Clinical and Practice Considerations in the Management of Iron Deficiency Anemia (IDA)

Jorge J. Garcia, PharmD, MS, MHA, MBA, FACHE
Assistant Vice President
Oncology, Infusion and Investigational Drug &
Research Pharmacy Services
Baptist Health

Background

Iron Deficiency Anemia (IDA)

- Reduction in circulating red blood cells (RDC)
- Insufficient utilizable body of iron stores
- Several etiologies
- Impacting ~ 5 million patients in U.S.
- Reduction in patient quality of life (QOL)

Prevalence:

- Vary by age, race, gender
- 2% in adult men
- 9-12% non-Hispanic white women
- 20% in black & Mexican-American women

Overview

Etiology of IDA

- Chemotherapy
- Blood loss after surgery
- Malnutrition
- Malabsorption

Contributing Factors:

- Hemolysis
- Hemophagocytic syndromes
- CKD
- ChT or RT-induced myelosuppression
- Bone Marrow Infiltration
- ESA
- Immuno-Inflammation

CKD – Chronic Kidney Disease | ChT – Chemotherapy | RT – Radiation Therapy

Overview

Absolute Iron Deficiency

Depletion of total body iron stores due to inadequate iron intake or blood loss

Functional Iron Deficiency

Total iron body stores are normal or increased, but iron cannot be metabolized

Iron Deficiency Anemia

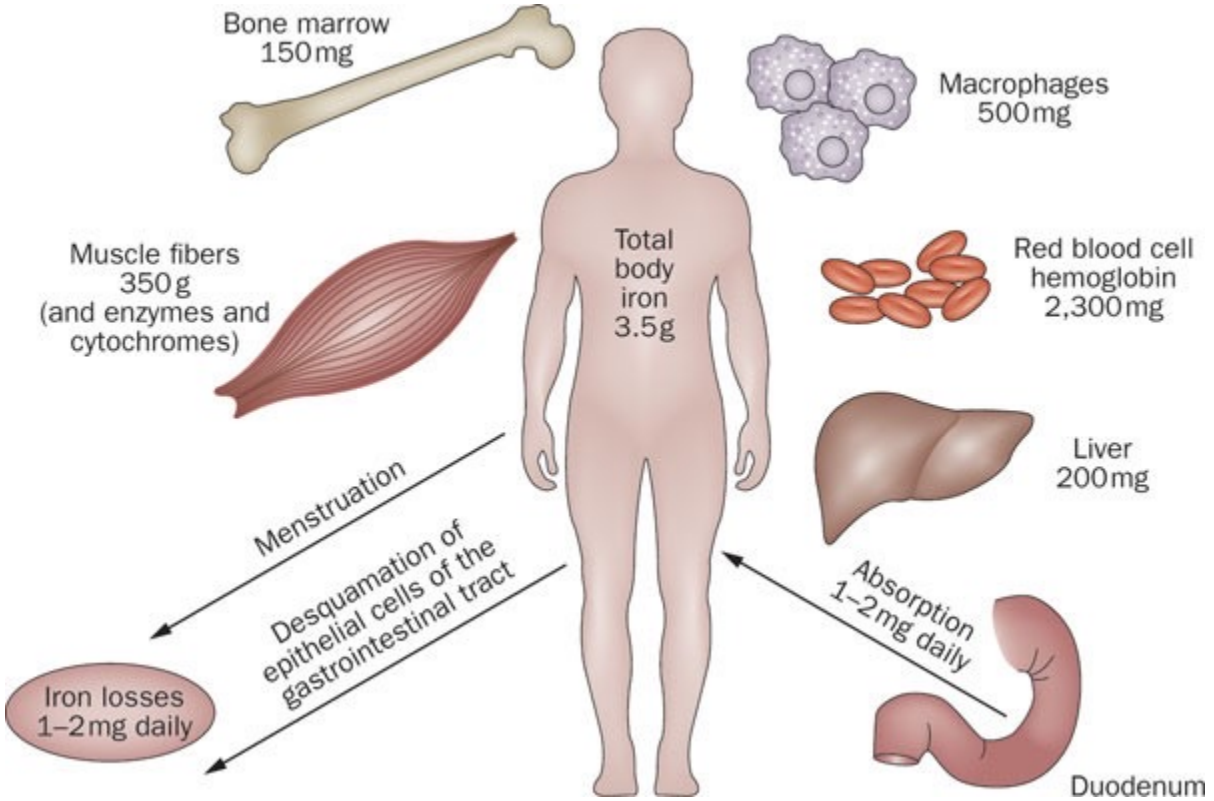
Symptomatology:

- Chest pain, fast heartbeat, or shortness of breath
- Headache, dizziness, or lightheadedness
- Pica
- Cold hands and feet
- Brittle nails
- Weakness
- Extreme fatigue

Iron Deficiency Anemia

Iron Homeostasis

- 1-2 mg iron is lost daily
  - Desquamation of epithelial cells of skin, GI tract, bile ducts and urinary tract
  - Menstruation
- 1-2 mg absorbed in duodenum



Iron Deficiency Anemia

IV Iron Therapy Evolution in the U.S.

1932	Iron hydroxide
1947	Iron saccharide
1954	High molecular weight iron dextran
1991	Low molecular weight iron dextran
1996	HMW-ID
1999	Ferric gluconate
2000	Iron sucrose
2009	Ferumoxytol
2013	Ferric carboxymaltose
2020	Ferric derisomaltose

Iron Deficiency Anemia

Safety Considerations for IV Iron Therapy

Pharmacist Consensus Statement

A panel of 12 pharmacists reviewed evidence regarding IV iron-associated AEs, including:

- 27 systemic reviews and review articles
- 35 RCTs, case reports & case series

Iron Deficiency Anemia
Pharmacist Safety Consensus Statement

Hypersensitivity Reactions / Infusion Related Reactions

1) Most mild-to-moderate HSRs, including IRRs, associated with IV iron preparations are Fishbane or CARPA reactions (e.g., pseudo-allergy) rather than anaphylactic reactions
2) Severe HSRs/IRRs rechallenging is NOT recommended; however, switching to a different IV formulation may mitigate reoccurrence of a severe HSR
3) Patients with previous IV iron-induced allergic reaction or a history of allergic reactions to multiple agents are at increased risk of developing a HSR
4) Premedication(s) or a test dose to mitigate the development of IV iron-associated HSR is generally not warranted

Iron Deficiency Anemia
Pharmacist Safety Consensus Statement

Hypersensitivity Reactions / Infusion Related Reactions

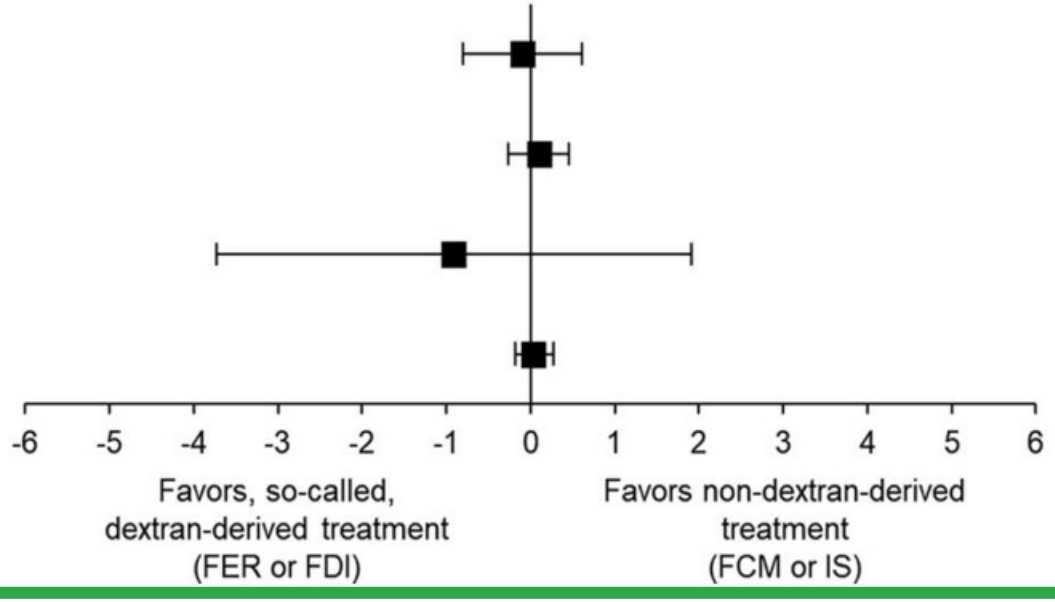
	IgE Mediated Reactions	CARPA Reactions
Mechanism of HSRs	Immune memory forms the specific IgE	Non-IgE-mediated activation of the complement system
Exposure	Typically arises upon re-exposure to allergen	Typically arises w/ first exposure to new molecule
Intensity	Increases w/ repeated exposure	Decreases with repeated exposure
Resolution	Reaction does not cease if treatment discontinued	Spontaneous resolution when infusion is paused or stopped

Reactions

1) For patients developing a mild-to-moderate Fishbane or CARPA reaction, consider rechallenging with the same product, at a slower rate, or switching with an iron product with a lower free iron load.

Iron Deficiency Anemia
Pharmacist Safety Consensus Statement

Study (dextran-derived treatment: non-dextran-derived treatment)	Incidence of HSRs, n/N (%) Dextran-derived treatment	Non-dextran-derived treatment	Risk difference (unadjusted 95% CI)
Adkinson (FER:FCM)	6/997 (0.60%)	7/1,000 (0.70%)	-0.10 (-0.80, 0.61)
FERWON (FDI:IS)	6/2,008 (0.30%)	2/1,000 (0.20%)	0.10 (-0.27, 0.46)
PHOSPHARE (FDI:FCM)	1/125 (0.80%)	2/117 (1.71%)	-0.91 (-3.73, 1.91)
Pooled (FER/FDI:FCM/IS)	13/3,130 (0.42%)	11/2,117 (0.52%)	0.04 (-0.18, 0.27)



1) Low risk of moderate-to-severe HSR
2) No statistically significant difference among products

 Achebe M, et al. Transfusion. 2020;60(6): 1154-1159

Iron Deficiency Anemia
Pharmacist Safety Consensus Statement

Patients at Increased Risk of HSR

1) Factors that increase the likelihood of HSRs

- Genetic disposition (asthma, other allergies)
- Acquired lasting factors (autoimmune diseases)
- Acquired Temporary Factors (anxiety, rate of infusion)

2) Factors that increase the likelihood of an adverse outcome to HSRs

- Advanced age
- Pre-existing severe respiratory or CVD
- Use of B-blockers or ACE inhibitors

Iron Deficiency Anemia
Pharmacist Safety Consensus Statement

Special Populations:

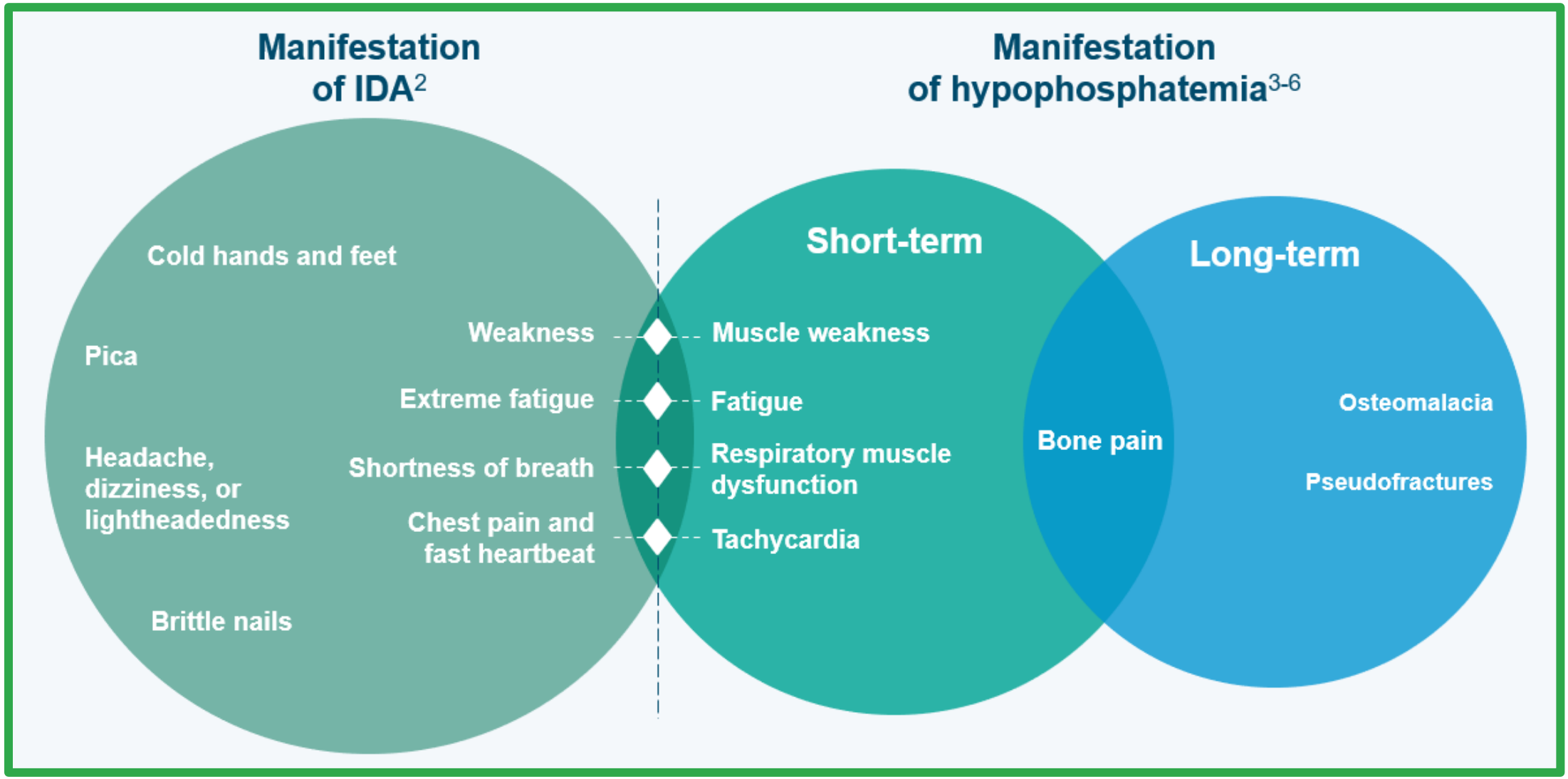
1) Selection of use in select populations (e.g., pregnancy, cardiac disease, IBD) should be based on formulation characteristics, ease of administration, AE profile, & social determinants of health.
2) Head-to-head and/or meta-analyses evaluating the use of IV iron products in select patient populations is limited
3) In patients with heart failure accompanied with a reduced ejection fraction and IDA, IV iron replacement is safe, effective and warranted.

Iron Deficiency Anemia
Pharmacist Safety Consensus Statement

Hypophosphatemia

1) The incidence of acute/persistent hypophosphatemia varies among formulations; the highest incidence of grade 3 hypophosphatemia (phosphate <2.0mg/dL) is associated with FCM
2) Monitoring serum phosphate levels is recommended for all patients receiving repeated courses of FCM, with extra vigilance for patients with low baseline serum phosphate or those who are at risk of developing osteomalacia
3) Persistent /reoccurring hypophosphatemia, after IV iron infusion, patients may benefit from:
    1) Using a formulation w/ lower risk of hypophosphatemia
    2) Phosphate supplementation
    3) Consulting renal expert for severe/refractory hypophosphatemia

Iron Deficiency Anemia
Hypophosphatemia

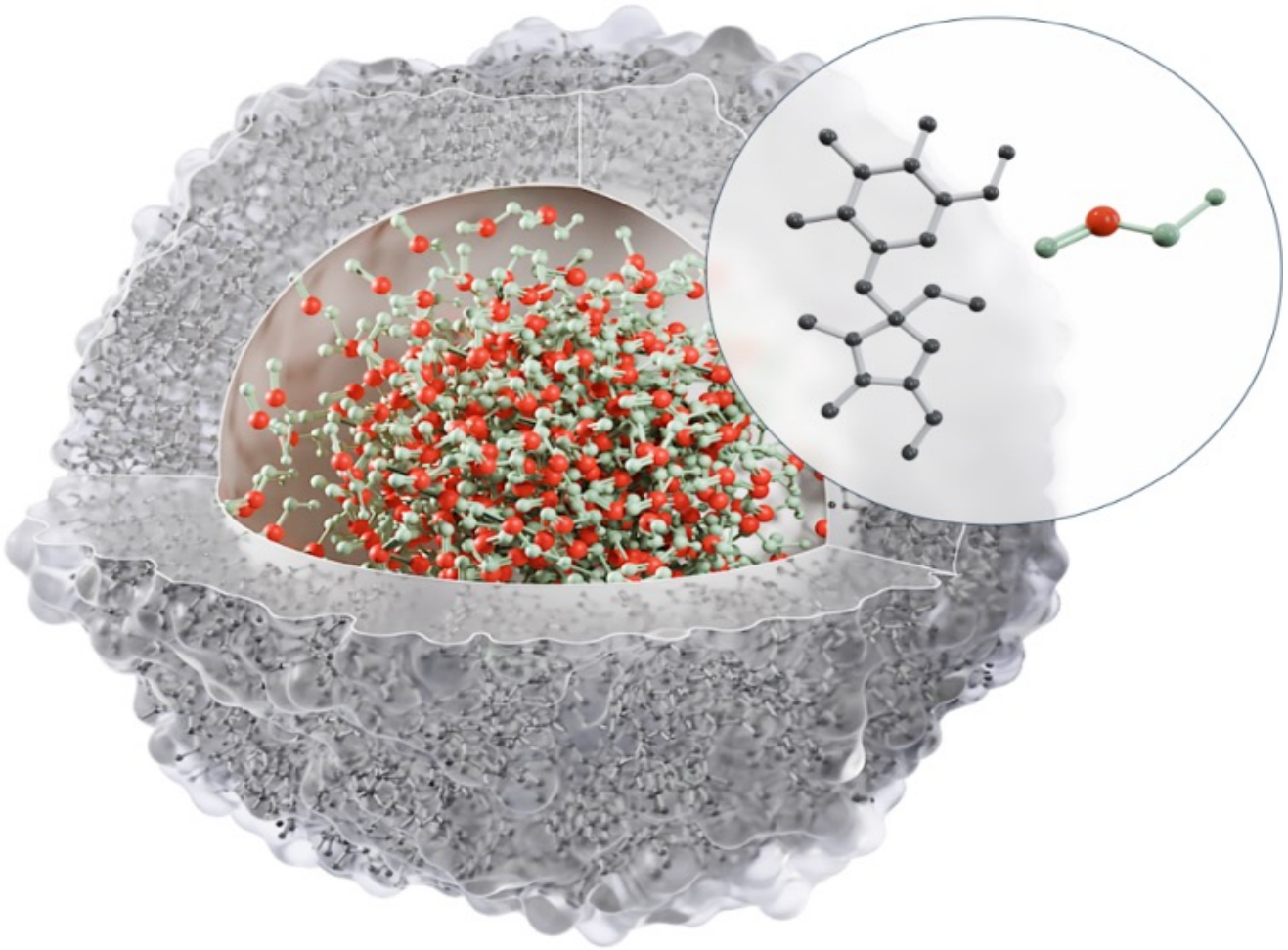


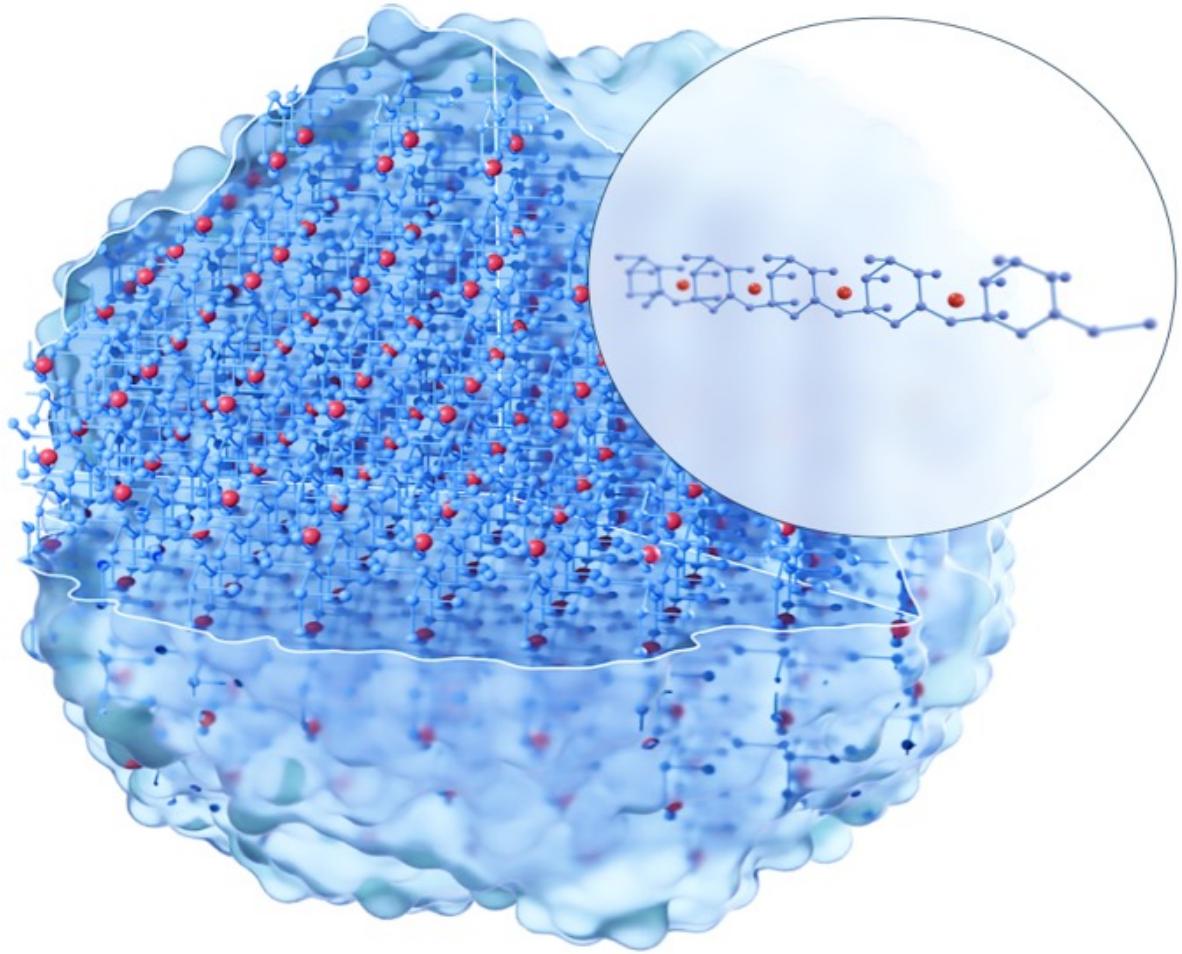
Iron Deficiency Anemia
Hypophosphatemia

Early Detection May Prevent Severe Complications:

1) Hemolysis
2) Rhabdomyolysis
3) Respiratory failure
4) Cardiac dysfunction
5) Neurological impairment

IV Iron Formulations





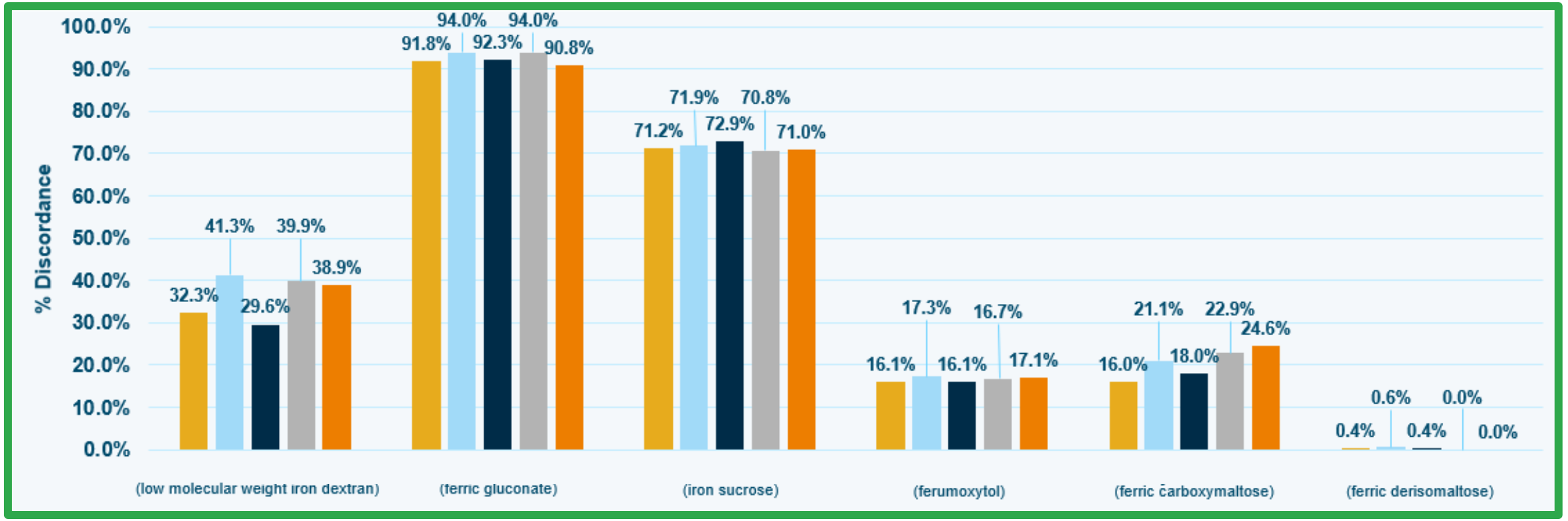
Iron Deficiency Anemia
IV Therapy Options & Considerations

Product	Dose	Visits	Infusion t	Test Dose	Boxed Warning
Iron Dextran	100 mg	[][][][][][][][][][] x10	≥ 2 mins	Yes	Yes (anaphylaxis)
Ferric Gluconate	125 mg	[][][][][][][][] x8	≥ 60 mins	No	No
Iron Sucrose	200 mg	[][][][][] x5	≥ 15 mins	No	No
Ferumoxytol	510 mg	[][] x2	≥ 15 mins	No	Yes (anaphylaxis)
Ferric Carboxymaltose	750 mg	[][] x2	≥ 15 mins	No	No
Ferric Derisomaltose	1000 mg	[] x1	≥ 20 mins	No	No

Iron Deficiency Anemia

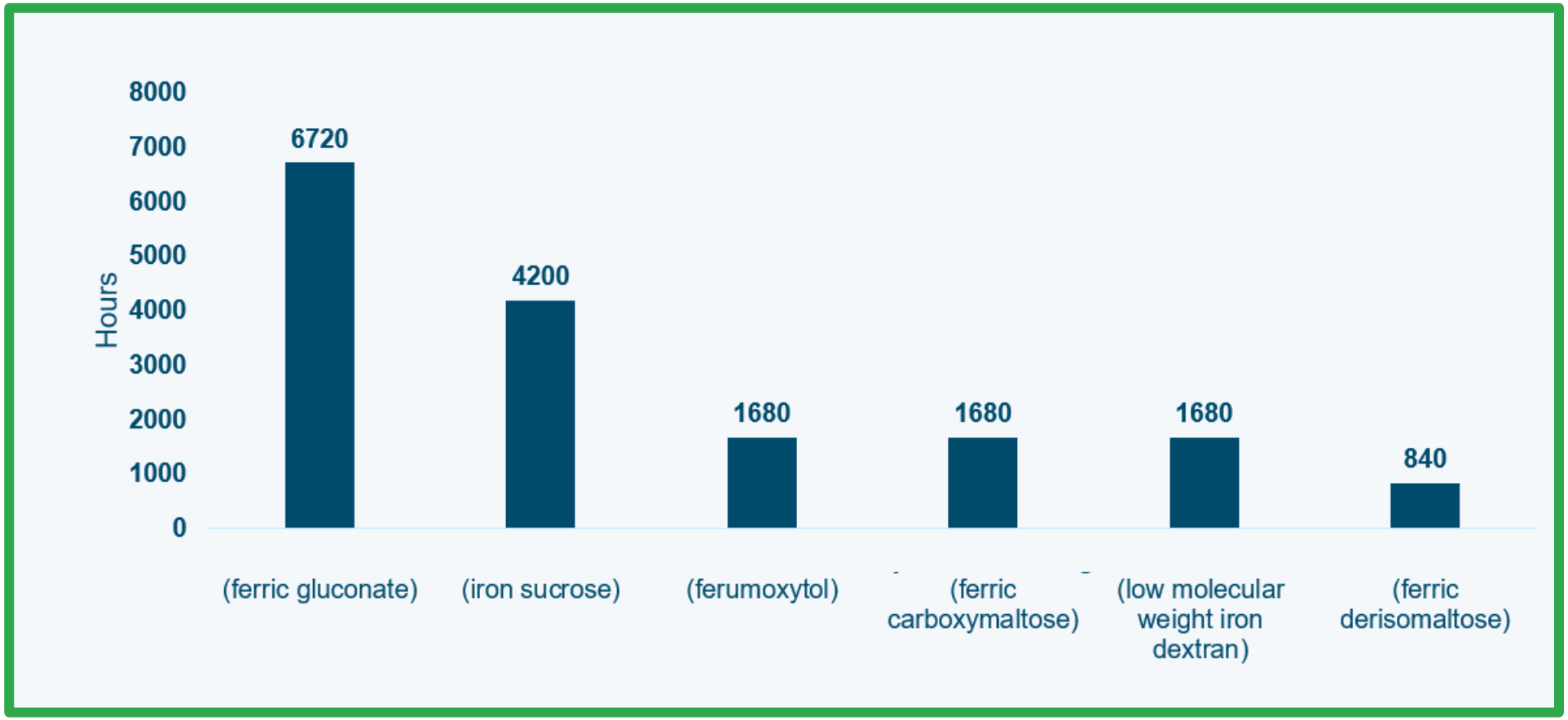
Treatment Discordance

Cumulative 6-week dose of less than 1,000 mg of iron



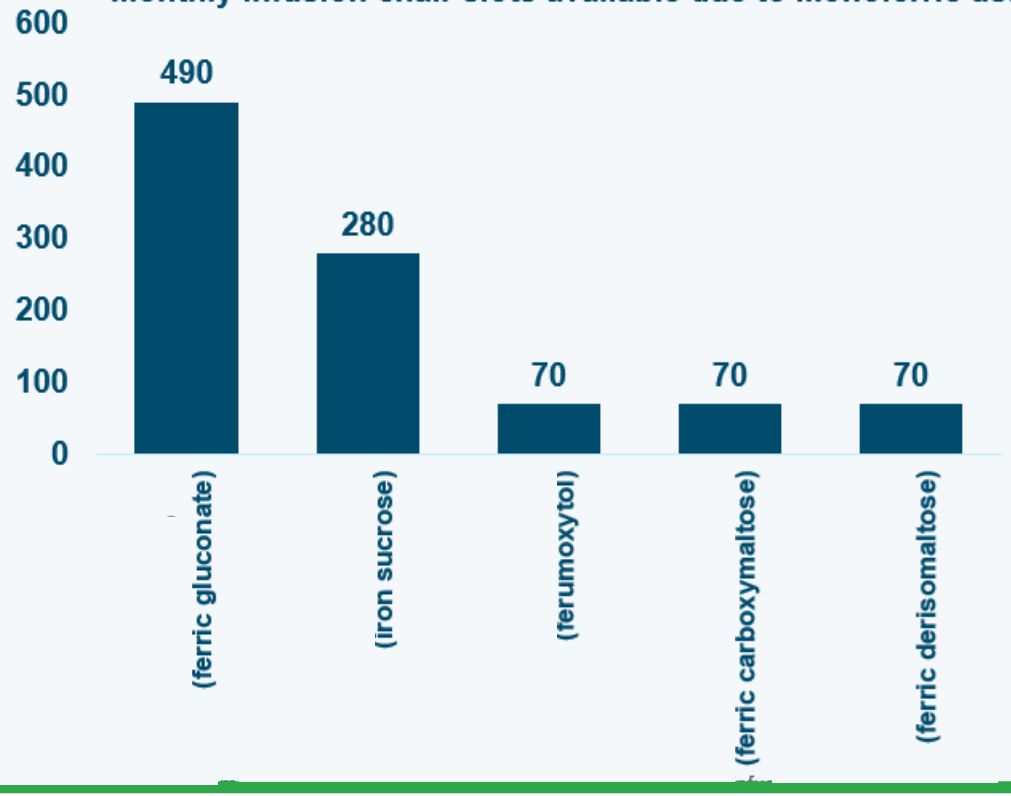
Iron Deficiency Anemia

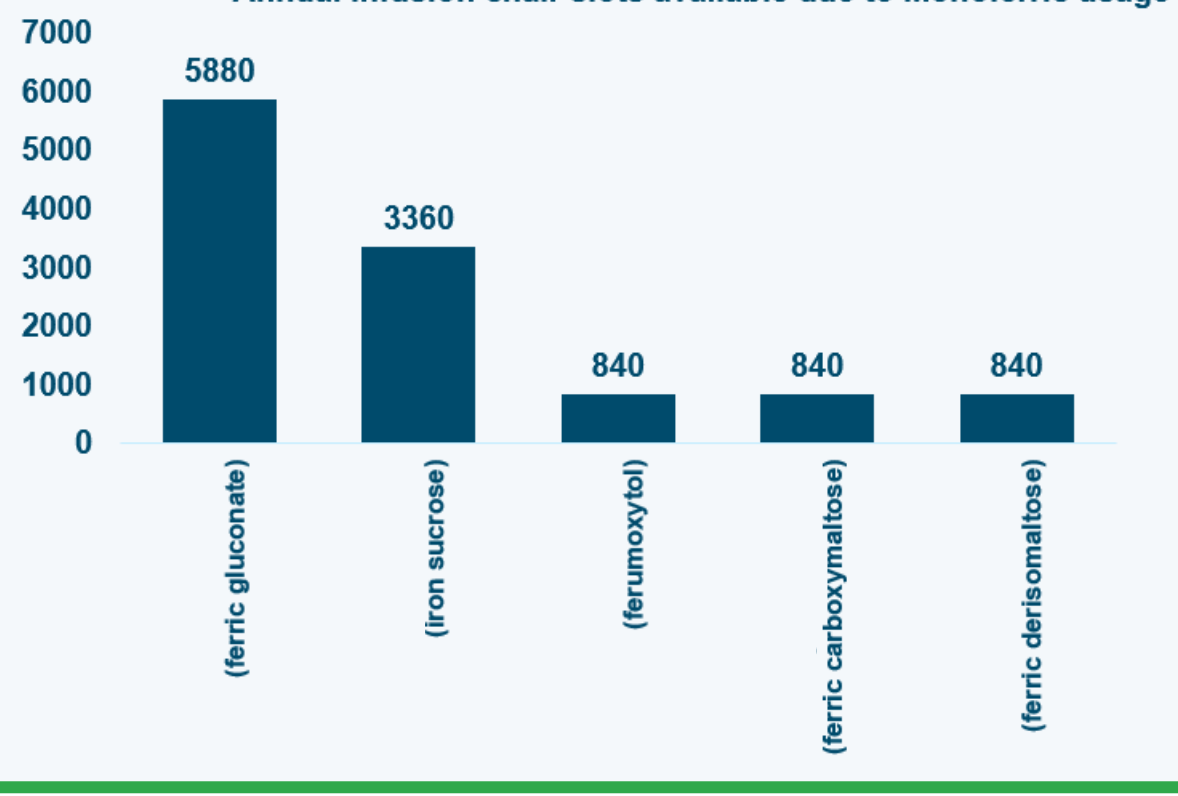
Chair Utilization by Time



Iron Deficiency Anemia

Chair Utilization by Infusion Slots





Iron Deficiency Anemia
IV Therapy Options

Other Considerations

1) CMS payable status indicator
2) Health plan coverage policy and authorizations
3) Patient out of pocket
4) Patient assistance
5) Transportation vulnerability
6) Provider economics
7) Tool for management of infusion capacity
8) Patient access gaps

Iron Deficiency Anemia

Summary

- Iron deficiency anemia affects a broad and large patient population
- Challenges accessing benign hematology specialty
- Challenges accessing infusion services
- Important IV iron replacement safety and efficiency considerations
- Coordinated iron infusion service can leverage
  - Patient access
  - Organizational value

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Q & A

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