# Describing and Comparing Patient Factors Associated with Use of Parenteral Iron before and after Implementation of an Order Set for Parenteral Iron (DECODE IRON)

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## ABSTRACT

**Background:** In select clinical scenarios, IV administration of iron is suitable for management of iron deficiency anemia; however, for most patients, oral administration of iron is the mainstay of treatment. At the Red Deer Regional Hospital Centre, in Red Deer, Alberta, high utilization of IV iron has resulted in limited access to this medication for the treatment of ambulatory patients, as well as significant usage of health care resources.

**Objectives:** The primary objective was to compare patient characteristics, specifically pretreatment laboratory test results and previous use of oral iron, among those receiving IV iron therapy in an ambulatory setting before and after implementation of an iron sucrose order set. For secondary objectives, the aforementioned groups were compared with regard to meeting the diagnostic criteria for iron deficiency anemia, with or without pretreatment oral iron or blood transfusion, and the dosing characteristics for IV iron.

**Methods:** A retrospective electronic chart review was performed for ambulatory patients who received IV iron between January 1, 2020, and January 31, 2022.

**Results:** A total of 436 unique treatment courses were included in the analysis. The following pretreatment laboratory results were observed before and after implementation of the iron sucrose order set: mean hemoglobin 105.8 (standard deviation [SD] 21.9) g/L versus 102.2 (SD 18.5) g/L; mean of mean corpuscular volume (MCV) 82.2 (SD 9.4) fL versus 79.2 (SD 8.9) fL; and median ferritin 7 (interquartile range [IQR] 4–12) µg/L versus 6 (IQR 4–11) µg/L. Only the difference in MCV values was statistically significant ($p = 0.001$).

**Conclusions:** The implementation of an iron sucrose order set for ambulatory patients did not have a significant effect on pretreatment laboratory parameters among patients for whom IV iron was prescribed. Further stewardship initiatives could be beneficial in improving the appropriateness of IV iron use.

**Keywords:** iron deficiency anemia, iron sucrose, IV iron, parenteral iron

## RÉSUMÉ

**Contexte :** Dans certains scénarios cliniques, l'administration de fer par voie intraveineuse (IV) convient à la prise en charge de l'anémie ferriprive; cependant, pour la plupart des patients, l'administration de fer par voie orale constitue le pilier du traitement. Au centre hospitalier régional Red Deer, à Red Deer, en Alberta, l'utilisation élevée du fer par IV a entraîné un accès limité à ce médicament pour le traitement des patients ambulatoires, ainsi qu'une utilisation importante des ressources de santé.

**Objectifs :** L'objectif principal consistait à comparer les caractéristiques des patients, en particulier les résultats de tests de laboratoire avant traitement et l'utilisation antérieure de fer par voie orale, chez ceux recevant un traitement de fer par IV en milieu ambulatoire avant et après la mise en œuvre d'un protocole de prescription de fer sucrosé. Les objectifs secondaires, quant à eux, étaient la comparaison des groupes susmentionnés en ce qui concerne la satisfaction des critères diagnostiques de l'anémie ferriprive, avec ou sans prétraitement de fer administré par voie orale ou par transfusion sanguine, ainsi que les caractéristiques posologiques du fer administré par IV.

**Méthodes :** Un examen rétrospectif des dossiers électroniques a été réalisé pour les patients ambulatoires ayant reçu du fer par IV entre le 1er janvier 2020 et le 31 janvier 2022.

**Résultats :** Au total, 436 traitements uniques ont été inclus dans l'analyse. Les résultats suivants de tests de laboratoire avant traitement ont été observés avant et après la mise en œuvre du protocole de prescription de fer sucrosé : hémoglobine moyenne 105,8 g/L (écart type [ÉT] 21,9) contre 102,2 g/L (ÉT 18,5); moyenne du volume corpusculaire moyen (VCM) 82,2 fL (ÉT 9,4) contre 79,2 fL (ÉT 8,9); et ferritine médiane 7 µg/L (intervalle interquartile [IIQ] 4–12) contre 6 µg/L (IQR 4–11). La seule différence statistiquement significative concernait les valeurs VCM ($p = 0,001$).

**Conclusions :** La mise en œuvre d'un protocole de prescription de fer sucrosé pour les patients ambulatoires n'a pas eu d'effet significatif sur les paramètres biologiques avant traitement chez les patients pour lesquels du fer par IV a été prescrit. D'autres initiatives de gestion pourraient être bénéfiques pour améliorer la pertinence de l'utilisation du fer IV.

**Mots-clés :** anémie ferriprive, fer sucrosé, fer IV, fer parentéral

## INTRODUCTION

Anemia affects approximately 1 to 2 billion people worldwide, with about 50%–80% of cases being due to iron deficiency anemia (IDA).[1-5] The causes of IDA include blood loss, inadequate iron intake, malabsorption of iron, and increased iron requirements, such as in pregnancy.[2,4-6] The most common symptoms are fatigue, weakness, pallor, and dyspnea on exertion.[2,4-6] The diagnosis of IDA is characterized by values for serum ferritin, hemoglobin (Hb), and mean corpuscular volume (MCV) below guideline-designated thresholds, with other iron studies, such as iron saturation and total iron binding capacity, also being used, particularly in cases where ferritin may be falsely elevated.[2,4-10]

Management of IDA includes identifying and addressing the underlying cause of iron deficiency and replenishing iron stores through supplementation, by either the oral or parenteral route.[10] Most guidelines recommend oral administration of iron as the preferred initial treatment for IDA in the majority of patients with uncomplicated IDA, because oral dosage forms are less expensive and more convenient than IV iron, while still being safe and effective.[2,5,7, 9-15] IV iron therapy is preferred over oral iron for selected patients, including those with concurrent inflammatory bowel disease, those with moderate to severe chronic kidney disease, and those with iron deficiency alongside symptomatic heart failure with reduced ejection fraction.[1,9,11,12,15-19]

Oral iron is inexpensive, readily accessible, and easily administered but can cause gastrointestinal adverse effects, such as nausea and constipation.[1,11] The IV form is associated with fewer gastrointestinal adverse effects and allows the patient to reach their Hb target level more quickly.[20,21] These benefits must be balanced against the pharmacoeconomic and health care resource impacts, as well as the risks associated with IV access and potential infusion reactions.[1]

In Canada, the costs of IV iron have been rising, and an environmental scan by CADTH (Canada's drug and health technology agency) stated that attempts to be more judicious with IV iron through the use of a standardized order form "have not yielded a decrease in utilization or cost."[22] The 2017 *Iron Summit Conference Report* stated that parenteral iron represents 4% of the total Alberta Health Services budget for ambulatory pharmacology, having grown 22% over the prior 2 years.[23] Iron sucrose is among the top drugs, in terms of expenditures, for Alberta Health Services, with utilization increasing year over year since 2015 (unpublished data).

Available research evaluating IV iron stewardship is sparse. A retrospective chart review of inpatients in a French hospital, published in 2018, reported that for 32 of the 89 study patients who received iron, there were no obvious reasons why IV iron had been used instead of an oral product.[24] A retrospective chart review of the use of IV iron in Calgary hospitals, conducted in 2018, found that, according to the 2018 Toward Optimized Practice (TOP) IDA guideline,[10] 648 (47.9%) of 1352 patients met the laboratory criteria for IDA diagnosis, and only 146 (20.1%) of the 726 patients in the inpatient cohort received IV iron in alignment with guideline recommendations.[25] These findings indicate that IV iron may have been overprescribed at these hospitals. The literature also shows that standardized order sets can lead to improved patient outcomes. For example, a systematic review of the literature up to 2009 evaluated the effects of order sets as the primary intervention for hospitalized patients and showed that most order sets led to positive outcomes, although the evidence was typically of lower quality.[26] This result was taken as further support for initiation of an iron sucrose order set at our hospital.

In February 2021, a mandatory iron sucrose order set (Appendix 1) was developed for the ambulatory Medical Day Room in our regional 370-bed Alberta Health Services hospital. The new order set incorporated guidance for prescribing IV iron that aligned with the 2018 TOP IDA guideline.[10] Before 2021, typical practice was for the hospital pharmacy to provide IV iron to the Medical Day Room upon request, with minimal restrictions. Pharmacy ensured appropriate dosing, using the Ganzoni equation to calculate the total dose required for iron repletion, and Medical Day Room staff booked patients for the number of iron infusions required to achieve the repletion dose. Development and implementation of the order set was a quality improvement, stewardship-based initiative undertaken in response to concerns about the increasing use of IV iron for ambulatory patients without robust screening for relevant laboratory values, comorbidities, or previous oral iron use, which had in turn led to problems with accessibility in the Medical Day Room. The new order set was implemented with the hope that IV iron would be prescribed only if the patient met the 2018 TOP IDA guideline recommendations for prescribing of IV iron or had contraindications to oral iron.

Before implementation of this order set, physicians prescribed IV iron for patients in the Medical Day Room with no criteria, restrictions, or guidance as to when oral iron should be used instead. Given the high costs and resources associated with IV administration of iron, ensuring its judicious use and optimizing oral iron therapy as an alternative could have a profound impact in terms of saving health care costs and increasing patients' access to ambulatory care.

The goal of this study was to describe and compare the population of adult ambulatory patients without chronic kidney disease who received iron sucrose, in terms of Hb, MCV, ferritin, and previous use of oral iron, in the periods before and after implementation of the iron sucrose order set. Secondary objectives were to compare the aforementioned groups with regard to whether they met the diagnostic criteria for IDA, with or without receiving pretreatment with oral iron or blood transfusions, and iron sucrose dosing characteristics.

## METHODS

### Study Design

A retrospective electronic chart review was performed for all ambulatory patients who received IV iron in the Medical Day Room of the Red Deer Regional Hospital Centre in Red Deer, Alberta, between January 1, 2020, and January 31, 2022. Ethics approval was obtained from the University of Alberta Health Research Ethics Board (ID Pro00115467), with granting of a waiver of consent.

### Study Population

The order set was implemented on February 8, 2021. Included in the analysis were treatment courses that began in the pre-implementation period (March 17, 2020, to February 7, 2021) and the post-implementation period (February 8, 2021, to December 31, 2021). The overall study period began a few weeks before the pre-implementation period and ended a few weeks after the post-implementation period to ensure capture of pertinent data for the treatment courses analyzed. Patients were included in the study if they were 18 years of age or older. Patients were included more than once if they had multiple distinct treatment courses, where a treatment course was defined as all doses of iron sucrose dispensed to a patient within 45 days of the previous dose. The 45-day threshold was based on discussion with Medical Day Room staff about the maximum interval between doses in a treatment course. Previous use of oral iron was defined by evidence of any dispensing of oral iron (as observed in the Pharmaceutical Information Network of Alberta Health Services, an electronic database capturing dispensed prescriptions for ambulatory patients and schedule II drug products in Alberta) in the 120 days before IV iron administration.

Patients with a documented estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73 $m^2$ according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation were excluded because prescribing guidelines for IV iron for patients with low eGFR[27] are different from the guidelines in the order set.

### Data Sources and Data Collection

Patients and treatment course details were retrieved from a medication search report in the pharmacy's Meditech system (Medical Information Technology, Inc). Laboratory values (eGFR, Hb, ferritin, and MCV) and dates of blood transfusions were obtained through Alberta Health Services Analytics, Data Integration, Measurement & Reporting. Dispensing data for oral iron were obtained through the Pharmaceutical Information Network.

### Outcomes

The primary outcome was a composite of the differences between treatment courses before and after implementation of the order set in terms of mean or median pretreatment Hb, MCV, and ferritin and the proportion of patients who received oral iron before IV iron. This outcome was constructed to demonstrate any differences in the "appropriateness of prescribing" in the absence of reliable symptom data. The various aspects compared were considered co-primary outcomes, with use of pretreatment laboratory values closest to the date of the first dose of IV iron.

The following secondary outcomes were also considered:

- The proportion of treatment courses that met the diagnostic criteria in the 2018 TOP IDA guideline[10] (for men, Hb < 135 g/L and at least one of the following: MCV < 75 fL or ferritin < 30 μg/L; for women, Hb < 120 g/L and at least one of the following: MCV < 75 fL or ferritin < 13 μg/L).[10] Where a pretreatment laboratory value was unavailable, then the missing element was deemed to have not met the diagnostic criterion.
- The proportion of treatment courses for which the patient met the aforementioned laboratory criteria and had either an oral iron trial in the previous 120 days or a blood transfusion in the previous 90 days.
- The proportion of treatment courses that did not meet the diagnostic criteria, but had evidence of a blood transfusion.
- Comparison of IV iron dispensing characteristics between pre-implementation and post-implementation groups, specifically the total dose of iron dispensed per treatment course and the number of iron sucrose doses dispensed per patient in a treatment course.

### Statistical Analysis

Outcomes were described using descriptive statistics. Categorical variables were presented using proportions and frequencies. Continuous variables were presented using means and standard deviations (SDs) for variables that were normally distributed or medians and interquartile ranges (IQRs) for those that were not normally distributed. Variables described using mean values were compared using an unpaired 2-sample *t* test, whereas medians were compared using the Mood median test. The proportions of treatment courses with a trial of oral iron were compared using a 2-proportion *z* test. Statistical analyses were performed with Microsoft Excel spreadsheet software.

## RESULTS

Of 2205 doses of IV iron initially identified, 436 treatment courses were included for analysis after screening: 208 in the pre-implementation period and 228 in the post-implementation period (Figure 1). Baseline characteristics are shown in Table 1.

Across both study periods, a total of 71 treatment courses were missing one or more pretreatment laboratory values. More specifically, 12 (5.8%) of the 208 pre-implementation treatment courses did not have Hb or MCV values,

and 19 (9.1%) were missing ferritin values. In the post-implementation group, 50 treatment courses (21.9%) had no Hb or MCV values, and 52 (22.8%) were missing ferritin values. Treatment courses with missing laboratory values were excluded from calculations involving these variables.

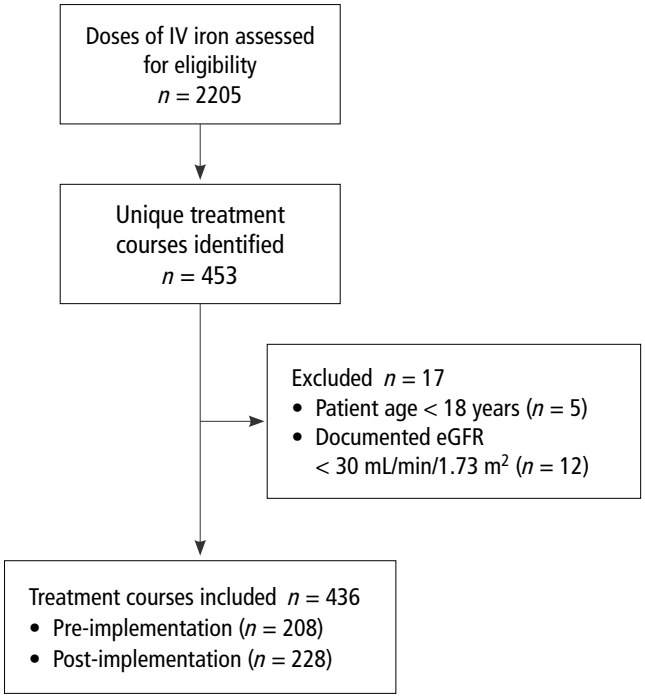


**FIGURE 1.** Study inclusion flow chart. IV = intravenous, eGFR = estimated glomerular filtration rate.

Pretreatment laboratory results are shown in Table 2. The differences in mean Hb and median ferritin between the pre-implementation and post-implementation groups were not statistically significant, whereas the difference in mean MCV was statistically significant.

In the pre-implementation group, 23 treatment courses (11.1%) had evidence of an oral iron trial within 120 days before the patient's first IV iron dose. In the post-implementation group, 18 treatment courses (7.9%) had evidence of a previous trial of oral iron. This difference was not statistically significant ($p = 0.26$).

In the pre-implementation group, 120 (57.7%) of the treatment courses met the diagnostic criteria for IDA, compared with 130 (57.0%) in the post-implementation group. Of the 186 treatment courses not meeting the IDA criteria (over the entire study period), 142 (76.3%) had Hb values either above threshold ($n = 80$, 56.3%) or missing ($n = 62$, 43.7%).

We determined the proportions of treatment courses for ambulatory patients that met both of the preceding requirements for appropriate iron sucrose therapy (i.e., oral iron dispensed within the previous 120 days and diagnostic criteria for IDA) and found that only 12 (5.8%) of the 208 courses in the pre-implementation group and 13 (5.7%) of the 228 courses in the post-implementation group would have qualified for IV iron according to these criteria. There was no statistically significant difference between the groups when blood transfusions received before IV iron therapy were taken into account as a surrogate indicator of clinically significant anemia, and only 21 (4.8%) of the

**TABLE 1. Patient Characteristics before and after Implementation of an Iron Sucrose Order Set[a]**

| Characteristic | Pre-implementation Treatment Courses ($n = 208$) | Post-implementation Treatment Courses ($n = 228$) |
|---|---|---|
| Patient age (years) (median and IQR) | 48 (36–63) | 47 (36–63) |
| Patient sex, female (no. and %) | 172 (82.7) | 196 (86.0) |
| Blood transfusion within 90 days before first dose of IV iron (no. and %) | 13 (6.3) | 13 (5.7) |

IQR = interquartile range.
[a]Data are presented in terms of IV iron treatment courses. Some patients are represented more than once, because they had multiple eligible courses of IV iron therapy in the study period.

**TABLE 2. Pretreatment Laboratory Values[a]**

| Variable | Pre-implementation Treatment Courses | Post-implementation Treatment Courses | *p* Value |
|---|---|---|---|
| Hemoglobin (g/L) (mean ± SD) | 105.8 ± 21.9 ($n = 196$) | 102.2 ± 18.5 ($n = 178$) | 0.08 |
| MCV (fL) (mean ± SD) | 82.2 ± 9.4 ($n = 196$) | 79.2 ± 8.9 ($n = 178$) | 0.001 |
| Ferritin (µg/L) (median and IQR) | 7 (4–12) ($n = 189$) | 6 (4–11) ($n = 176$) | 0.77 |

IQR = interquartile range, MCV = mean corpuscular volume, SD = standard deviation.
[a]Data are presented in terms of IV iron treatment courses. Some patients are represented more than once, because they had multiple eligible courses of IV iron therapy in the study period.

treatment courses met the diagnostic criteria for IDA while also having evidence of a recent blood transfusion.

Iron dispensing characteristics are shown in Table 3. The median total dose (mg) of iron per treatment course was significantly lower in the post-implementation group ($p < 0.001$). There was also a decrease in the total number of IV iron doses dispensed: 939 doses across all pre-implementation treatment courses and 830 doses across all post-implementation treatment courses.

## DISCUSSION

This study aimed to describe and compare IV iron treatment courses for ambulatory patients, before and after implementation of an iron sucrose order set.

Overall, the distribution of relevant laboratory values between study periods was similar, with no clinically significant change observed after implementation of the order set. This finding implies that the order set did not lead to any change in baseline characteristics among patients referred for IV iron therapy, as it was designed to do. Dispensing of oral iron before IV iron therapy was also similar (no statistically significant difference) before and after implementation of the order set. The low proportion of treatment courses with prior trialling of oral iron, both before and after implementation of the order set, suggests that IV iron may be frequently prescribed irrespective of the patient's tolerance of or treatment success with oral iron. Furthermore, the proportion of treatment courses meeting the diagnostic criteria for IDA in the 2018 TOP guideline was similar in the 2 study periods. More than 40% of treatment courses in each period did not meet the criteria for IDA, albeit with a large proportion of treatment courses failing to meet the criteria because of missing laboratory values (16.3%). These results demonstrate that implementation of the order set did not have the intended effect, and thus there may be a large proportion of individuals for whom IV iron is being prescribed even though it is not the first-line treatment option.

The presence or absence of anemia symptoms is an important consideration in determining the appropriateness of IV iron therapy. The TOP guideline suggests that IV iron may be appropriate as first-line therapy for patients who have confirmed IDA and Hb less than 100 g/L and who are symptomatic (shortness of breath, chest pain, lightheadedness, syncope, or suspected ongoing bleeding).[10] Given the retrospective nature of this study and the limited information available in patients' charts, the presence of anemia symptoms before IV iron treatment could not be determined for the study population. Instead, we reviewed the number of treatment courses that met the IDA diagnostic criteria alongside evidence of oral iron dispensing or blood transfusion, from which we could infer that IV iron had been prescribed according to guidelines. The proportion of treatment courses with a previous trial of oral iron or previous blood transfusion was similarly low in both groups; however, this does not necessarily indicate that IV iron was prescribed injudiciously in these patients. If patients are showing symptoms of anemia, it may be appropriate to use IV iron as first-line therapy, without attempting oral therapy. Given that less than 5% of all treatment courses met IDA diagnostic criteria and also had evidence of recent blood transfusion, it is unlikely that pretreatment laboratory values were inflated by transfusions.

Although implementation of the order set does not appear to have had a significant impact on the number of patients with pretreatment trial of oral iron or on ensuring that current Hb, ferritin, and/or MCV values correspond with an IDA diagnosis, the order set may have helped to limit the amount of IV iron ordered by prescribers, given the statistically significant decrease in median total dose per treatment course. There was also a decrease in the total amount of IV iron dispensed after the order set was implemented. However, these reductions do not necessarily demonstrate improvement in IV iron stewardship, given that the percentage of treatment courses that followed the TOP IDA guideline remained essentially unchanged. Furthermore, we could not determine whether the decrease in IV iron prescribed per treatment course was attributable more to a change in dosing assessment (with potential underdosing) or to the order set. This also makes the decrease in total amount of IV iron dispensed unreliable, in terms of determining a direct correlation with the order set.

This study had some limitations that bear mentioning. The retrospective study design precluded detailed evaluation of patients' anemia symptoms, and determination of the appropriateness of IV iron therapy was hindered by

**TABLE 3. Dispensing Characteristics of Iron Sucrose[a]**

| Characteristic | Pre-implementation Treatment Courses (*n* = 208) | Post-implementation Treatment Courses (*n* = 228) |
|---|---|---|
| Total dose of iron per treatment course (median and IQR) | 1200 (900–1600) mg | 900 (600–1200) mg |
| No. of doses per treatment course (median and IQR) | 4 (3–6) doses | 4 (2–5) doses |

IQR = interquartile range.

[a]Data are presented in terms of IV iron treatment courses. Some patients are represented more than once, because they had multiple eligible courses of IV iron therapy in the study period.

reliance on the limited amount of clinical documentation that was available; in this regard, we reviewed the order sets completed by physicians and found that the data available did not include symptoms, diagnosis, or prior oral iron therapy. Use of oral iron was captured from administrative data only and was not confirmed through patient interviews. Therefore, it is possible that for some patients, oral iron was dispensed without being included in the dispensing record, which would lead to an underestimate of oral iron trials. Furthermore, adherence and duration of use of oral iron could not be captured. Relevant comorbidities for which IV iron is more broadly indicated, without a previous trial of oral iron, were not identified, which hindered our ability to analyze appropriateness. The number of missing laboratory values may have affected the statistical analyses, given the larger-than-expected proportion of treatment courses with no pretreatment laboratory values. For example, only those with documented eGFR less than 30 mL/min/1.73 $m^2$ were excluded, but there may have been patients with no available eGFR who would have met the exclusion criteria. Lastly, the study was conducted during the COVID-19 pandemic, which could have had implications for the number of patients or appointments for IV iron therapy, given the hospital's efforts to limit non-urgent appointments. Although the COVID-19 pandemic may have affected some patients' ability to have samples drawn for laboratory testing, the high proportion of treatment courses with missing values suggests that IV iron may frequently be prescribed on the basis of historical laboratory data.

The order set included stringent criteria for pertinent pretreatment laboratory values and previous oral iron trials, and it is therefore possible that the lack of changes observed in these parameters may have been due to ineffective enforcement of the order set. Post hoc observations indicated that clinic staff were not strictly enforcing adherence to the order set, but rather were using it more as a suggestion for prescribers. Although the body of literature on IV iron stewardship is small, the results of this study are comparable to those of the 2018 chart review conducted in Calgary, which also found that a large proportion of patients did not meet the criteria for IDA.[25] Together, the results of these studies show that iron stewardship is not just a local issue, and that direct intervention, rather than passive intervention, is likely needed for change to occur.

## CONCLUSION

Building upon previous iron deficiency and supplementation research conducted in Alberta,[25] this study evaluated the effect of a new iron sucrose order set, with robust prescribing criteria, on the use of IV iron in an ambulatory setting. Implementation of the order set did not significantly affect pretreatment characteristics of patients who received IV iron, including relevant pretreatment laboratory parameters, previous trials of oral iron, and proportion of patients meeting diagnostic criteria for IDA. These results suggest that further strategies to optimize prescribing of IV iron could be beneficial in ensuring its judicious use and could lead to cost savings for the health care system. Such strategies might include increasing education to prescribers about iron stewardship or considering formulary restriction of IV iron to individuals with evidence of enhanced efficacy and/or when a reasonable trial of oral iron has been ineffective or not tolerated.

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**Competing interests:** None declared.

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## APPENDIX 1 (part 1 of 2). Iron sucrose order form created for use in the Medical Day Room of the Red Deer Regional Hospital Centre.[a]

**Check the following as applicable for iron sucrose indication**

**Comorbidities** (check if answer "yes" to any of the following)

- Chronic kidney disease (dialysis-dependent and/or requiring erythrocyte-stimulating agents for CKD-anemia)
- Ongoing bleeding (eg., menorrhagia, cancer, GI source)
- Malabsorption syndrome (e.g., inflammatory bowel disease, Celiac disease, bariatric surgery)
- Symptomatic heart failure with reduced ejection fraction (LVEF less than or equal to 40%) and low iron (ferritin less than 100 mcg/L or ferritin 100–299 mcg/L and TSAT less than 20%)

***If checked "yes" to any of the above, proceed to iron sucrose dosing section****

**Laboratory Criteria for Iron Deficiency Anemia (IDA)** (check all of the following that apply):

Low hemoglobin (Hb) and low ferritin below reference ranges are required to meet diagnostic criteria for IDA

- Hb less than 100 g/L ***AND*** symptomatic of IDA (dyspnea, chest pain, light-headed, syncope/presyncope, ongoing bleeding)

**OR**

- Hb less than 60 g/L

**AND:**

- Ferritin less than 30 mcg/L (male); less than 13 mcg/L (female)

***If above criteria are not met, proceed to next section, otherwise proceed to iron sucrose dosing section****

**Pregnant?** ☐ yes / ☐ no ***If checked "no", skip to next section regarding previous oral iron use***

Is patient beyond 14 weeks gestational age? ☐ yes / ☐ no

***If less than 14 weeks gestational age, iron sucrose is contraindicated****

If greater than 14 weeks gestational age, check all of the following that apply (at least 1 of the following required):

- Most recent Hb less than 80 g/L AND ferritin less than 30 mcg/L
- IDA diagnosed at greater than 34 weeks gestational age with Hb less than 110 g/L AND ferritin less than 30 mcg/L
- Failed an adequate trial of oral iron (minimum of 4 weeks with Hb increase less than 20 g/L)
- Patient did not tolerate at least 1 oral iron regimen:

*Oral iron formulations trialed. Include dose(s), duration, and reason(s) for failed trial:*

1. _____
2. _____

**Has Patient Previously Trialed Oral Iron?**

☐ Yes. Select all of the following that apply:

- Inadequate response (Hb increase less than 10 g/L after minimum 12 weeks of oral iron therapy)
- Hb continues to decline to less than 90 g/L while adherent to oral iron therapy
- Patient did not tolerate a reasonable trial of at least 2 different oral iron regimens

*Oral iron formulations trialed. Include dose(s), duration, and reason(s) for failed trial:*

1. _____
2. _____

☐ No. *Oral iron therapy should be considered prior to initiating iron sucrose.* An adequate oral iron trial must include at least 60 mg of elemental iron daily for at least 12 weeks to show evidence of Hb improvement and replenish iron stores.

## APPENDIX 1 (part 2 of 2). Iron sucrose order form created for use in the Medical Day Room of the Red Deer Regional Hospital Centre.[a]

**Iron Sucrose Dosing**

*Consider using the Ganzoni formula to calculate total iron deficit (mg) and determine iron repletion dose; available from AHS provincial parenteral monograph for iron sucrose or at: https://www.mdcalc.com/ganzoni-equation-iron-deficiency-anemia.*

- Iron sucrose (Venofer) 200 mg in 100 mL 0.9% sodium chloride IV over at least 15 minutes
- Iron sucrose (Venofer) 300 mg in 250 mL 0.9% sodium chloride IV over at least 90 minutes
- Other: _____
- Repeat the above IV iron dose every _____ week(s) × _____ (number of weeks)

*****Medical Day Room will not provide iron sucrose infusions of greater than 300 mg/infusion to avoid prolonged administration time and to facilitate appointment booking*****

**Pre-Medication (Optional)**

| | |
|---|---|
| ☐ DiphenhydrAMINE (Benadryl®) 50 mg IV or PO × 1 | ☐ 30 minutes prior **OR** ☐ PRN during or after infusion |
| ☐ MethylPREDNISolone (Solu-Medrol®) 125 mg IV × 1 | ☐ 30 minutes prior **OR** ☐ PRN during or after infusion |
| ☐ Acetaminophen (Tylenol®) 650–1000 mg PO × 1 | ☐ 30 minutes prior **OR** ☐ PRN during or after infusion |

**Patient Monitoring**

*Anaphylaxis from iron sucrose is exceedingly rare (less than 1%); however, isolated symptoms of hypersensitivity (e.g., IV site irritation, urticaria, nausea, diarrhea, abdominal pain) or "Fishbane reactions" resulting from free iron (e.g., facial flushing, chest tightness, joint pains) may occur. These patients may be treated by pausing the infusion, providing an H1 antagonist, and resuming the infusion at a slowed rate if symptoms resolved.*

- Vital signs prior to infusion, post-infusion, and as per the AHS parenteral monograph.
- Observe patient for 30 minutes after the infusion for signs/symptoms of hypersensitivity.
- Provide teaching: delayed reactions occurring more than 30 min after the end of infusion are rare; however, may occur as late as 24-48h after initiating iron infusion. Symptoms are generally mild and self-limiting. Patient to contact ordering provider if symptoms persist or proceed to emergency department for urgent concerns.

**Post Iron Replacement Laboratory Monitoring**

- Ordering provider to provide patient with a laboratory requisition for CBC and ferritin samples to be drawn 2–4 weeks after the last iron sucrose infusion. Results to prescriber. Note: Medical Day Room staff will not receive or review results.
  - Optional: iron studies
- Notify prescriber when orders have been completed.

**Other Important Information**

- See AHS Drugs and Therapeutic Backgrounders for assistance with iron dosing and administration, strategies to optimize oral iron absorption and tolerability, and considerations for iron replacement in specific patient populations
  - Available from AHS Insite > Teams > Pharmacy Services > Publications > Drugs & Therapeutics Backgrounder [internal resource]

AHS = Alberta Health Services, CBC = complete blood count, CKD = chronic kidney disease, GI = gastrointestinal, Hb = hemoglobin, LVEF = left ventricular ejection fraction, TSAT = transferrin saturation.

[a]Form in use at the time of the reported study; use of this form has since been discontinued in favour of another system.