage Kidney Disease (Adult) in Haemodialysis - Fraser Coast Renal Services”. The two specified protocols are a part of the PLAM trial.

## Scope

This Guideline provides information for all Queensland Health employees (permanent, temporary and casual) and all organisations and individuals acting as its agents (including Visiting Medical Officers and other partners, contractors, consultants and volunteers) in the Fraser Coast renal services.

## General information

TSAT and ferritin are generally good indication of iron stores and availability. Ferritin levels can be an effective marker for systemic inflammation (ie. Infection, malignancies and autoimmune diseases), and therefore must be interpreted with caution. In these cases ferritin maybe falsely elevated.

Iron formulations used for this purpose

**Ferrosig®** arrives in a 2mL ampoule containing 318 mg of iron polymaltose equivalent to 100 mg elemental iron (III). Ferrosig® (Iron polymaltose) is the intravenous iron formula of choice for routine iron infusions with Haemodialysis (100mg injections)<https://www.mimsonline.com.au/Search/AbbrPI.aspx?ModuleName=Product%20Info&searchKeyword=ferrosig&PreviousPage=~/Search/QuickSearch.aspx&SearchType=&ID=65580001_2>

If the patient is unable to receive Ferinject® or Ferrosig® due to a previous reaction, then **Venofer®** (iron sucrose) is the alternative choice for intravenous iron infusion. Venofer® comes in a 5 mL ampoule and contains 2.7g of iron sucrose corresponding to 100 mg elemental iron (III). For bolus infusion of Venofer® refer to product information, for routine iron infusions with Haemodialysis (100mg infusions), see administration procedure below. <https://www.mimsonline.com.au/Search/AbbrPI.aspx?ModuleName=Product%20Info&searchKeyword=iron+sucrose&PreviousPage=~/Search/QuickSearch.aspx&SearchType=&ID=71360001_2>

**Ferinject®** (Ferric Carboxymaltose) is the intravenous iron formulation for bolus 500mg to 1g infusions. Ferinject® arrives as either: 100mg/2ml, or 500mg/10ml, both contained in a glass vial. Ferric Carboxymaltose is not routinely used in Haemodialysis patients. <https://www.mimsonline.com.au/Search/AbbrPI.aspx?ModuleName=Product%20Info&searchKeyword=Ferric+carboxymaltose&PreviousPage=~/Search/QuickSearch.aspx&SearchType=&ID=91220001_2>

## Procedure

Early intervention is necessary in avoiding iron deficiency anaemia for the patient with CKD and ESRF. Routine iron studies are performed for the assessment of Serum Ferritin and Transferritin Saturation levels. Markers for Serum Ferritin levels are 200-500 μg/L and Transferritin Saturation (TSAT) at 20 – 40%.

Haemodialysis patients receive routine intravenous iron of 100mg ONCE a week if medically indicated as per the table 1 below. The routine schedule is for patients who are prescribed an ESA. Iron prescriptions for patients who are not prescribed a regular ESA may be individualised by the treating doctor.

Table 1: Standard prescription of Iron

|  |  |
| --- | --- |
| If ferritin is <200μg/L or TSAT <20% | Start or recommence iron administration  |
| If ferritin is 200-500μg/L and TSAT is 20-40% | No change, continue current status. |
| If ferritin is >500μg/L or TSAT >40% | Stop iron administration |
| If there is conflict between TSAT % and ferritin levels, consult the CNC or Doctor. |

Iron studies are to be performed monthly. Iron studies cannot be performed more frequently as laboratories will not perform the test more often than monthly. Results are to be reviewed at the next dialysis session. Nurses are to review the result of their allocated patients and results are to be checked by another nurse. Dose adjustments are to be made in accordance with table 1 above.

## Risk and Precautions

Very rarely anaphylaxis or anaphylactoid reaction may occur with intravenous iron infusions and administrations. This generally happens with the first several minutes of administration and is characterised by sudden onset of hypotension and or bronchospasm and or upper airway obstruction. This is the rational for the slow infusion guide. Iron infusions should be administered within the vicinity of a fully equipped emergency trolley, including Promethazine 25 mg and Hydrocortisone 100 mg (both in intravenous form) Pre-medication or the presence of a medical officer (even with first dose of IV Iron, including satellite units) is not routinely required (Newnham 2006 et al). Please take note that there are different iron preparation available and care is required in selecting the correct product for the correct patient. The three intravenous iron preparations available are listed above in iron formulations.

## Iron Management in Haemodialysis

Iron polymaltose preparation is routinely used for the treatment and maintenance of iron management in haemodialysis patients.

## Test Dose

* Medical officer must be notified and be available on call in the hospital for the duration of the infusion
* Emergency trolley and emergency drugs for the treatment of anaphylactic reaction must be readily available throughout the procedure.
* Dilute 100mg of Iron Polymaltose in 100ml of normal saline 0.9% and complete and attach additive label
* Administer via infusion pump and venous bubble trap at 25mg over 20 minutes in the last hour of dialysis.
* If no reaction occurs, infuse the remaining 75mg over the remaining 40 minutes.
* Monitor and document vital signs every 5 minutes for 15 minutes then every 15 minutes until infusion is completed.

## Subsequent Iron Infusion

* Check if there was any sensitivity during the test dose. If a dose of iron has not been given in 6 months or over, perform another test dose. (Refer to test dose above).
* Using a 20ml syringe, draw up 100mg of intravenous iron and make up to 4.9ml with 0.9% normal saline
* Complete and attach additive label
* Administer via heparin pump over the last hour of dialysis. Set pump at a rate of 4.9ml/hour
* Observe patient for signs of adverse reactions during the administration of intravenous iron.
* Bolus heparin not required at the time of the syringe change as some heparin will be present in the line. Observe extracorporeal circuit for evidence of clotting and record as appropriate.
* If the patient has chronically low haemoglobin, TSAT% and ferritin level for >3 months and other causes iron deficiency anaemia have been excluded, give the patient a bolus 500mg of iron polymaltose in 100ml to 250ml of normal saline depending on the patient’s current fluid status. The 500mg of iron in normal saline bolus should be administered over 1 hour in the last hour of dialysis. Observations every 5 minutes for the first 15 minutes should be checked, followed by every 30 minutes thereafter if no reaction occurs. The extra 100ml to 250ml of fluid can be removed from the patient via dialysis.

## Iron infusion with CAPD

* Check if any sensitivity during the test dose
* Using a 20ml syringe, draw up 100mg of intravenous iron and make up to 4.9ml with 0.9% normal saline
* Complete and attach additive label
* Administer via heparin pump over the last hour of dialysis. Set pump at a rate of 4.9ml/hour
* Observe patient for signs of adverse reactions during the administration of intravenous iron.
* Bolus heparin not required at the time of the syringe change as some heparin will be present in the line. Observe extracorporeal circuit for evidence of clotting and record as appropriate.

## Administration

* Wash hands as per Qld Health policy and using aseptic technique draw up the prescribed dose and add to the required dose of sodium chloride 0.9% if required.
* 100mg of Iron polymaltose is to be injected intravenously in the last hour of dialysis as stated above in the subsequent iron infusion.
* If doses above 100mg are required, the dose should be mixed into an appropriate dilution of sodium chloride 0.9%. If the patient is receiving 1500mg of iron polymaltose or less then it can be put in a 250mL of normal saline 0.9%.
* If the Haemodialysis patient has had no reaction in the past to the iron polymaltose, doses above 100mg can be infused intravenously at the fast rate.
* Dilute the calculated dose (up to 1500mg) in 250 mL of sodium chloride 0.9%. Infuse at a rate of 250 mL/hour. If an infusion-related reaction occurs, temporarily stop the infusion and restart at a reduced rate of 60 mL/hour.

Monitoring

* The patient should have baseline observations- temperature, heart rate and blood pressure as a minimum
* Then measure and document the patient’s vital signs (temperature, heart rate and blood pressure) every 15 minutes for the first 50mL of infusion, or the first 50mg of iron polymaltose.
* Also check vitals 15 minutes after the infusion rate has been increased as some patients react to the rapid escalation of infusion rate.

Adverse Reactions

* If there are any adverse reactions, **stop infusion immediately and notify a medical officer**
* Immediate symptoms of an adverse event:
	+ Hypotension with circulatory collapse
	+ Bronchospasm with dyspnoea
	+ Tachycardia
	+ Facial flushing, faintness, joint and muscle pains
	+ Headache
	+ Nausea and vomiting
* Delayed symptoms of an adverse event:
	+ Dizziness/ syncope
	+ Chest and/or back pain
	+ Stiffness in limbs and face
	+ Chills and fever
	+ Urticaria and rash
	+ Generalised lymphadenopathy
	+ Angioneurotic oedema

## Iron Management in Home Dialysis

Please refer to the guidelines for haemodialysis. Patients can be trained for self administered doses once the initial test dose in hospital has been preformed.

## Iron Management in Peritoneal Dialysis

Generally, all patients on EPO receive oral iron as tolerated such as Ferro-Gradumet 325mg 1-2 tablets daily. If response to EPO is suboptimal and Ferritin <200 or TSAT <20%, IV iron may be given after discussion with the nephrologists. Schedule for IV iron for Ferric Carboxymaltose 500mg. For work instruction for ferric carboxymaltose, please refer to iron management in CKD below.

Intravenous iron may be necessary when response to erythrocyte stimulating agents (ESA) like EPO is inadequate and iron indices show reduced iron stores. IV iron may be used for the management of anemia in absents of ESA therapy.

## Intravenous Iron Supplementation using Ferinject® (Iron Carboxymaltose) for the Chronic Kidney Disease (CKD) / Renal Patient

# Wide Bay Hospitals and Health Service – Fraser Coast Renal Services

## 1. Purpose

This workplace instruction outlines the safe and appropriate process for administration of intravenous iron infusions using Ferinject® (Iron Carboxymaltose) for the Chronic Kidney Disease Patient (CKD) within Fraser Coast Renal Services.

## 2. Scope

This workplace instruction relates to medical and nursing staff employed by Fraser Coast Renal Services caring for any CKD patient (including general nephrology, conservative management and pre-dialysis patients) under the care of the Fraser Coast Renal Services.

## 3. Procedure for administration of (IV) Ferinject® (Iron Carboxymaltose) for the CKD patient

#### Points to Acknowledge:

* Early intervention is essential in avoiding iron deficiency anaemia for the patient with CKD.
* Measurement of iron stores must be deferred for 1 week following an intravenous iron dose of ≤ 200mg, and for two weeks following iron dose ≥ 200mg or blood transfusion administered.

##### Iron formula:

Ferinject® (Iron Carboxymaltose) is the intravenous iron formula of choice for CKD patients. Ferinject® is available in either 100mg/2ml, or 500mg/10ml, both contained in a glass vial with bromobutyl rubber stopper and aluminium cap.

##### Preparation and administration:

Procedure is to be booked into Hervey Bay Renal Unit Procedure Room in consultation with Home Therapies staff.

A fully equipped emergency trolley, including Promethazine 25mg and Hydrocortisone 100mg (both in intravenous form) must be available within the patient’s vicinity for the duration of the procedure. Pre-medication or the presence of a medical officer (even with first dose of IV Iron) is not routinely required. (Newnham 2006 et al).

##### Prior to the procedure:

* A medical order for IV iron must be obtained.
* Before the iron infusion is commenced, establish if any history of previous reactions, allergies or sensitivities to iron have ever been documented or voiced by the patient. If allergies or sensitivities identified, notify medical officer – consider avoiding iron administration.
* Inform the patient of signs to notify staff, i.e. breathlessness, chest tightness, racing heart, nausea or pain at cannula site.
* Insert an intravenous cannula. This must be done by a medical or nursing staff member who has completed a venipuncture and/or cannulation competency. (Back of the hand is the preferred cannulation site. An AV fistula/graft should not be accessed solely for an intravenous iron infusion unless deemed absolutely necessary. If necessary, AV fistula/graft cannulation is to be performed by a doctor/nurse who is competent in fistula/graft cannulation.

###### Preparation of the infusion:

*Equipment-*

* Alaris® volumetric pump
* Intravenous giving set
* Iron ampoules
* Sodium chloride 0.9% 100ml/250ml bag
* Additive label
* 20ml syringe and 18g drawing up needle for drawing up iron
* 18g sharp needle for adding solution to the sodium chloride bag
* Alcohol swabs

**Dilution**

|  |  |  |  |
| --- | --- | --- | --- |
| **Ferinject** | **Iron** | **Amount of 0.9% Sodium Chloride** | **Minimum administration time** |
| **2-4 mL** | **100-200 mg** | **100 mL** | **3 minutes** |
| **>4-10 mL** | **>200-500 mg** | **100 mL** | **6 minutes** |
| **> 10-20 mL** | **> 500-1000 mg** | **250 mL** | **15 minutes** |

**Adding iron to the infusion fluid**-

* Wash hands and don gloves
* Add Iron to 0.9% Normal Saline as per above table.
* Enter infusion documentation on additive label. This will include patient’s name, UR, DOB, or place patient identification label onto additive label. Then add to label IV fluid, drug added, total volume, prepared by, checked by and time and date commenced.

**Administration via infusion pump:**

**1000 mg Iron/250mls 0.9% Sodium Chloride**: Volume to be infused = 270 mLs, rate = 1080 mLs/hr.

Total delivered – 1000mg Iron over 15 minutes

**500mg Iron /100mLs 0.9% Sodium Chloride:** Volume to be infused = 110mLs, rate = 1100mLs/hr

Total delivered – 500mg Iron over 6 minutes.

**200mg Iron/100mL 0.9% Sodium Chloride:** Volume to be infused = 104mLs, rate = 1040mLs/hr.

Total delivered – 200mg Iron over 6 minutes

NOTE: dilution must not be less than 2mg/ml

* Turn the infusion bag to mix the contents.
* Spike the IV administration set and prime the line.
* Insert the administration set into the volumetric pump.
* Wash hands
* Connect giving set to intravenous access
* Establish baseline blood pressure and pulse
* Commence infusion at appropriate rate

- Assess patient (including cannulation site) and monitor blood pressure and pulse 5 minutely until the end of the infusion.

- If adverse reactions are noted:

* Cease infusion immediately
* Notify medical officer
* Obtain IV hydrocortisone in preparation
* Stay with patient; provide supportive care/resuscitation as required

- At the discretion of the medical officer, once the patient has stabilised, the infusion may be recommenced at half the infusion rate (540mls/hour).

- Once the infusion has completed, remove intravenous cannula prior to discharge.

- Document events.

**Adverse effects:**

**(Vifor Pharma 2011)**

* Anaphylaxis – usually within the first few minutes of administration and characterised by a sudden onset of respiratory difficulties, tachycardia and hypotension.
* Flushing, sweating, chills, fever, chest and back pain
* Nausea, vomiting
* Headache, dizziness
* Joint/muscle pain, sensation of stiffening arms, legs or face
* Anxiety, loss of consciousness, syncope, vertigo
* Tachycardia, hypotension, hypertension, circulatory collapse
* Bronchospasm, dyspnoea
* Generalised lymphadenopathy
* Dermatitis, erythema, rash, urticaria, angioneurotic oedema

**If adverse effects are suspected:**

* Cease infusion immediately
* Notify a medical officer
* Initiate nursing interventions as appropriate (i.e. administer bolus normal saline, apply oxygen therapy, provide comfort measures, basic/advanced life support).
* If anaphylaxis is evident/suspected, or patient condition warrants immediate medical attention, contact the medical emergency response services at your location, retrieve resuscitation equipment and prepare IV adrenaline.
* Document adverse reaction appropriately, including PRIME.

**Tissue infiltration (extravasation) with iron**

Iron is considered a vesicant. The important indicator of the severity of the extravasation is **PAIN.** Therefore, where possible, avoid iron administration in sedated patients.

In the event of the iron infusion infiltrating tissue surrounding the intravenous cannula insertion site;

* Immediately cease the infusion. Contact the medical officer immediately.
* Apply a cold compress. Recommendations: For a small amount of extravasated iron, apply 1% hydrocortisone cream. Adults: administer 100mg IV hydrocortisone and 10 to 25mg oral Promethazine.
* Do **NOT** cover the site with bandages.
* Mark the initial demarcated area with an indelible pen and observe hourly for 24 hours.
* If more serious symptoms develop, or if the extravasation is thought to be severe, contact a plastic surgeon immediately. A flush out of the site may be required under local or general anaesthetic. (NHS Tayside, 2008)

## 4. Supporting documents

Anderson, G., McMahon, L., Olynuk, J., Gibson, P. & Robinson, K. (2008) Which way for iron? Report on a forum on intravenous iron. Newsletter. Aspen Pharmacare.

Cairns & Hinterland Hospital & Health Service (2011). Iron Polymaltose Infusion. Retrieved 5th November 2012 from the Queensland Health Electronic Publishing service website, <http://qheps.health.qld.gov.au/>

Fremantle Hospital and health Service Department of Pharmacy (2010) Specialised Drug Guideline Iron Polymaltose.

Townsville Health Service District (2010). Standing Order:Intravenous Iron. Retrieved 14th September 2011. <http://qheps.health.qld.gov.au/tville/policies/thsdcli/thsdcli090457.pdf>

Iron infusion – Western health [http://docs.health.vic.gov.au/docs/doc/C4CBE7CC665EA259CA257CF900785805/$FILE/WH%20Iron%20Infusion.pdf](http://docs.health.vic.gov.au/docs/doc/C4CBE7CC665EA259CA257CF900785805/%24FILE/WH%20Iron%20Infusion.pdf)

## 5.Definition of terms

|  |  |  |  |
| --- | --- | --- | --- |
| **Term** | **Definition** | **Source**  | **See also** |
| Iron Infusion | Generally have either 1 or both of the following:1. Hb ≤ 100
2. TSAT ≤ 20% Seri, Ferritin ≤ 200µg/L
 | Roger, S., 2005. Haematological Targets-Iron, CARI guidelines, Viewed 11th July 2011Http://www.cari.org.au/DIALYSIS bht published/Iron.pdf. |  |
| Vesicant | A drug capable of causing tissue necrosis when extravasated | Mosby’s medical, Nursing & Allied Health Dictionary (2006). 6th edition. |  |

## References and Suggested Reading

## Cairns & Hinterland Hospital & Health Service (2012) Procedure document Intravenous Iron Supplementation for the Chronic Kidney Disease (CKD)/Renal Patient

* + MIMS Online (2017). Ferrosig Injection. Retrieved 5th May 2017 from the Queensland Health Electronic Publishing service website, <http://qheps.health.gld.gov.au/>
	+ NHS Tayside. (2008). Clinical extravasation policy for all drugs, chemotherapy and non-chemotherapy.
	+ CARI Guidelines – Haematological Targets – Iron <http://www.cari.org.au/DIALYSIS>
	+ MIMS Online (2017) Venofer (Iron Sucrose) Product information Retrieved 5th May 2017 from the Queensland Health Electronic Publishing service website, <http://qheps.health.gld.gov.au/>
	+ Vifor Pharma Pty Ltd 2011, Ferinject Product Information, Melbourne, Australia.
	+ Australian injectable drugs handbook (SHPA) 6th ed. (2017) <http://aidh.hcn.com.au/browse/about_aidh>
	+ Newnham E, Ahmad I, Thornton A, Gibson P., (2006) *Safety of Iron Polymaltose given as a Total Dose Iron Infusion*, Internal Medicine Journal, Vol 36. 672–74

* **Consultation**

 Key stakeholders who reviewed this document are:

* Renal clinical Service team
* Nephrologist
* Renal Pharmacist
* Nurse Unit Manager
* Nurse Practitioner (Renal)
* Clinical Facilitator (Renal)
* Renal Anaemia Coordinator
* UQ research council
* Director of Pharmacy WBBHS south

|  |  |
| --- | --- |
| **Version No.** | **Modified by** |
| Level of risk | Low |
| Audit strategy | RISKMAN reviews |
| Audit tool attached | No |
| Audit date | Annual |
| Audit responsibility | Renal Anaemia Coordinator |
| Key elements/ indicators / outcomes | 100% of chronic kidney disease patients ordered iron will have it administered as per this procedure, unless a specific medical order dictates otherwise. |

## Iron management in Chronic Kidney Disease (CKD)

Intravenous Iron Supplementation using Ferinject® (Ferric Carboxymaltose) for the Chronic Kidney Disease (CKD).

## 4. Supporting / Relating documents

* Queensland Health List of Approved Medications

**Authorising Policy / Standard/s / Legislation:**

*

**Procedures, Guidelines and Protocols:**

*
*

**Forms and templates:**

*

## 5. Definition of Terms

|  |  |
| --- | --- |
| **Term** | **Definition / Explanation / Details** |
| EPO | [Erythropoietin agonists](https://www.amh.net.au/online/view.php?page=chapter7/class2haemopoietics.html#haemopoietics) |
| CKD | Chronic Kidney Disease Patient  |
| ESRF | End Stage Renal Failure  |
| PD | Peritoneal Dialysis |

## 6. References and Suggested Reading

* Product information Ferrosig®. Sigma Pharmaceuticals (Australia) Pty Ltd, Victoria Australia.

## 7. Procedure Development / Revision and Approval History

|  |  |  |  |
| --- | --- | --- | --- |
| **Version No.** | **Modified by** | **Amendments authorised by**  | **Approved by** |
|  |  |  |  |

**7.1 This version supersedes/replaces:**

* Document 532s75v1: Iron Infusion (Adult) IV

## 8. Audit Strategy

|  |  |
| --- | --- |
| **Version No.** | **Modified by** |
| Level of risk | Low |
| Audit strategy | Compliance will be assessed through reported medication incidents involving Ferrosig® and RISKMAN reviews |
| Audit tool attached | No |
| Audit date | Annual |
| Audit responsibility | Renal Anaemia Coordinator |
| Key elements / indicators / outcomes | 100% of chronic kidney disease patients ordered iron will have it administered as per this procedure, unless a specific medical order dictates otherwise. |

**9. Communication Plan of Procedure**

|  |  |  |  |
| --- | --- | --- | --- |
| **Audience** | **Facilities** | **Accountable Officer** | **Timeframe** |
|  |  |  |  |

## 10. Approval and Implementation

**Procedure Initiator/Review Officer:** <<Daniel Bermingham, Renal Pharmacist>>

**Authority:** <<Dr Krishan Madhan>>

**Approving Officer:** <<Director of Renal Medicine >>

|  |  |
| --- | --- |
| **Date approved by Policy and Procedure Committee** |  |
| **Date published on WBHHS QHEPS page.** |  |
| **Next Review Date:** |  |

|  |  |
| --- | --- |
| **Version No.:** | <<1.0>> |
| **Keywords:** | Iron, Ferrosig, Iron Polymaltose, Iron Infusion, Iron carboxymaltose |
| **Accreditation References:** | EQuIP and other criteria and standards* <<insert EQuIP National Standards>>
 |

## 11. Appendices

Fraser Coast Renal Service  

Participant Information Sheet/Consent Form

|  |  |
| --- | --- |
| **Title** | **Pharmacist led decision support protocol for the management of anaemia utilising erythrocyte stimulating agents in patients undergoing haemodialysis** |
| **Short Title** | The PLAM trial  |
| **Principal Investigator** | Daniel Bermingham, Renal Unit, PO Box 592, Hervey Bay 4655. Wide Bay Hospital and Health Service District. Ph 43256610 or 0401351859 |
|  |  |
| **Location** | Fraser Coast Renal Service, Wide Bay Hospital and Health Service |

**1 Invitation**

You are invited to take part this research project – The (Pharmacist Lead Anaemia Management), PLAM study. This research is part of my Masters studies. You have been invited because you have chronic kidney disease (CKD) stage 5 on dialysis within the Fraser Coast renal Service. The research study is testing a pharmacist led anaemia management plan that will set up a protocol to ensure a high-level anaemia management plan under the supervision of the nephrologist.

The main goals of the study are to:

* Make decision-making smother and easier for treatment of iron repletion
* Make decision-making smother and easier for treatment of haemoglobin in dialysis patients
* Improve knowledge regarding the benefits and risks of protocol driven decision making
* Lower iron and haemoglobin related complications in dialysis patients
* Aid in future clinical decisions making and expansion in roles for pharmacist and other health professionals

This Participant Information Sheet/Consent Form tells you about the research study. It explains the tests and research involved. Knowing what is involved will help you decide if you want to take part in the research. Please take your time to make a decision.

Please read this information carefully. Ask questions about anything that you don’t understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or local doctor.

Participation in this research is voluntary. If you don’t wish to take part, you don’t have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

• Understand what you have read.

• Consent to take part in the research project.

• Consent to the tests and research that are described.

• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

You will not receive any different care than you are receiving now, if you do not want to participate in this study.

**2 What is the purpose of this research?**

The purpose of this research is to assess the PLAM trial iron management and haemoglobin management decision making protocol to gain an understanding on how to support your anaemia requirements whilst undergoing treatment for your dialysis dependent stage 5 kidney disease. The Pharmacist lead protocol has been developed using the best current information about treatment of anaemia in patients with CKD stage 5.

This research will also inform clinicians about other issues such as stability of haemoglobin and iron repletion, as well as the extension of the pharmacist role towards proactive clinical decision making rather than the current reactive nature of the profession.

The research:

* Has been initiated by me (Daniel Bermingham) in undertaking a Masters of Clinical Pharmacy at the University of Queensland (UQ).
* Is being conducted across 2 hospitals in Queensland and I am not being funded by any means.
* The results of this research will be used by the principle investigator (myself) to obtain a Masters of Clinical Pharmacy.

**3 Do I have to take part in this research study?**

Being in this study is voluntary. You can choose to not be in this study, or leave this study at any time.

You have the right to ask questions about the study at any time. If you have questions about your rights as a participant or you want to leave the study, please contact me on 43256610 or 0401351859.

If you choose to not take part or to leave this study, your regular clinical care will not be affected in any way.

* Even if you withdraw from the study, the information collected from your participation will be included in the study evaluation, unless you specifically ask that it not be included.
* There are no additional costs associated with participating in this study, nor will you be paid.

**4 About the study**

If you choose to accept, you will be participating in a cohort study. The cohort will be all participants within the Wide Bay Hospital and Health Service dialysis unit. In this study, I am testing the effectiveness of Pharmacist led anaemia management plan. The Pharmacist led anaemia management plan consists of work unit guidelines and dose adjustment charts that will allow for easier assessment and anaemia control.

It is difficult to know the best way to manage anaemia in dialysis patients. Judgment is mostly made based on the current treatment plan set in place, and the effective results seen in the monthly bloods. Work unit guidelines help to make a standardised judgment for the patients receiving erythropoietin’s and iron preparations to help management your anaemia. The decisions made will help to stabilise both your iron and haemoglobin levels on a month to month basis. These tools will help the Doctors prescribe the best choice of erythropoietin and iron for your anaemia management.

In this study, the patients in the Fraser Coast renal service dialysis group will be the intervention and the control. This group will partake if you so choose in the change in practice. Data collection of the past will serve as the control. Data collection will be done retrospectively for the months of July, August, September and October of 2017. This will allow the author to compare the past data versus the data after the change has occurred. There will be no change to the usual medications, medications information, and appropriate care as you did before. The difference lies in the manner of your medication management, where by the Fraser Coast renal service pharmacist will lead the management of anaemia, and the control being the past data will remain as the physician based management.

The study is an open label study with no blinding. This means that you and I will know which group you have been allocated too, as well as the doctors and nurses.

This study has been designed to make sure I interpret the results in a fair and appropriate way and it will stop me from jumping to conclusions.

There are no costs associated with participating in this research project, nor will you be paid.

**5 What does participation in this study involve?**

The study will last four months. The nurses normally take bloods from you on dialysis, and send to the pathology your blood samples for testing in the first week of the month. Your haemoglobin and iron requirements whilst on dialysis are normally monitored by the nephrologist on the second Tuesday of the month. The changes to your monthly anaemia management plan are handed to the nurses and the pharmacy for dose adjustments and you continue to receive treatment as per standard protocol. All these processes will not change to you or your treatment. The only area that will change will be the pharmacist comes in ONE step ahead to help manage your anaemia under the supervision of the nephrologist. You will not need to give any more blood than what is standard practice nor will you need to pay any additional money for services like pathology or medications.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Monthly plan** | **First Week** | **Second Week** | **Three Week** | **Forth Week** |
| **Pathology collection, Pharmacist intervention** | 🗸 |  |  |  |
| **Nephrologist bloods reviews** |  | 🗸 |  |  |
| **No intervention**  |  |  | 🗸 |  |
| **Pathology requests**  |  |  |  | 🗸 |

Once you have decided to participate in this study, all the study work and anaemia management will be done in the background of your standard dialysis treatment.

Data will be collected from the past to serve as the control and will not require any additional input from yourself. Data will be stored and analysed only on a work computer.

**6 What do I have to do?**

You should continue with your normal daily activities. There will be no change you’re your current dialysis treatment, now will there be of any additional treatment, medications or pathology requirements other than standard care.

**7 What are the other treatment choices?**

You don’t have to take part in this study to be treated at this hospital. The other option available is to continue with the usual care where the doctor provides you with the standard treatment for your anaemia associated with your renal disease.

It is possible that the standard treatment that is provided by the doctor would be very similar to what you would receive if you joined this study.

If you decide you do not want to join this research study, your medical care will not be affected in any way.

**8 What are the possible benefits of taking part?**

Taking part in this study may improve your knowledge about your treatment plans and assist with you to understanding about haemoglobin and anaemia.

I do know that the information from this study will help pharmacist, nurses and doctors learn more on how to support patients in anaemia management and also gain an understanding about pharmacist progression and scope of practice as decision makers.

This information could help other patients with kidney disease in the future.

**9 What are the possible risks and disadvantages of taking part?**

As this is a trial assessing the impact of a decision-making tool, there may be clinical side effects. However, all decisions made will be supervised by the consultant nephrologist to ensure the right decisions are made consistently. Your safety and clinical outcomes are the top priority of this outcome. You will be observed closely to ensure you don’t find the experience too distressing.

Iron and haemoglobin management can be a very tricky medical complication of end stage renal disease, and there is a possibility that your anaemia may become uncontrolled whilst on the study. There have been placed many check points in the study tools that will make sure that your iron and haemoglobin’s do not go above or below the reference ranges without the consultant doctor’s knowledge and intervention. All decisions made will be under the supervision of the consultant nephrologist, and any changes in the pharmacist plans will be documented and followed up to ensure that you as the patient gets the best treatment possible. It is highly unlikely that your haemoglobin and or iron stores in your body will go beyond that of the standard reference ranges, however if this does occur the nephrologist will take over treatment until your biomarkers are once again within range

**10 What if new information arises during this research study?**

During this research study, if new information regarding outcomes for either haemoglobin management of iron management arises, I will discuss this with the kidney specialist and my research team and decide whether this needs to be included in the research project.

1. **Can I receive other education while in this study?**

You will receive the usual education that the pharmacist and nurses provided. It is a step of the standard practice that will only differ.

**12 What if I withdraw from this research study?**

You can change your mind at any time about allowing me to use your results and health information for research. Please let the me of the doctors know that you wish to withdraw. Letting them know will give me the chance to discuss any requirements linked to withdrawing from the study.

**13 Could this research study be stopped unexpectedly?**

 This research study may be stopped unexpectedly for many reasons. These may include reasons such as:

* Further research indicates the pharmacist led tool is not advisable.
* Decisions made by local regulatory/health authorities.

**14 What happens when the research study ends?**

Once the study is complete and the results are known, a summary of the research can be provided to you. If you would like to receive this you can request a copy from me. You will not be able to receive anything specific to yourself, as the information collected about you has not been linked to your name.

**15 What will happen to information about me?**

By signing the consent section, you consent to me and other research staff, collecting and using personal information about you for this research project. All information obtained in connection with this research project that can identify you will remain confidential. This information will be stored on a secure computer and will be password locked with a 128bit lock, with only myself and the research team allowed to access this. Any information I get from this research study that can identify you will remain confidential and will only be used for medical reasons. It will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the research team accessing health records if they are relevant to your participation in this research project.

Your health records and any information obtained during the research project are subject to inspection for the purpose of verifying the procedures and the data. This review may be done by the relevant authorities and authorised representatives of the Townsville Human Research Ethics Committee and or University of Queensland Human Ethics Committee, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant research personnel and regulatory authorities as noted above.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified. Any information obtained for the purpose of this research project that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

All data will be stored in a coded way (no name, date of birth or hospital ID) for 15 years on a hard drive in a locked filing cabinet. After 15 years, all data will be destroyed.

Information about you may be obtained from your medical record held at this, and other, health services such as from your local doctor or other hospitals, but only for this research.

**16 Can I see my information and data?**

The data is non-identifiable unless it is necessary for medical purposes or you withdraw from the study. You will not be able to view any information collected about you. This has been undertaken to ensure your confidentiality**.**

**17 What happens if I am injured as a result of participating in this research study?**

There is a minimal likelihood of you suffering any injuries or complications, as the treatment is a decision tool to aid in better clinical choices about standard treatments. Nether the less, all precautions will be considered, and all decisions made are under the care of the nephrologist. Any medical complication that may arise because of treatment within the dialysis unit will be attended to by the hospital nurses and doctors. In the event of a medical emergency, the hospital staff are well trained and knowledgeable to manage any complication that may arise as a result of your treatment.

**18 Who is organising and funding the research?**

The research study is part of my masters in clinical pharmacy, and is not being funded by any governing bodies. No member of the research team will receive a personal financial benefit from your involvement in this research study (other than their ordinary wages). All medication costs will be covered under the PBS and all pathology tests will be covered under Medicare.

**19 Who has reviewed the research study?**

The Human Research Ethics Committee of Townsville Hospital and UQ have approved the ethical aspects of this research study. The Human Research Ethics Committee’s business is to protect the interests of people who agree to participate in human research studies.

**20 Who can I contact about the study?**

The person you may need to contact will depend on the nature of your query.

If you want any further information about this study or if you have any medical problems, which may be related to your involvement in the study, you can contact me on 0401 351 859 or the pharmacy department on 07 4325 6610

 24 Hour Clinical contact persons

|  |  |
| --- | --- |
| Name | Daniel Bermingham |
| Position | Principle Investigator |
| Telephone | 0401351859 |
| Email | Daniel.Bermingham@health.qld.gov.au |

**Complaints**

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

|  |  |
| --- | --- |
| Reviewing HREC name | Townsville Human Research Ethics Committee |
| HREC Executive Officer | Associate Professor Nikola Stepanov |
| Telephone | 07 4433 1440 |
| Email | TSV-Ethics-committee@health.qld.gov.au |

**Reviewing HREC**

**Academic Supervisor at University of Queensland contact details**

|  |  |
| --- | --- |
| Name | Judy Burrows |
| Position | Course coordinator |
| Telephone | 07 33461956 |
| Email | j.burrows@uq.edu.au |

UQ is committed to research integrity and the ethical conduct of research projects. However, if you do have any concerns or complaints about the ethical conduct of the project you may contact the UQ Research Ethics Unit on 0733653560 or email dvc.research@uq.edu.au. The UQ Research Ethics Unit is not connected with the research project and can facilitate a resolution to your concern in an impartial manner.

**Consent Form**

|  |  |
| --- | --- |
| **Title** | **Pharmacist led decision support protocol for the management of anaemia utilising erythrocyte stimulating agents in patients undergoing haemodialysis**. |
| **Short Title** | The PLAM trial |
|  |  |
| **Principal Investigator** | Daniel BerminghamRenal UnitPO Box 592Hervey Bay 4655Wide Bay Hospital and Health Service District 0401 351 859 |
|  |  |
| **Location**  | Fraser Coast renal service |

**Declaration by Participant**

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

|  |
| --- |
|   |
|  | Name of Participant |  |  |
|  |  | (please print) |  |
|  | Signature |  | Date |  |  |
|  |

**Declaration by Principal Investigator**

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

|  |
| --- |
|  |
|  | Name of Research Assistant |  |  |
|  |  | (please print) |  |
|  | Signature |  | Date |  |  |
|  |

Note: All parties signing the consent section must date their own signature.

**Form for Withdrawal of Participation**

|  |  |
| --- | --- |
| **Title** | **Pharmacist led decision support protocol for the management of anaemia utilising erythrocyte stimulating agents in patients undergoing haemodialysis.** |
| **Short Title** | *The PLAM trial* |
|  |  |
| **Principal Investigator** | Daniel BerminghamRenal UnitPO Box 592Hervey Bay 4655Wide Bay Hospital and Health Service District 0401 351 859 |
|  |  |
| **Location** | Hervey Bay and Maryborough Hospital |

**Declaration by Participant**

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Fraser Coast renal service, Wide Bay Hospital and Health Service South.

|  |
| --- |
|   |
|  | Name of Participant |  |  |
|  |  | (please print) |  |
|  | Signature |  | Date |  |  |
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|  |

**Declaration by Principal Investigator**

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

|  |
| --- |
|  |
|  | Name of Research Assistant |  |  |
|  |  | (please print) |  |
|  | Signature |  | Date |  |  |
|  |

Note: All parties signing the consent section must date their own signature.