NURSE OR PHARMACIST-LED ANEMIA MANAGEMENT
PROTOCOL EDUCATIONAL PACKAGE

TABLE OF CONTENTS:


Page 16: CANN-NET Anemia Management: Draft Policy and Procedures

For more information please contact the project lead at brimbles@mcmaster.ca.
IT IS CRITICAL THAT ALL STAFF MEMBERS INTENDING TO ADMINISTER THE ANEMIA MANAGEMENT PROTOCOL REVIEW THIS DOCUMENT IN DETAIL.

Introduction: In 2012 the Kidney Disease: Improving Global Outcomes (KDIGO) work group published updated clinical practice guidelines for anemia management in Chronic Kidney Disease (CKD) patients. Subsequently, the Canadian Society of Nephrology (CSN) anemia work group published a commentary on the KDIGO clinical practice guideline. The objective was to establish a consistent nation-wide guideline to improve the quality of health care delivered to CKD patients in Canada, and to inform optimal anemia management in CKD patients.

Purpose: The nurse or pharmacist-led anemia management protocol, developed by the Canadian Kidney Knowledge Translation and Generation Network (CANN-NET), is based on protocols graciously provided by the BC Renal Agency, and seeks to provide medical direction for the adjustment of the following medications, as they are used in the management of renal anemia associated with chronic renal failure: Darbepoetin alpha (Aranesp®), Epoetin alpha (Eprex®), Sodium Ferric Gluconate (Ferrlecit®), Iron dextran (DexIron®), and / or Iron Sucrose (Venofer®).

What is Anemia?
Anemia is a common complication of CKD because the kidneys are unable to manufacture enough erythropoietin (EPO), a hormone that regulates the production of red blood cells (RBC). Erythropoietin Stimulating Agents (ESAs), such as Eprex® (Epoetin alpha) or Aranesp® (Darbepoetin alpha), are manufactured versions of a protein that may be administered to stimulate erythropoiesis in the absence of kidney function. Patients with kidney failure also have trouble absorbing and processing iron, and as such, iron therapy (typically administered intravenously in hemodialysis patients) is usually required.

This educational document will provide you with an overview of the CANN-NET Anemia Management Protocol. We will conduct a comprehensive review of each page of the protocol, including pictures and explanations of individual sections of each page and areas to note for future use of the algorithm.
**IMPORTANT POINTS TO REMEMBER:**
**INITIATION OF THE ANEMIA MANAGEMENT PROTOCOL REQUIRES A PHYSICIAN ORDER FOR EACH PATIENT.**

Contraindications to using the CANN-NET Anemia Management Protocol:
A patient should **not** start the protocol if:
1. They have a known allergy to any ESA or intravenous iron medication, UNLESS the renal program has access to alternative medications that are safe for the patient. *(ie: the patient is allergic to Darbepoetin, but Epoetin is available and the patient has no known allergy to Epoetin)*
2. The patient’s physician does not feel they are appropriate for the protocol.
3. They are currently on an ESA dose greater than the recommended maximum of 150 mcg weekly of Darbepoetin or 30,000 units weekly of Epoetin.
4. They are currently an inpatient.
5. They are currently receiving chemotherapy for malignancy.

Medication Specifics: Iron and ESA Therapy
1. Given that renal programs vary in terms of labwork schedules (6-week vs 4-week) and erythropoietin administration (intravenous vs subcutaneous), there are differing protocols for these specifications. For simplicity we present the six week protocol with IV ESAs in this document, though the educational messages apply to all variations of the protocol.
2. The physician will determine which iron medication the patient will receive among the following suitable iron products: Sodium Ferric Gluconate (Ferrlecit®), Iron Dextran (DexIron®), and Iron Sucrose (Venofer®). Your centre may not use all of these formulations.
   a. Your centre may also use Ferumoxytol (Feraheme®) as an iron preparation, currently there is no recommended maintenance dosage regimen, and as such this product is not included in the CANN-NET Anemia Management Protocol.
3. If a patient is on antibiotic therapy, iron therapy may be held until antibiotics are complete or the infectious process is resolved. Verification from a physician is required.
4. The physician will determine which ESA product the patient will receive, Epoetin alpha (Eprex®) or Darbepoetin alfa (Aranesp®). Your centre may not use both of these formulations.
5. Dose adjustments will be made and determined by the nurse or pharmacist (refer to Page 3 of the anemia protocol – Dosage Adjustment Tables).
6. The recommended starting dose of Epoetin alpha (Eprex®) is 100 U/kg/wk and Darbepoetin alfa (Aranesp®) is 0.45 mcg/kg/wk.
7. The recommended maximum dose of Epoetin alpha (Eprex®) is 10,000 U 3x q weekly, and Darbepoetin alfa (Aranesp®) is 150 mcg q weekly.
CANN-NET Anemia Management Protocol: Educational Document

OVERVIEW OF PAGE ONE: HEMOGLOBIN ASSESSMENT

The following protocol is an order of physician transfers anemia management of hemodialysis patients to nonphysician staff (i.e., nurses and renal pharmacists). The following protocol is intended to serve as a guide and cannot replace your clinical judgment. ESA’s are not recommended in patients with active malignancy or a stroke in last 3 months. The recommendations included may also be inappropriate for other clinical situations (e.g., patients with hemochromatosis, thalassemia, PRCA, allergy to IV iron or an ESA, etc.). The lowest ESA dosage to achieve acceptable Hgb range should be used.

Any decrease in Hgb ≥ 15 g/L, OR If Hgb < 85g/L → Notify MD

Hgb 85 - 94 g/L

- YES
  - Re-measure iron bloodwork, if not done in past week. Refer to page 5.
  - If no dose increase in past 5 weeks, increase ESA dosage by 30% of ESA Dosage Adjustment Table on page 2.
  - If dose was increased in past 5 weeks, maintain that dose until next bloodwork, or 6 weeks.
  - Notify MD if Hgb is not in target range after 3 consecutive doses increases. Refer to ESA Hypersensitivity Reaction Table on page 5.

If there has been no dosage reduction in the past 5 weeks, reduce ESA dosage as per ESA Dosage Adjustment Table on page 3.

If there has been dosage reduction in the past 6 weeks, maintain current dose and re-check Hgb in 6 weeks to reassess ESA dosage.

Hgb 95 to 115 g/L

- NO
  - ESA on hold or discontinued

Hgb > 115 g/L

- YES
  - Erythropoietin (EPO): a glycoprotein hormone, secreted chiefly by the kidney which acts on the bone marrow cells to stimulate erythropoiesis (formation of red blood cells).
  - Erythropoietin Stimulating Agent (ESA): The manufactured version of a protein that may be administered to stimulate erythropoiesis in the absence of a functioning kidney (e.g., Aranesp® or Eprex®).

Important Definitions:

Hemoglobin: is the iron-containing oxygen-transport metalloprotein in red blood cells.

Erythropoietin: (EPO): a glycoprotein hormone, secreted chiefly by the kidney which acts on the bone marrow cells to stimulate erythropoiesis (formation of red blood cells).

Hemoglobin/Erythropoietin Stimulating Agent (ESA): The manufactured version of a protein that may be administered to stimulate erythropoiesis in the absence of a functioning kidney (e.g., Aranesp® or Eprex®).

Here is a breakdown of page one of the anemia protocol, Hemoglobin/ESA Assessment.

The headings: this indicates that this particular page is to be used only for Hemodialysis patients/units using a 6-week bloodwork schedule.

Furthermore, the blue heading indicates that this page refers to the Hemoglobin/Erythropoietin Stimulating Agents aspect of the protocol. The protocol works as a complete package, however, it is to be used in a sequential order. Therefore, please ensure that this first page, Hgb/ESA assessment, is
followed first when reviewing a patient’s anemia status and that the second page, Iron assessment, is addressed only after the first page has been completed.

The Target Hemoglobin is 95 to 115 g/L. This is consistent with the KDIGO clinical practice guidelines for anemia management in CKD patients and the CSN commentary on these guidelines for application in the Canadian health care system.

The Statement:
- This specifies that a written order must be issued from a physician to start the CANN-NET Anemia Protocol for any patient.
- This protocol is to be used as a guide and cannot replace a physician’s clinical judgment.
- Erythropoietin Stimulating Agents (ESA’s) are not recommended in patients with active malignancy or history of a stroke within the past 3 months.
  - This recommendation comes from the CSN commentary on the KDIGO clinical practice guidelines for anemia in CKD patients since studies suggest that patients on active chemotherapy have an increased risk of mortality while on ESA therapy. Additionally, evidence suggests that patients with a history of stroke may have an increased risk of experiencing a subsequent stroke while on ESA therapy. It is the responsibility of the physician to determine whether the benefits of ESA therapy outweigh the risks in these two circumstances.
- Please be aware that the recommendations included throughout the protocol may be inappropriate for specific clinical situations, such as, patients with hemochromatosis, thalassemia, PCRA, allergy to IV iron or an ESA, etc. Physicians should consider these situations prior to ordering the anemia protocol.
- The lowest ESA dosage to achieve acceptable Hgb range should be used.

If any decrease in Hgb greater than 15 g/L is noted between successive bloodwork values, drawn for anemia management only, notify the physician.

Any decrease in Hgb ≥ 15 g/L, OR if Hgb < 85g/L → Notify MD

Patients may be placed in one of three hemoglobin ranges within the Hgb/ESA assessment page, these are as follows:
1) Low Hgb range: Hgb 85 – 94 g/L,
2) Target Hgb range: Hgb 95-115 g/L, and
3) Elevated Hgb range: Hgb >115g/L.
For the **low Hgb range: 85-94 g/L.**
First, ensure that the patient’s anemia bloodwork indicates their **Hgb level is within the 85-94 g/L range.**

Next, is this patient receiving ESA currently?
Regardless of whether the patient is currently receiving ESA therapy or not, the initial step remains the same.

Note that the patient’s iron bloodwork should be re-measured, if not done in the past week, and you are directed to page 2: **Iron Assessment** (though please continue to follow the ESA page to completion as the protocol is intended to work in a sequential manner). We will review page 2 shortly, but the overall goal is to ensure that the iron stores are replete. A review of clinical practice and research shows that ESA therapy and IV iron work in a complementary manner. As such, it is important to ensure that the patient has adequate iron stores, as this will help improve the Hgb level and potentially decrease the dosage of ESA required to reach the target Hgb level.

**If “Yes on ESA”,** review the recent ESA dosage adjustments.

- If **NO dosage increase** has occurred within the past 5 weeks, then an increase in ESA dosage should be done according to the ESA Dosage Adjustment Tables on page 3 of the Anemia Protocol.
- If the **ESA dose** has been increased within the past 5 weeks, then the current ESA dose should be maintained (No change to ESA dosage) until the next bloodwork is drawn in 6 weeks and the patient’s anemia status is reassessed.
  - It is important to note that the physician should be notified if the patient’s hemoglobin does not reach the target Hgb range after 3 consecutive ESA dose increases. At this point, we recommend that the physician refer to the ESA Hyporesponsiveness Flowchart, located on page 5 of the Anemia Protocol.

**If “Not on ESA”,** the physician should be consulted to consider ESA therapy initiation. Please note that a Dr. Order must be obtained, including the type of ESA (Epoetin or Darbepoetin and the initial dosage). The CSN commentary recommends an initial starting dose for each ESA therapy: Epoetin: 100 units/kg/wk; Darbepoetin: 0.45 mcg/kg/wk (see ESA dosage adjustment tables).
Target Hemoglobin Range: 95-115 g/L

First, ensure that the patient’s anemia bloodwork indicates their Hgb level is within the 95 – 115 g/L range.

Next, is this patient receiving ESA currently?

If “Not on ESA”, then the patient does not require ESA therapy and they may continue with normal Hgb monitoring with bloodwork every 6 weeks for anemia status assessment.

If “Yes on ESA”, then the patient may maintain their ESA dosage and continue with normal Hgb monitoring with bloodwork every 6 weeks for anemia status assessment.

If “ESA is on Hold”, then the patient must have their ESA therapy restarted, but at a reduced dose. This reduced dose is based on their previous ESA dosage, prior to having the ESA therapy put on hold. Refer to the ESA Dosage Adjustment Tables on page 3. Finally, they may also continue normal Hgb monitoring with bloodwork every 6 weeks for anemia status assessment.
Elevated Hemoglobin Range: Hgb >115 g/L

First, ensure that the patient’s anemia bloodwork indicates their Hgb level is above 115 g/L.

Next, is this patient receiving ESA currently?

If “Not on ESA”, then the patient does not require ESA therapy and they may continue normal Hgb monitoring with bloodwork every 6 weeks for anemia status assessment.

If “Yes on ESA”, then consider which Hgb range the patient fits into?

- **Hgb 116-125 g/L**: review the recent ESA dosage adjustments.
  - If “No ESA dosage reductions in past 5 weeks” (since last anemia bloodwork was drawn), then reduce the patient’s ESA dose according to the ESA Dosage Adjustment Tables on page 3 of the Anemia Protocol.
  - If “There have been ESA dosage reductions in the past 5 weeks” (since last anemia bloodwork was drawn), then maintain current ESA dose and continue normal Hgb monitoring with bloodwork every 6 weeks for anemia status assessment.

- **Hgb >126 g/L**: Hold ESA.
  - Measure Hgb in 2 weeks to reassess anemia status.
  - Note: If Hgb has been greater than 126 g/L for 18 weeks, discontinue the patient’s ESA. Also, continue with routine Hgb monitoring with bloodwork every 6 weeks for anemia status assessment.

If “ESA is on Hold OR Discontinued”, then consider which Hgb range the patient fits into?

- **Hgb 116-125 g/L**: How much has the patient’s Hgb changed since their last bloodwork?
  - IF the patient’s Hgb has changed <10 g/L, then continue to HOLD ESA.
  - IF the patient’s Hgb has changed ≥ 10 g/L, then resume the ESA at a reduced dose. (Consult the ESA Dosage Adjustment Tables on Page 3)

- **Hgb >126 g/L**: Hold ESA. Measure Hgb in 2 weeks to reassess anemia status.
  - Note: If Hgb has been greater than 126 g/L for 18 weeks, discontinue the patient’s ESA. Also, continue with routine Hgb monitoring with bloodwork every 6 weeks for anemia status assessment.

**Note:** the yellow box indicating abbreviations and symbols (>, <, ≥, ≤) is simply for your information.
CANN-NET Anemia Management Protocol: Educational Document

After Hgb/ESA Assessment is complete:

Regardless of which hemoglobin range the patient is in, at the end of the hemoglobin and ESA therapy assessment, you should continue to page 2 for the iron status assessment.  
**Note:** If the hemoglobin is 95 or greater, then iron bloodwork does not need to be re-drawn and analysed to assess page 2: Iron/IV Iron Assessment. You can simply refer to the patient’s most recent iron bloodwork.
**OVERVIEW OF PAGE TWO: IRON ASSESSMENT**

**Why is this important?** Hemodialysis patients become iron deplete for several reasons: decreased GI absorption of iron, increased iron loss due to ongoing blood loss, and blood loss from blood testing and/or clotting in the dialyzer.

Also, ESA’s increase the body’s utilization of iron; which means every ESA administration requires a certain amount of available iron in the body for RBC production. Thus, IV iron is administered in any of the following forms (depending on your renal program): Sodium Ferric Gluconate (Ferrlecit®), Iron Dextran (DexIron®) or Iron Sucrose (Venofer®).

**Important Fact:** when a patient receives a *blood transfusion*, do not administer a scheduled dose of IV iron. Each unit of blood has the equivalent of 200-250 mg of iron. If you administer the blood and the IV iron dose on the same day, you *risk overdosing your patient with iron.*

---

**Important definitions:**

- **Ferritin:** an iron-binding protein that stores iron in the body. About 30% of iron is stored in the liver and the reticuloendothelial system in a form that is bound with ferritin.
- **Transferrin:** an iron-binding protein that carries iron in the plasma.
- **Transferrin Saturation (TSAT):** is a measure of the proportion of serum iron bound to transferrin ÷ a measure of circulating transferrin.

---
Here is a breakdown of page two of the anemia protocol, Iron/IV Iron Assessment.

The top left heading: this indicates that this particular page is to be used only for Hemodialysis patients/units using a 12 week iron bloodwork schedule.

The large middle heading: this indicates that this page refers to the Iron/IV Iron aspect of the protocol. Due to the fact that the protocol works as a complete package, it is to be used in a sequential order. As such, please ensure that a thorough review of page one, Hgb/ESA assessment, has been completed prior to initiating page 2.

**FIRST:** What is the patient’s Hgb?

- If Hgb >115 g/L, you should hold the patients IV iron dose.
- If Hgb ≤ 115 g/L, you should continue the iron assessment on page 2.

**Important Note:** The administration of IV Iron should be held if at any point the patient’s Hgb reaches a level greater than 115 g/L. Furthermore, you should notify the physician to assess the patient’s iron status and IV iron use, if the patient presents with any of the following:

- Serum ferritin greater than 1000 µg/L (*notify MD only once and reassess in 12 weeks),
- Patient is on IV antibiotics,
- Patient has signs and symptoms of sepsis (e.g. temperature greater than 38°, chills, rigors, unexplained hypotension)

**Unusual Bloodwork Note:** This is simply to serve as a reminder to staff using the Anemia Protocol that they should always be monitoring the progression of their patient on Hemodialysis. You can track the patient’s anemia status on the Anemia Management Log on page 4 of the Anemia Protocol. It is important to notice inconsistent or unusual bloodwork results, or drastic changes in a patient’s anemia status. Remember in some circumstances there could have been an error with the bloodwork.

The CSN commentary on the KDIGO clinical practice guideline recommends that the minimum TSAT is 30%, although we sought to give some leeway on this measure. The inclusion of a TSAT <20% range focuses on ensuring adequate iron supplementation to fully support RBC production. Moreover, when the anemia protocol was tested using a target TSAT of 25-49%, hemodialysis units noted a significant increase in iron use with no reduction in the average ESA use.

**Acronym Legend:** the yellow box indicating abbreviations and symbols (> , <, ≥, ≤) is simply for your information.
Patients may be placed in one of three TSAT ranges within the Iron/IV Iron assessment page, these are as follows: 1) TSAT <20% - indicating that Iron Stores Require Repletion, 2) TSAT 20% - 49% - indicating to Maintain Iron Stores, and 3) TSAT ≥ 50% - indicating possible Iron Overload.

Examine **TSAT <20% - Replete Iron Stores:**

First, ensure that the patient’s anemia bloodwork indicates their TSAT is below 20%. They must also have a Hgb level equal to or less than 115 g/L. These measures indicate that the patient requires their iron stores be repleted.

Next, is this patient receiving ESA currently?

**If “Yes on ESA”, start an iron loading dose.** If the patient has not previously received IV iron, be sure to obtain a physician’s order to start the patient’s iron loading dose. Depending on the type of IV Iron that your HD centre uses, please refer to the recommended IV iron loading dose (9 consecutive doses).

- Ferrlecit®: 125 mg IV 3 times/week for 3 weeks
- DexIron®: 100 mg IV 3 times/week for 3 weeks
- Venofer®: 100 mg IV 3 times/week for 3 weeks

**If possible, be sure that the patient has discontinued their oral iron intake.**

**Following Iron Loading Dose Completion:** the patient should be started on a maintenance dose of IV iron every 2 weeks. It is recommended that the following dosing be used as initial iron maintenance dosing, depending on the IV iron drug type.

- Ferrlecit®: 125 mg IV every 2 weeks
- DexIron®: 100 mg IV every 2 weeks
- Venofer®: 100 mg IV every 2 weeks

**Important note:** You should note that no more than 2 consecutive courses of iron loading may be administered to a patient. If the patient’s iron indices (TSAT %, Hgb level) remain low, notify the physician. This is due to the potential for iron toxicity to occur.

**If “Not on ESA”,** the patient should continue or initiate IV iron maintenance dosage for every 4 weeks and reassess their iron status and dosage regimen in 12 weeks.

**Reassessment:** Regardless of the patient’s current IV iron use, they should always have their TSAT and Ferritin re-measured in 12 weeks (or 3 months) at which point the patient’s iron dosage regimen and iron status should be assessed.
**TSAT 20% - 49%: Target Range - Maintain Iron Stores**

First, ensure that the patient’s anemia bloodwork indicates their TSAT level is within the TSAT 20% - 49% range.

**Important Note:** Studies suggest that patients with Ferritin less than 200 will have an increase in their Hgb if given iron. As such, in patients with a Hgb less than 95g/L and a Ferritin level of less than 200, notify the physician to consider initiating an iron loading dose.

Next, is this patient receiving IV Iron currently?

If “receiving Maintenance Iron”, the patient should continue with their current maintenance dose of IV iron. This is found on the Anemia Management Log on page 4 of the Anemia Protocol.

If “Iron is currently on Hold”, the patient should be restarted on an iron maintenance dose every 4 weeks. It is recommended that the following dosing be used, depending on the IV iron drug type.

- Ferrlecit®: 125 mg IV every 4 weeks
- DexIron®: 100 mg IV every 4 weeks
- Venofer®: 100 mg IV every 4 weeks

If “Not on IV Iron”, the patient should be started on an IV Iron maintenance dose. A Physician Order is required to administer iron, and should include the IV Iron drug type and specific dose. It is recommended that the starting IV iron maintenance dose be every 4 weeks as follows, depending on the IV iron drug type. (Ensure that the patient has discontinued their oral iron intake, if relevant.)

- Ferrlecit®: 125 mg IV every 4 weeks
- DexIron®: 100 mg IV every 4 weeks
- Venofer®: 100 mg IV every 4 weeks

**Reassessment:** Regardless of the patient’s current IV iron use, they should always have their TSAT and Ferritin re-measured in 12 weeks (or 3 months) at which point the patient’s iron dosage regimen and iron status should be assessed.
TSAT ≥ 50% : Elevated TSAT Range - Possible Iron Overload

First, ensure that the patient’s anemia bloodwork indicates their TSAT level is equal to or greater than 50%.

Next, the patient should have their Iron Held, as it is above the target range. The patient should have their anemia bloodwork drawn in 12 weeks to assess their iron status (TSAT and Ferritin) and iron dosage regimen.

Important Note: You must notify the physician if the iron indices remain high for 3 consecutive measurements.
OVERVIEW OF PAGE 3: ESA DOSAGE ADJUSTMENT TABLES

The following tables provide guidance for most dosage adjustments. If a patient’s Hb cannot be maintained within the desired range with 3 consecutive dose modifications using the dosage schedule below, contact the physician for advice.

If a patient’s erythropoiesis stimulating agent (ESA) dosage is not available in the tables below, please contact a physician for ESA dosage modification. The lowest ESA dosage to maintain Hb within acceptable range should be used.

### Darbepoetin (Aranesp®) Dosage Adjustment Table
Pre-filled syringes available for CKD patients include: 10 mcg, 20 mcg, 50 mcg, 40 mcg, 50 mcg, 60 mcg, 80 mcg, 100 mcg, 150 mcg and 200 mcg.

<table>
<thead>
<tr>
<th>Current Dose</th>
<th>Increase Dose</th>
<th>Decrease Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mcg every 1 week</td>
<td>10 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>20 mcg every 1 week</td>
<td>20 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>30 mcg every 1 week</td>
<td>30 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>40 mcg every 1 week</td>
<td>40 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>50 mcg every 1 week</td>
<td>50 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>60 mcg every 1 week</td>
<td>60 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>70 mcg every 1 week</td>
<td>70 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>80 mcg every 1 week</td>
<td>80 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>90 mcg every 1 week</td>
<td>90 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>100 mcg every 1 week</td>
<td>100 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>110 mcg every 1 week</td>
<td>110 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>120 mcg every 1 week</td>
<td>120 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>130 mcg every 1 week</td>
<td>130 mcg every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
</tbody>
</table>

### Epoetin alpha (Eprex®) Dosage Adjustment Table
Pre-filled syringes available for CKD patients include: 1000 units, 2000 units, 3000 units, 4000 units, 5000 units, 6000 units, 8000 units and 10,000 units.

<table>
<thead>
<tr>
<th>Current Dose</th>
<th>Increase Dose</th>
<th>Decrease Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000 units every 1 week</td>
<td>2000 units every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>2000 units every 1 week</td>
<td>3000 units every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>3000 units every 1 week</td>
<td>4000 units every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>4000 units every 1 week</td>
<td>5000 units every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>5000 units every 1 week</td>
<td>6000 units every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>6000 units every 1 week</td>
<td>8000 units every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>8000 units every 1 week</td>
<td>10,000 units every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
<tr>
<td>10,000 units every 1 week</td>
<td>15,000 units every 1 week</td>
<td>D/C check Hb in 2 weeks</td>
</tr>
</tbody>
</table>

Note: This dosage adjustment table is applicable to hemodialysis units which dispense Eprex® or Aranesp® to patients. For units where patients purchase their own ESA and bring it to the HD unit, changing their dose is usually done by changing the frequency with which the ESA is administered. If this is the case for your unit, please go to [www.cann-net.ca](http://www.cann-net.ca) or contact Scott Brimble ([brimbles@mcmaster.ca](mailto:brimbles@mcmaster.ca)) for an alternate Dosage Adjustment Table.

For units which dispense the ESA to the patient, the above CANN-NET ESA Dosage Adjustment Table is applicable, and each column is equivalent to a dosage step. In moving across the table, using the current dose, you may increase or decrease one dosage step, depending on the patient’s bloodwork. Please keep in mind, that the maximum ESA doses should not be exceeded. In the event a patient appears to require moving past the recommended maximum ESA doses (Aranesp: 150 mcg/week, Eprex: 30,000 units/week), please notify the physician for further instruction on treatment.
**OVERVIEW OF PAGE 4: ANEMIA MANAGEMENT LOG**

<table>
<thead>
<tr>
<th>DATE</th>
<th>Hgb Draw Date</th>
<th>TSAT &amp; Ferr Draw Date</th>
<th>Current ESA Dose</th>
<th>Current Iron Dose</th>
<th>Change ESA Dose To</th>
<th>Change Iron Dose To</th>
<th>Follow up Bloodwork and Draw Date</th>
<th>Other Comments</th>
<th>Staff Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>04/12/2013</td>
<td>Hgb 95 (04/12/2013)</td>
<td>N/A</td>
<td>40mcg weekly</td>
<td>N/A</td>
<td>Maintain Aranesp (40 mcg weekly)</td>
<td>N/A</td>
<td>January 2014 MBW</td>
<td>YES</td>
<td>Dates: 12/12/2013, 15/01/2014</td>
</tr>
<tr>
<td>15/01/2014</td>
<td>Hgb 97 (15/01/2014)</td>
<td>N/A</td>
<td>40mcg weekly</td>
<td>N/A</td>
<td>Maintain Dose</td>
<td>N/A</td>
<td>February 2014 MBW</td>
<td>YES</td>
<td>Jane Doe</td>
</tr>
<tr>
<td>20/01/2014</td>
<td>Hgb 97 (15/01/2014)</td>
<td>TSAT 17%, Ferr 788 (17/01/2014)</td>
<td>N/A</td>
<td>N/A</td>
<td>Venoferr 100mg IV, 3x/week for 9 doses</td>
<td>N/A</td>
<td>11/04/2014 Fe BW</td>
<td>YES</td>
<td>John Smith</td>
</tr>
<tr>
<td>17/02/2014</td>
<td>Hgb 98 (24/02/2014)</td>
<td>TSAT 24%, Ferr 738 (14/02/2014)</td>
<td>N/A</td>
<td>N/A</td>
<td>Venoferr 100mg IV, x9 doses</td>
<td>N/A</td>
<td>Fe BW - 12/03/2014, F/U 19/03/2014</td>
<td>YES</td>
<td>As per Anemia Protocol</td>
</tr>
</tbody>
</table>

In the Anemia Management Log above, you will note that we have included examples of a patient’s anemia management while on the anemia protocol. You will see that each successive line is a new anemia evaluation by the nursing staff, using the patient’s regularly scheduled labwork or iron bloodwork. The nurse has written in the patient’s lab values, along with the dates, the previous ESA or iron dose and finally, the next course of action for this patient. As you can see, this patient has had their iron dose changed during the most recent iron bloodwork assessment (circled in red).

**OVERVIEW OF PAGE 5: ESA HYPORESPONSIVENESS CHART**

It is important to note that the ESA Hyporesponsiveness Chart, page 5 of the Anemia Management Protocol, is for informational purposes only and should act as a guide for physician assessment of ESA therapy hyporesponsiveness on a patient case-by-case basis. As a nurse or pharmacist you will not be required to use this page.
1. **PURPOSE:** To achieve and maintain the recommended hemoglobin and iron levels in chronic kidney disease (CKD) patients undergoing hemodialysis treatment with a nurse or pharmacist-led anemia management protocol.

The nurse or pharmacist-led anemia management protocol, developed by the Canadian Kidney Knowledge Translation and Generation Network (CANN-NET) based on protocols graciously provided by the BC Renal Agency, seeks to provide medical direction for the adjustment of the following medications, as they are used in the management of renal anemia associated with chronic renal failure.

Darbepoetin alpha (Aranesp®), Epoetin alpha (Eprex®), Sodium Ferric Gluconate (Ferrlecit®), Iron dextran (DexIron®), and / or Iron Sucrose (Venofer®).

2. **DEFINITIONS:**

**Hemoglobin:** is the iron-containing oxygen-transport metalloprotein in red blood cells.

**Ferritin:** an iron-binding protein that stores iron in the body. About 30% of iron is stored in the liver and the reticuloendothelial system in a form that is bound with ferritin.

**Transferrin:** an iron-binding protein that carries iron in the plasma.

**Transferrin Saturation (TSAT):** is a measure of the proportion of serum iron bound to transferrin: a measure of circulating transferrin.

**Total Iron Binding Capacity (TIBC):** represents the amount of iron that can bind to transferrin to provide 100% saturation at the binding sites.
Erythropoietin (EPO): A glycoprotein hormone, secreted chiefly by the kidney which acts on the bone marrow cells to stimulate erythropoiesis (formation of red blood cells).

Erythropoietin Stimulating Agent (ESA): The manufactured version of a protein that may be administered to stimulate erythropoiesis in the absence of kidney function (e.g. Aranesp® or Eprex®).

3. **EQUIPMENT/ SUPPLIES:**
   3.1. CANN-NET Anemia Management Protocol: Hemoglobin/ESA Assessment (Page 1)
   3.2. CANN-NET Anemia Management Protocol: Iron/IV Iron Assessment (Page 2)
   3.3. CANN-NET Anemia Management Protocol: ESA Dosage Adjustment Tables (Page 3)
   3.4. CANN-NET Anemia Management Protocol: Anemia Management Log (Page 4)
   3.5. CANN-NET Anemia Management Protocol: ESA Hyporesponsiveness Chart (Page 5)

4. **PERSONNEL PERMITTED TO PERFORM PROCEDURE:**
   It is recommended that the following staff members complete the CANN-NET Anemia Management Protocol Staff Learning Module prior to employing the Anemia Management Protocol in everyday practice.
   4.1. REGISTERED NURSES *
   4.2. REGISTERED PHARMACISTS

* Other nurse categories may administer the anemia program subject to local renal program-specific policies and procedures.

5. **TARGETS:**
   5.1. Target Hemoglobin (Hgb) range is 95 -115 g/L.
   5.2. Target Iron Saturation % (TSAT) range is 20% - 49%.
6. CONTRAINDICATIONS:

6.1. Any patient with a known allergy to any of the following medications should not start the Anemia Management Protocol, UNLESS the renal program has access to alternative medications that are safe for the patient. (i.e: Patient has allergy to Darbepoetin, but Epoetin is available and patient has no known allergy to Epoetin). A physician should be consulted prior to administration.

I. Darbepoetin (Aranesp®)
II. Epoetin (Eprex®)
III. Sodium Ferric Gluconate (Ferrlecit®)
IV. Iron dextran (DexIron®)
V. Iron Sucrose (Venofer®)

6.2. Any patient deemed inappropriate by the physician (requiring a written order stating patient is not to commence Anemia Management Protocol).

6.3. Any patient receiving doses of Darbepoetin or Epoetin outside the defined dose range (greater than 150 mcg weekly of Darbepoetin or 10,000 units 3x weekly of Epoetin).

6.4. When a hemodialysis patient is admitted to hospital, the order to follow the Anemia Management Protocol is to be discontinued, unless specifically ordered to be continued (or resumed) by the attending physician.

7. POLICY:

7.1. Conditions:

I. A physician order is required to initiate Anemia Management Protocol. This order must include the specific ESA drug and initial dose.
   - Initial Iron dose should not be started until patient has had at least three (3) previous dialysis runs unless specifically ordered by the physician.

II. Patient anemia status assessment, utilizing the Anemia Management Protocol algorithms, will be completed every 4 (or 6) weeks (depending on the frequency with
which hemoglobin labs are measured) on the dialysis run following the drawing of patient’s regular bloodwork.

III. The patient must be an outpatient at the local hemodialysis centre or satellite clinic.

IV. When a hemodialysis patient is admitted to hospital, the order to follow the Anemia Management Protocol is to be discontinued, unless specifically ordered to continue by the attending physician.
   - Following patient discharge from hospital, an order from a physician is required to resume anemia protocol after a review of discharge ESA dose.

V. Dose adjustments will be made to achieve and maintain a target hemoglobin of 95-115 g/L.

VI. Dose adjustments for ESAs will not be made more frequently than every five weeks according to the Anemia Management Protocol Dosage Adjustment Tables, unless otherwise specified by the physician.

VII. If for any reason the patient is to stop the Anemia Management Protocol, an order is to be written by the physician to discontinue the protocol.

VIII. Hemoglobin and iron bloodwork values, actions to be taken, and other comments are to be charted on the Anemia Management Log at each assessment.

IX. In order to individualize and provide the best care for the patient, the physician may write orders to supplement the Anemia Management Protocol for that individual. If this occurs, confirmation with the physician should be made to determine if the Anemia Management Protocol is to be continued or discontinued.

X. Ensure the physician is notified where indicated within the Anemia Management Protocol.

7.2. Iron and ESA Medications:

I. The physician will determine which iron medication the patient will receive depending on locally available iron products: Sodium Ferric Gluconate (Ferrlecit®), Iron dextran (DexIron®), and Iron Sucrose (Venofer®).
Due to the current absence of a recommended maintenance dosage regimen for Ferumoxytol (Feraheme®), this product has been omitted from the CANN-NET Anemia Protocol. However, should the physician order this iron preparation and dosage, it could simply be inserted into Page 2: Assess Iron Status of the anemia protocol and tracked in the same manner on Page 4: Anemia Management Log.

II. If patient is on antibiotic therapy, iron therapy may be held until antibiotics are complete or the infectious process is resolved. Verification from a physician is required.

III. If a patient is being treated for an active malignancy, the Canadian Society of Nephrology (CSN) recommends using ESA therapy with great caution, if at all, and in particular when cure is the anticipated outcome.

IV. If a patient has experienced a stroke within the past 3 months, the Canadian Society of Nephrology (CSN) recommends using ESA therapy with great caution, and aiming for a lower target.

- The CSN suggests initiating ESA at a Hgb of 90 g/L and using a target Hgb range of 90-105 g/L in patients with a recent stroke; therefore the CANN-NET Anemia Management Protocol may be inappropriate for these patients and is at the discretion of the physician.

V. The physician will determine which ESA product the patient will receive, Epoetin alpha (Eprex®) or Darbepoetin alfa (Aranesp®).

VI. Dose adjustments will be made and determined by the nurse or pharmacist (refer to page 3 of protocol - Dosage Adjustment Tables).

VII. The recommended starting dose of Epoetin alpha (Eprex®) is 100 U/kg/wk and Darbepoetin alfa (Aranesp®) is 0.45 mcg/kg/wk.

VIII. The recommended maximum dose of Epoetin alpha (Eprex®) is 10,000 U 3x q weekly, and Darbepoetin alfa (Aranesp®) is 150 mcg q weekly.
7.3. Bloodwork:

I. All CKD patients require baseline bloodwork completed prior to initiation of the Anemia Management Protocol; relevant bloodwork (hemoglobin and iron) must be within previous two weeks.

II. Draw CBC, Ferritin, TSAT according to local practice and protocol.

III. N.B. If bloodwork has not been drawn, draw appropriate tests prior to adjusting and administering iron and erythropoietin as per the Anemia Management Protocol.

IV. Hemoglobin levels are drawn every 4 (or 6) weeks, (depending on the frequency with which hemoglobin labs are measured) but no sooner than every 2 weeks, unless clinically indicated. Iron bloodwork (Ferritin, TSAT) is drawn every 12 weeks, unless clinically indicated otherwise.

8. Modification of the CANN-NET Anemia Management Protocol:

We strongly recommend that the CANN-NET anemia protocol is implemented without changes, though you are free to use the ESA and iron products that your hemodialysis units normally use. This anemia protocol has been designed for hemodialysis units monitoring hemoglobin every 4 or 6 weeks, and monitoring iron bloodwork every 12 weeks.

Once hemodialysis units are familiar with the protocol, they may wish to make some modifications. For instance, some units currently using this anemia protocol have decided that physicians do not need to be notified when the ferritin is above 1000ug/l. To facilitate these types of minor changes, CANN-NET is pleased to provide modifiable protocols for your use.

9. EXTERNAL REFERENCES:


10. DEVELOPED BY:

CANN-NET acknowledges the significant contribution of the British Columbia Renal Agency and thanks them for generously allowing CANN-NET to adapt an updated anemia management protocol from the pre-existing and well-functioning BC 4-week Hemodialysis Anemia Protocol.

Dr. Scott Brimble, MD, MSc, FRCPC; Associate Professor, Division of Nephrology, Department of Medicine, McMaster University; Staff Nephrologist, St. Joseph’s Healthcare Hamilton, Hamilton, Ontario, Provincial Lead, Early Detection and Prevention of Progression, Ontario Renal Network.

Dr. Braden Manns, MD, MSc, FRCPC; Professor, Departments of Medicine and Community Health Sciences, University of Calgary; Staff Nephrologist, Foothills Medical Centre, Calgary, Alberta

Lauren Galbraith, BScH; Research Assistant, Division of Nephrology, Department of Medicine, University of Calgary

11. IN CONSULTATION WITH:

Dr. Louise Moist, MD, MSc, FRCPC; Associate Professor, Division of Nephrology, Schulich School of Medicine, University of Western Ontario; Lead Vascular Access, Ontario Renal Network; Staff Nephrologist, London Health Science Centre, London, Ontario

Dr. Dan Martinusen, BScPharm, PharmD, ACPR; Chair, Pharmacy and Formulary Committee, British Columbia; Clinical Pharmacy Specialist, Nephrology, Royal Jubilee Hospital, BC Provincial Renal Agency

Dr. Jennifer Macrae, MD, MSc, FRCPC; Associate Professor, Division of Nephrology and Department of Cardiac Sciences, University of Calgary; Medical Director for hemodialysis, home hemodialysis and vascular access for the Southern Alberta Renal Program; Staff Nephrologist, Foothills Medical Centre, Calgary, Alberta

Keyword Assignment: Anemia, Chronic Renal Failure, Algorithm