



SABM[®]
SOCIETY FOR THE ADVANCEMENT
OF BLOOD MANAGEMENT

ANEMIA IN THE PRESURGICAL PATIENT

RECOGNITION, DIAGNOSIS
AND MANAGEMENT

New Insights and Concepts
for the Primary Care Provider

“Anemia is a significant and modifiable risk factor for increased perioperative morbidity and mortality and should be diagnosed and treated before elective surgery.”

Irwin Gross, M.D., Senior Medical Advisor, Accumen, Inc., San Diego, CA

WHAT IS THE UNMET NEED IN SURGICAL PATIENTS?

ANEMIA IS EPIDEMIC – A COMMON COMPLICATION OF COMMON DISEASES

- 30-60% of patients with rheumatoid arthritis.
 - 30-80% of patients with inflammatory bowel disease.
 - 30-50% of patients with chronic heart failure.
 - 20-40% of diabetics without overt renal failure.
 - 40-60% of patients with chronic kidney disease.
- All of these are related to iron absorption and metabolism.

“Anemia is so common that it’s becoming accepted as normal. Many physicians are under the misconception that anemia is relatively harmless and best managed with transfusion when symptomatic.”

WHY CARE (MORE) ABOUT ANEMIA?

ANEMIA IS A SIGNIFICANT MODIFIABLE RISK FACTOR IN SURGICAL PATIENTS

PREVALENCE OF UNDIAGNOSED ANEMIA

At least 1/3 of patients undergoing non-emergent surgical procedures have potentially treatable anemia.¹

ANEMIA INCREASES PERIOPERATIVE MORBIDITY AND MORTALITY

A large retrospective study of almost 8000 non-cardiac surgical patients found that the prevalence of preoperative anemia was almost 40%. Preoperative anemia was associated with a nearly five-fold increase in the odds of postoperative mortality.²

Even mild preoperative anemia (Hb 10-12 g/dL in women; 10-13 g/dL in men), is independently associated with a 41% increased risk of mortality and a 31% increase in morbidity in patients undergoing major non-cardiac surgery. Perioperative transfusion is associated with an additional increase in morbidity and mortality.³

PREOPERATIVE ANEMIA IS THE MOST FREQUENT PREDICTOR OF PERIOPERATIVE TRANSFUSION⁴

A systematic review of 62 studies shows that preoperative anemia is the most frequent predictor of perioperative transfusion. Other factors include advancing age, female gender, and small body size.

“There is a common misconception that transfusion should be the default management strategy for anemia, that it is low risk, high benefit, despite robust clinical evidence to the contrary.”

PREOPERATIVE ANEMIA DIAGNOSIS AND TREATMENT IMPROVES PATIENT OUTCOMES⁵⁻⁷

- Improves readiness for surgery.
- Reduces transfusion risk in the perioperative period.
- Reduces anemia and transfusion associated morbidity and mortality.
- Helps identify co-morbidities.
- Effective clinical management of anemia improves patient outcomes in chronic diseases (e.g., chronic heart failure, chronic kidney disease, inflammatory bowel disease, rheumatoid arthritis, etc).
- Anemia may be an indicator of an undiagnosed underlying disease process (e.g., iron deficiency suggesting occult malignancy).

WHAT LABORATORY TESTS ARE NEEDED FOR A PRESURGICAL ANEMIA EVALUATION?

GOALS OF PREOPERATIVE ANEMIA LABORATORY TEST ALGORITHM

- Allow diagnosis of common causes of anemia.
- Avoid the need for patients to return for another blood sample.
- Draw CBC and sample for additional testing to “hold” for additional tests if needed.
- Eliminate unnecessary lab studies.

FIRST TIER LABORATORY TESTS

Complete Blood Count (CBC)

Reticulocyte Count

- Absolute reticulocyte count.
 - Reticulocyte hemoglobin content if available (a functional measure of iron status).
-

Vitamin B12

Folate

FIRST TIER LABORATORY TESTS

Iron Studies

- Transferrin Saturation.
 - Ferritin.
 - Iron.
 - Iron Binding Capacity.
-

Serum Creatinine

Additional studies predicated on initial test results, or if a diagnosis cannot be made based on initial tests:

SECOND TIER LABORATORY TESTS

Thyroid Stimulating Hormone (TSH)

Direct Antiglobulin Test

C-Reactive Protein

Soluble Transferrin Receptor

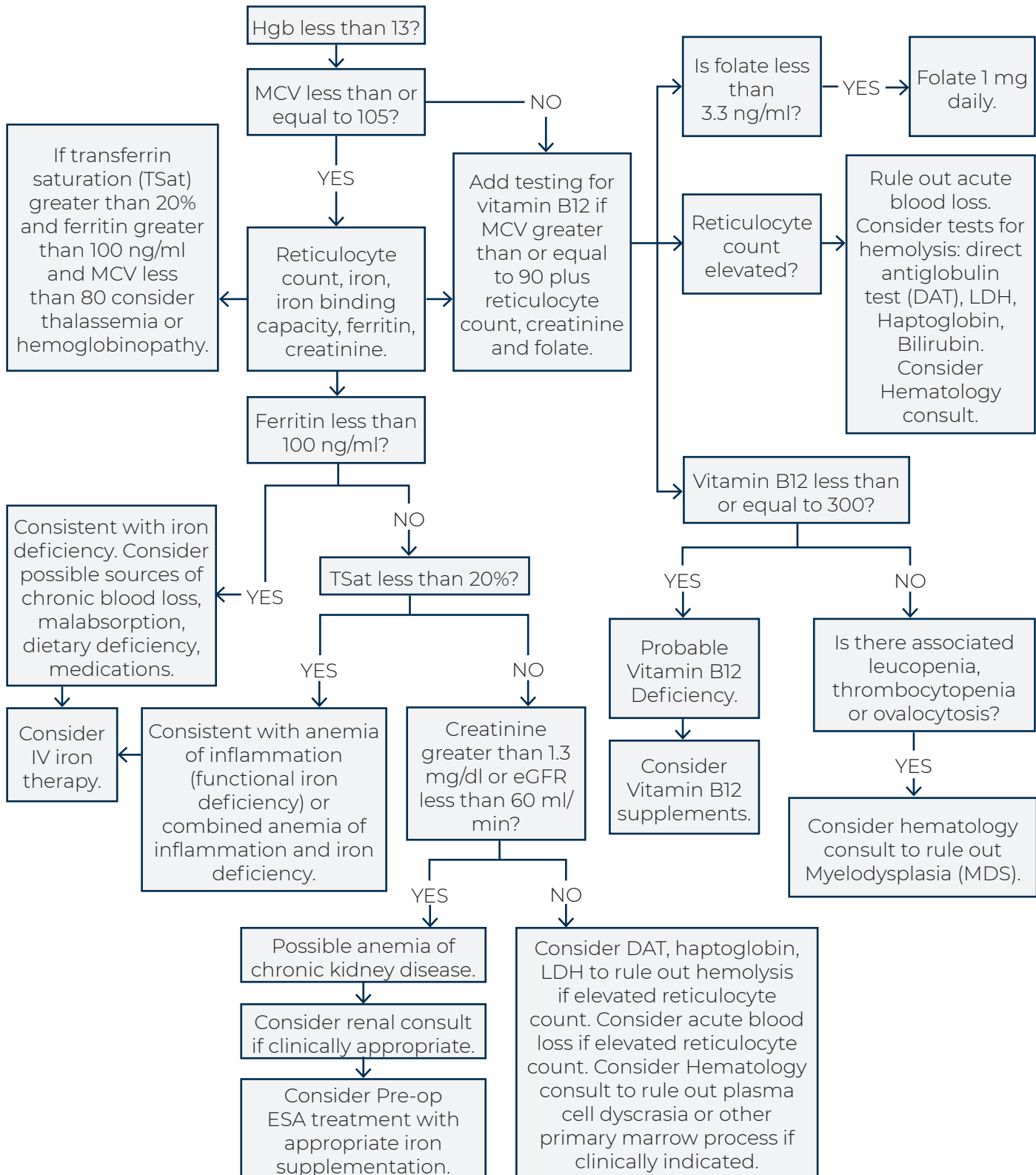
Methyl Malonic Acid

Serum Protein Electrophoresis

Erythropoietin

Haptoglobin

PREOPERATIVE ANEMIA MANAGEMENT ALGORITHM



NOTES TO PREOPERATIVE ANEMIA MANAGEMENT ALGORITHM:

1. If absolute iron deficiency is detected and cause is unknown, gastroenterologist or other appropriate referral to rule out malignancy as a source of chronic blood loss is indicated.⁸
2. If ferritin, iron saturation values, or both or other markers of iron-restricted erythropoiesis are inconclusive, further evaluation to rule out iron deficiency or iron sequestration due to inflammation/chronic disease may be necessary.⁸
3. A therapeutic trial of oral iron therapy would confirm absolute iron deficiency but may be impractical in the presurgical patient. No response to iron therapy may not rule out absolute iron deficiency because of patient non-compliance, ongoing blood (iron) losses in excess of oral iron absorption, and/or diminished gastrointestinal absorption and transport of iron due to inflammation.⁸
4. Anemia in the setting of decreased transferrin saturation (< 20%) in the setting of decreased glomerular filtration rate (GFR < 60) will often respond to intravenous iron. Referral to a nephrologist may be indicated.⁸
5. Additionally, iron-restricted erythropoiesis due to iron sequestration, functional deficiency, or both must be considered.⁸

WHAT ANEMIA TREATMENT STRATEGIES SHOULD BE CONSIDERED FOR THE ANEMIC PRESURGICAL PATIENT?

CORRECT NUTRITIONAL DEFICIENCIES

IRON THERAPY

- Choice of therapy is based on:
 - Timescale before surgery.
 - Tolerance of oral iron.
 - Iron status.
- Consider oral iron if:
 - Adequate time (2-4 months).
 - No ongoing blood loss.
 - No inflammatory process or co-morbidity.
 - Normal GFR.
 - Patient is tolerant.

NOTE: Relatively slow iron repletion with a high incidence (30-40%) of gastrointestinal intolerance; co-morbid inflammatory states reduces iron uptake. Need to re-evaluate anemia studies 4 weeks before surgery to determine effectiveness.
- Intravenous iron is the most common intervention in presurgical anemia.
 - Better tolerated and much faster than oral iron.
 - Effective—even in inflammation.
 - Less expensive than ESAs.
- Vitamin B12.
- Folate.
- Erythropoiesis Stimulating Agents (ESA).
 - When nutritional anemia has been ruled out and/or corrected.
 - Use conservatively, lowest dose and shortest administration time.
 - Prescribe supplemental iron throughout the course of ESA therapy to optimize presurgical red blood cell production and minimize ESA-induced functional iron deficiency.
 - ESA therapy combined with supplemental iron may reduce the subsequent need for blood transfusion.

TREAT COMORBIDITIES

DELAY SURGERY IF NECESSARY TO OPTIMIZE SURGICAL OUTCOME AND REDUCE TRANSFUSION RISK

NOTE: EXPECTED HEMOGLOBIN OPTIMIZATION RESPONSE TO ANEMIA TREATMENT

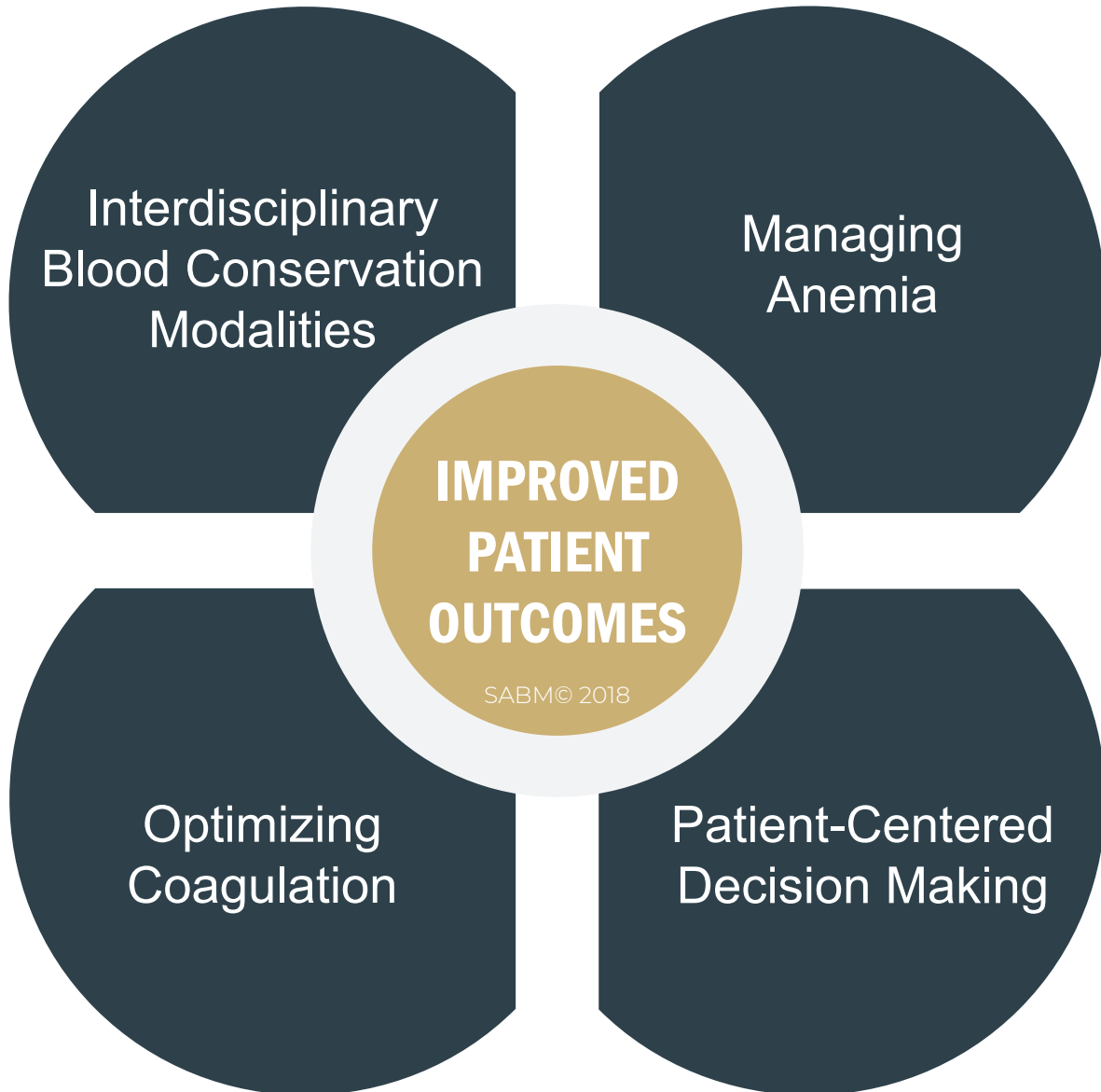
Most patients can expect to have a hemoglobin rise between 0.5g/dL- 1.0g/dL per week with use of IV iron and or ESA therapy as per prescribing information.

	IRON DEXTRAN	IRON SUCROSE	FERRIC GLUCONATE	FERUMOXYTOL	FERRIC CARBOXYMALTOSE
Trade Name(s)	InFeD (Sanofi Aventis)	Venofer (American Regent Inc)	Ferrlecit (Sanofi Aventis US)	Feraheme (AMAG Pharmaceuticals)	Injectafer (American Regent Inc)
FDA Approved Indication	Iron deficiency in patients whom oral administration is unsatisfactory or impossible.	Iron deficiency anemia in adult and pediatric patients with chronic kidney disease (CKD).	Iron deficiency anemia in adult and pediatric patients with chronic kidney disease (CKD) receiving hemodialysis who are receiving supplemental EPO therapy.	Iron deficiency anemia in adult patients with chronic kidney disease (CKD).	Iron deficiency anemia in adult patients who have intolerance to oral iron or have had unsatisfactory response to oral iron; or who have non-dialysis dependent chronic kidney disease.
Black Box Warning	Yes	No	No	No	No
Route of Administration	IV injection IV infusion IM injection (not recommended)	IV injection IV infusion	IV injection IV infusion	IV infusion	IV injection IV infusion
Maximum FDA Approved Single Dose	100mg	400 mg	125mg	510 mg	750 mg

	IRON DEXTRAN	IRON SUCROSE	FERRIC GLUCONATE	FERUMOXYTOL	FERRIC CARBOXYMALTOSE
Dosing	<p>Doses less than or equal to 300 mg, slow IV push at a rate not to exceed 50 mg/minute; or diluted in 100-250 ml normal saline.</p> <p>For administration of a 1000mg total dose infusion, the total calculated dose should be diluted in 500 ml (range of 250 to 1000 ml) of normal saline. After a test infusion, the solution may be infused over 1 or more hours.</p>	<p>100mg IVP over 2-5 minutes; 100 mg/100ml 0.9% NS over 15 minutes; 200mg / 250ml 0.9%NS over 2 - 4 hours for a TDI of 1,000mg over a 14-day period.</p> <p>300 mg/ 250ml 0.9% NS infusion over 1.5 hours.</p> <p>400 mg/ 250ml 0.9% NS infusion over 2.5 hours.</p>	<p>Administer 125 mg diluted in 100 ml normal saline over 60 minutes daily for 5 doses maximum per week. May need to continue to a cumulative dose of 1 gram.</p>	<p>Up to 510mg IV push in 17 seconds.</p> <p>However, due to free iron with the rapid infusion, it is recommended that the 17 ml injection be given in 60-90 seconds.</p> <p>Intravenous infusion 510mg/ 50-200mL 0.9%NS or 5% Dextrose over at least 15 minutes.</p> <p>Observe patients for signs and symptoms of hypersensitivity during and after administration for at least 30 minutes and until clinically stable.</p>	<p>Up to 750 mg can be delivered in a single dose. Give 2 doses separated by at least 7 days for a total cumulative dose of up to 1500 mg per course.</p> <p>Administer as intravenous infusion over at least 15 minutes.</p> <p>Slow push injection at the rate of approximately 100 mg (2 mL) per minute over at least 7.5 minutes.</p> <p>For patients weighing less than 50 kg (110 lb), give each dose as 15 mg/kg body weight.</p> <p>† When administered via infusion, dilute up to 750 mg of iron in no more than 250 mL of sterile 0.9% sodium chloride injection, USP, such that the concentration of the infusion is not <2 mg of iron per mL and administer over at least 15 minutes. When administering as a slow intravenous push, give at the rate of approximately 100 mg (2 mL) per minute.</p>

ADOPT CONCEPT OF PATIENT BLOOD MANAGEMENT

“The timely application of evidence-based medical and surgical concepts designed to manage anemia, optimize hemostasis, and minimize blood loss in order to improve patient outcomes.” - Society for the Advancement of Blood Management (SABM.org)



REFERENCES

1. Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence and outcomes of anemia in surgery: a systematic review of the literature. *Am J Med.* 2004 Apr 5;116 Suppl 7A:58S-69S.
2. Beattie WS, Karkouti K, Wijeyesundera DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. *Anesthesiology.* 2009 Mar;110(3):574-81.
3. Musallam KM, Tamim HM, Richards T, Spahn DR, Rosendaal FR, Habbal A, Khreiss M, Dahdaleh FS, Khavandi K, Sfeir PM, Soweid A, Hoballah JJ, Taher AT, Jamali FR. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. *Lancet.* 2011 Oct 15; 378(9800): 1396-407.
4. Khanna MP, Hébert PC, Fergusson DA. Review of the clinical practice literature on patient characteristics associated with perioperative allogeneic red blood cell transfusion. *Transfus Med Rev.* 2003 Apr; 17(2): 110-9.
5. Cuenca J, García-Erce JA, Muñoz M. Efficacy of intravenous iron sucrose administration for correcting preoperative anemia in patients scheduled for major orthopedic surgery. *Anesthesiology.* 2008 Jul; 109(1): 151-2.
6. Yoo YC, Shim JK, Kim JC, Jo YY, Lee JH, Kwak YL. Effect of single recombinant human erythropoietin injection on transfusion requirements in preoperatively anemic patients undergoing valvular heart surgery. *Anesthesiology.* 2011 Nov;115(5):929-37.
7. Bacuzzi A, Dionigi G, Piffaretti M, Tozzi M et al Preoperative methods to improve erythropoiesis. *Transplantation Proceedings* 2011; 43(1): 324-326.
8. Goodnough LT, Maniatis A, Earnshaw P, Benoni G, Beris P, Bisbe E, Fergusson DA, Gombotz H, Habler O, Monk TG, Ozier Y, Slappendel R, Szpalski M. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. *Br J Anaesth.* 2011 Jan;106(1):13-22.
9. Noorani A, Hippelainen M, Nashef SA. Time until treatment equipoise: a new concept in surgical decision making. *JAMA Surg.* 2014 Feb;149(2):109-11.
10. InFeD [package insert]. Morristown, NJ: Watson Pharma; 2009.
11. Venofer [package insert]. Shirley, NY, American Regent; 2012.
12. Ferrlecit [package insert]. Bridgewater, NJ: Sanofi Aventis US; 2011.
13. Feraheme [package insert], Lexington, MA: AMAG Pharmaceuticals; 2012.
14. Injectafer [package insert]. Shirley, NY: American Regent; 2013.



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