In the name of God

Anemia of Iron Deficiency & Rational use of Iron Supplements

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content

- Introduction
- Symptoms
- Indications for treatment
- Oral versus IV iron
- IV iron
- Pregnancy
- Choice of oral preparation

- iron replacement products
- oral preparation
  - *over-the-counter preparations*
  - *daily versus alternate-day dosing*
  - *Number & Amount of doses per day*
  - *enteric-coated or sustained-release capsules*
  - *The duration of treatment*
  - *Side effects (oral iron)*
  - *Strategies to improve tolerability*

- Intravenous iron
  - *Premedication*
  - *Routes of use*
  - *Dosing*
  - *IV products*

INTRODUCTION

- More than one-quarter of the world's population is anemic, with approximately one half of the burden from iron deficiency.

- The prevention and treatment of iron deficiency is a major public health goal, especially in women, children, and individuals in low income countries.

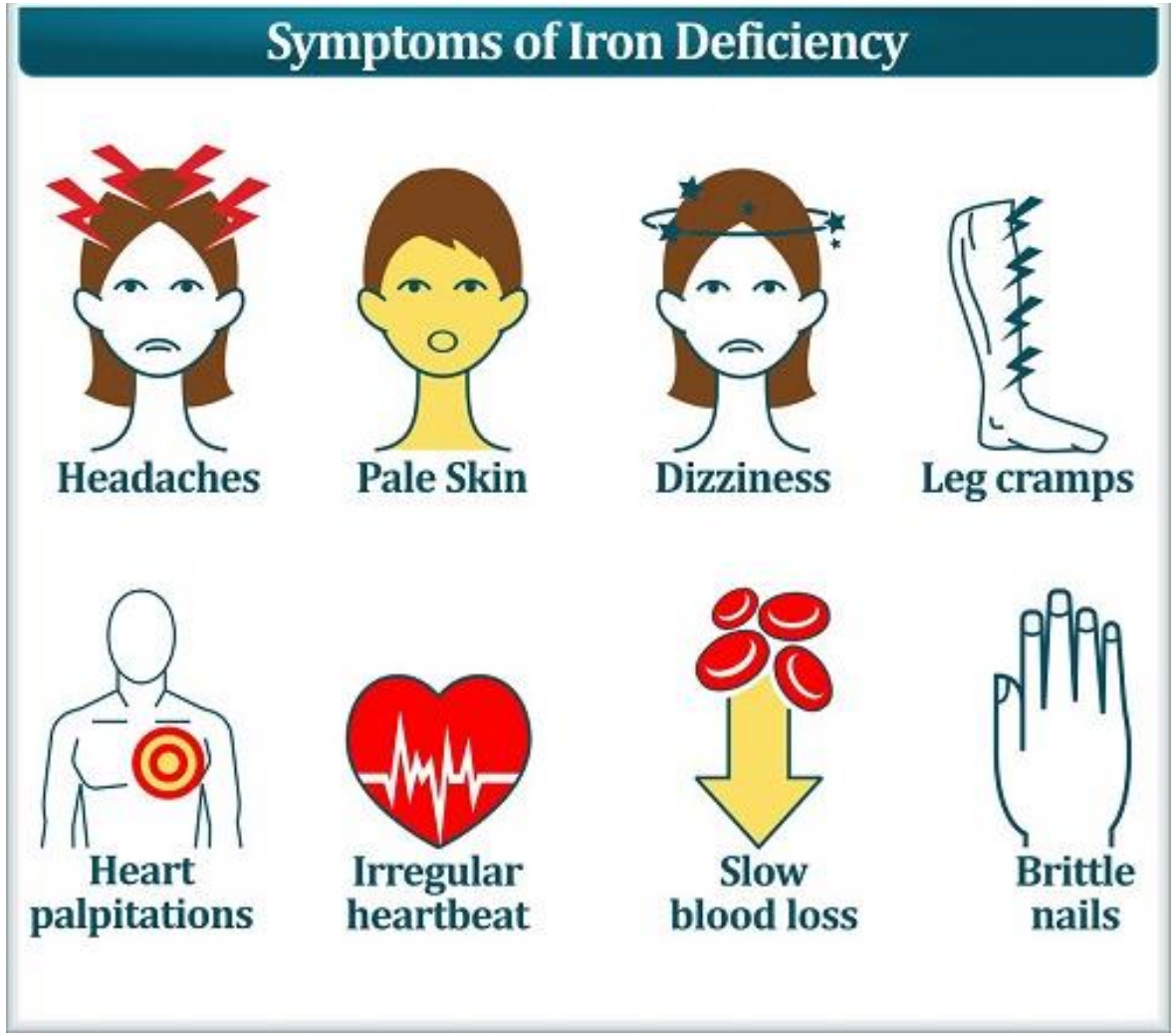
- Challenges in the treatment of iron deficiency include finding and addressing the underlying cause and the selection of an iron replacement product that meets the needs of the patient.

symptoms

Some patients with iron deficiency anemia will be asymptomatic

Symptoms of anemia, which may include

- weakness, headache, decreased exercise tolerance, fatigue, irritability, or depression
- Neurodevelopmental delay (children)
- Pica and pagophagia (ice craving)
- Beeturia (reddish urine after eating beets)
- Restless legs syndrome



	Normal	Iron deficiency without anemia	Iron deficiency with mild anemia	Severe iron deficiency with severe anemia
Hemoglobin	Normal range*	Normal range*	**9 to 12 g/dL (90 to 120 g/L)**	**6 to 7 g/dL (60 to 70 g/L)**
Red blood cell size and appearance	Normal	Normal	**Normal or slight hypochromia (slight decrease in MCHC)**	**Microcytosis (decrease in MCV) and hypochromia (decrease in MCHC)**
Serum ferritin	40 to 200 ng/mL (40 to 200 mcg/L; 89.9 to 449 picoM/L)	**<40 ng/mL¶ (<40 mcg/L; <89.9 picoM/L)**	**<20 ng/mL (<20 mcg/L; <45 picoM/L)**	**<10 ng/mL (<10 mcg/L; <22.5 picoM/L)**
Serum iron	60 to 150 mcg/dL (10.7 to 26.7 microM/L)	60 to 150 mcg/dL (10.7 to 26.7 microM/L)	**<60 mcg/dL (<10.7 microM/L)**	**<40 mcg/dL (<7.1 microM/L**
Total iron-binding capacity (TIBC; transferrin)	300 to 360 mcg/dL (53.7 to 64.4 microM/L)	300 to 390 mcg/dL (53.7 to 69.8 microM/L)	**350 to 400 mcg/dL (62.6 to 71.6 microM/L)**	**>410 mcg/dL (>73.4 microM/L)**
Transferrin saturation (serum iron/TIBC)	20 to 50%	20%	**<15%**	**<10%**
Reticulocyte hemoglobin [1]	30.6 to 35.4 pg	22.3 to 34.7 pg	14.8 to 34.0 pg	Data not available
Bone marrow iron stain	Adequate iron present	**Iron absent**	**Iron absent**	**Iron absent**
Erythrocyte zinc protoporphyrin, ng/mL RBC	30 to 70	30 to 70	**>100**	**100 to 200**

Indications for treatment

- Regardless of the presence of symptoms, **all** patients with iron deficiency anemia and most with iron deficiency without anemia should be treated.

- The rationale is that there is risk for further organ damage/ischemia and progression of anemia unless the underlying cause of the deficiency is addressed and adequate iron stores are replenished.

treatment

- When treatment is indicated, the usual approach is repletion of iron.
- Blood transfusion should not be used as treatment for iron deficiency unless the individual has **severe anemia with hemodynamic instability**.

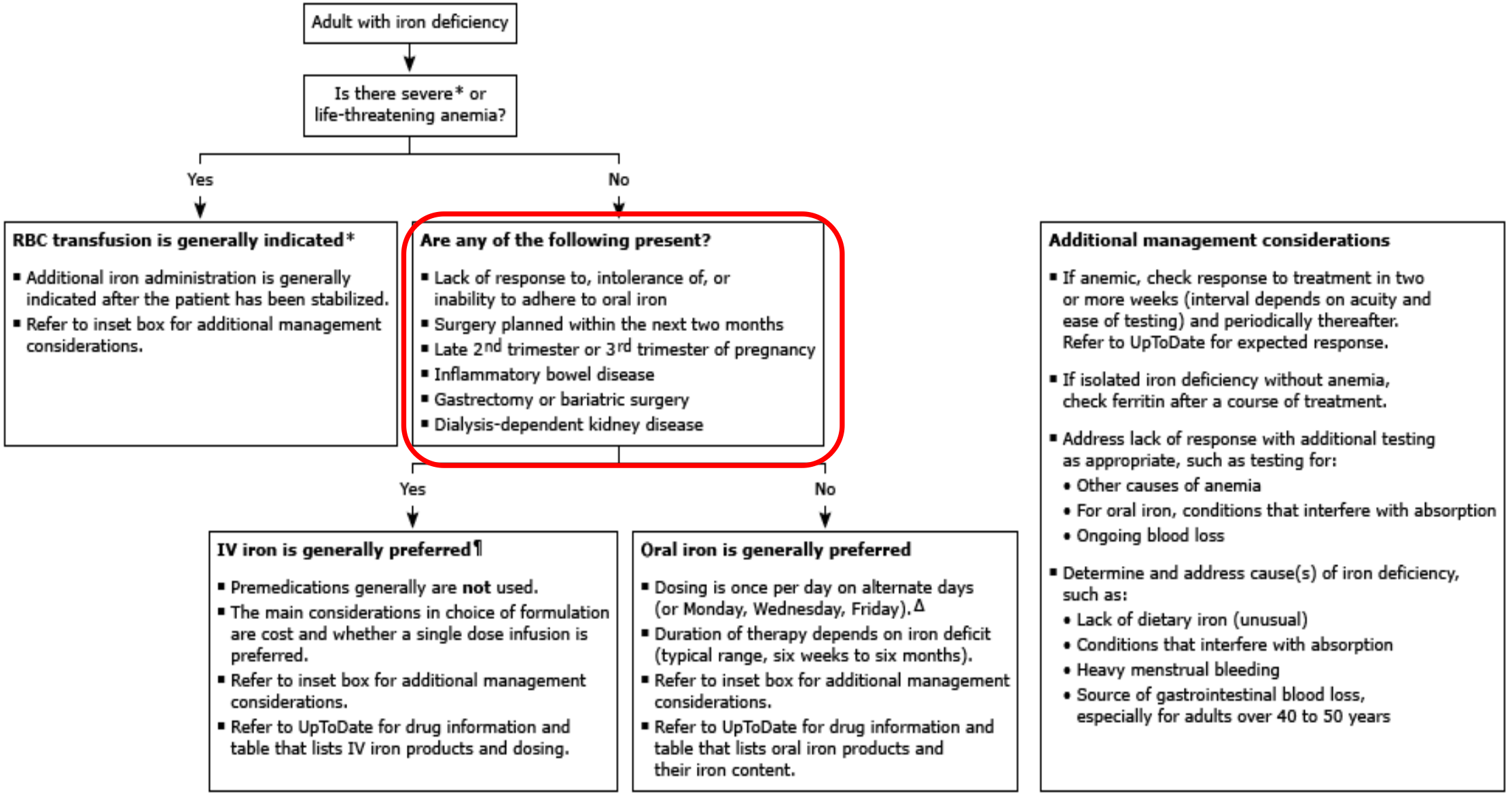
- Routine iron administration to **individuals without iron deficiency** is not advised. Rarely, some experts will treat a patient who has symptoms compatible with iron deficiency (pagophagia [ice craving] or restless legs syndrome) without overt laboratory evidence of reduced iron stores if all other interventions have been exhausted.

IRON REPLACEMENT PRODUCTS

Oral versus IV iron

- The choice between oral and intravenous (IV) iron depends on a number of factors including the acuity of the anemia, costs and availability of different iron replacement products, as well as the ability of the patient to tolerate oral iron preparations.

- Most patients are treated with oral iron because it is generally effective, readily available, inexpensive, and safe. However, up to **70 percent** of patients for whom oral iron is prescribed (especially ferrous sulfate) report gastrointestinal side effects.


Adult with iron deficiency
Is there severe* or life-threatening anemia?
Yes
No
RBC transfusion is generally indicated*
Additional iron administration is generally indicated after the patient has been stabilized.
Refer to inset box for additional management considerations.
Are any of the following present?
Lack of response to, intolerance of, or inability to adhere to oral iron
Surgery planned within the next two months
Late 2nd trimester or 3rd trimester of pregnancy
Inflammatory bowel disease
Gastrectomy or bariatric surgery
Dialysis-dependent kidney disease
Yes
No
IV iron is generally preferred¶
Premedications generally are not used.
The main considerations in choice of formulation are cost and whether a single dose infusion is preferred.
Refer to inset box for additional management considerations.
Refer to UpToDate for drug information and table that lists IV iron products and dosing.
Oral iron is generally preferred
Dosing is once per day on alternate days (or Monday, Wednesday, Friday).Δ
Duration of therapy depends on iron deficit (typical range, six weeks to six months).
Refer to inset box for additional management considerations.
Refer to UpToDate for drug information and table that lists oral iron products and their iron content.
Additional management considerations
If anemic, check response to treatment in two or more weeks (interval depends on acuity and ease of testing) and periodically thereafter. Refer to UpToDate for expected response.
If isolated iron deficiency without anemia, check ferritin after a course of treatment.
Address lack of response with additional testing as appropriate, such as testing for:
Other causes of anemia
For oral iron, conditions that interfere with absorption
Ongoing blood loss
Determine and address cause(s) of iron deficiency, such as:
Lack of dietary iron (unusual)
Conditions that interfere with absorption
Heavy menstrual bleeding
Source of gastrointestinal blood loss, especially for adults over 40 to 50 years

IV iron

- IV iron is appropriate for patients who are **unable to tolerate gastrointestinal side** effects of oral iron. Examples include older individuals, individuals with **abnormal uterine bleeding** in which oral iron cannot keep up with losses, individuals who are **pregnant** (who may already have gastrointestinal symptoms related to the pregnancy), and individuals with existing **gastrointestinal disorders**, which may be exacerbated by the gastrointestinal side effects of oral iron.
- Use of IV iron allows administration of nearly full-replacement doses in one or two infusions, depending on the product. In contrast, it has been estimated that the maximum amount of elemental iron that can be absorbed with an oral iron preparation is 25 mg per day.

pregnancy

In the second trimester of pregnancy, if the Hb is less than 10.5 g/dL, or at any time in the third trimester, at which oral iron is unlikely to supply adequate iron to the developing fetus.

Choice of oral preparation

- Numerous oral iron formulations are available, and for the most part all are equally effective, as long as they are taken.
- The most appropriate form is a liquid (allows for dose titration) or tablet containing ferrous salts.
- Side effects are generally similar among different preparations. Use of alternate day dosing and a liquid form that can be titrated may reduce side effects

Ferrous fumarate – 324 or 325 mg tablet (contains 106 mg elemental iron per tablet) (33%)

181mg

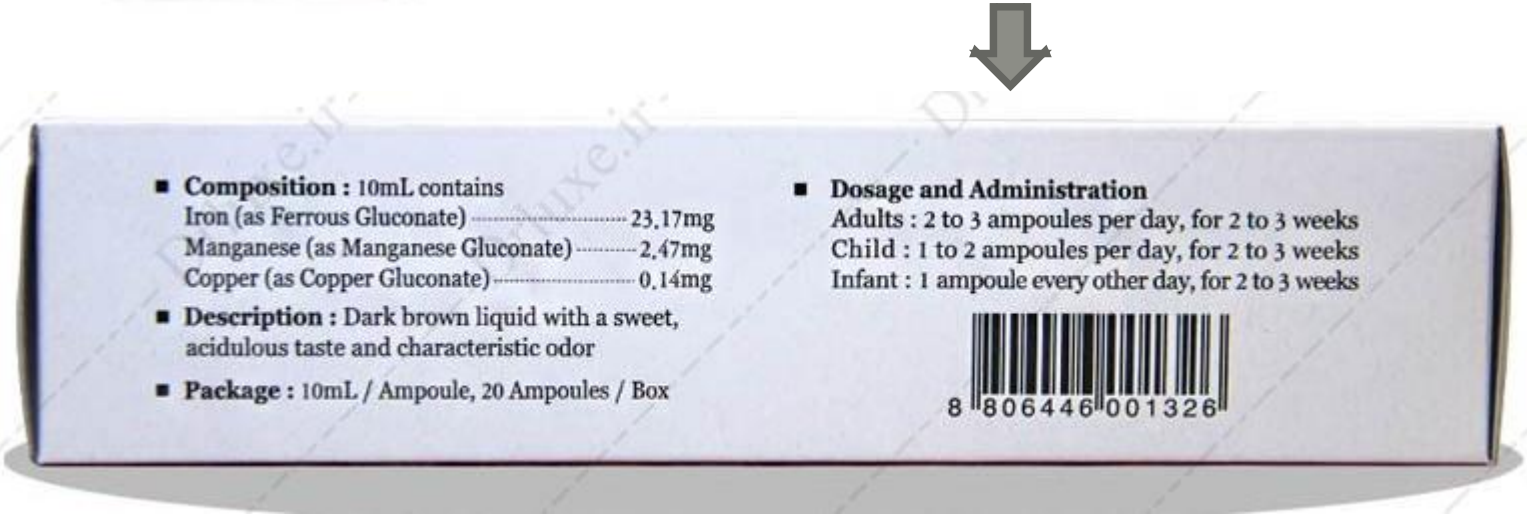
Ferrous gluconate (12%)

- 240 mg tablet (contains 27 mg elemental iron per tablet)
- 324 mg tablet (contains 38 mg elemental iron per tablet)
- 325 mg tablet (contains 36 mg elemental iron per tablet)


GERICARE
NDC 57896-724-01
FERROUS GLUCONATE
240 mg
Elemental Iron 27 mg
IRON SUPPLEMENT
100 Tablets

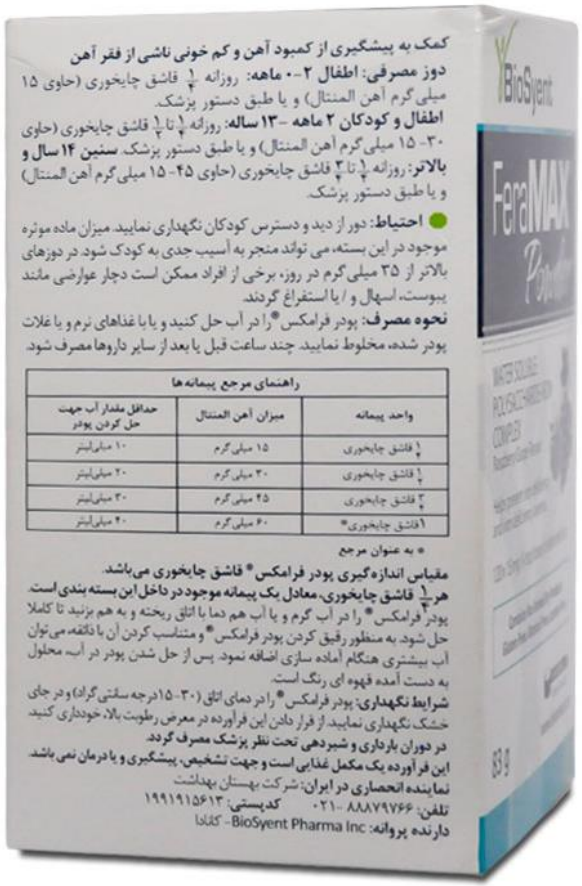

21ST CENTURY
DIETARY SUPPLEMENT
Iron 27 mg
Ferrous Gluconate
Essential Mineral Helps Production Of
Red Blood Cells And Specific Enzymes*
110 Tablets


G M P
Anti-Anemic·Anti-Asthenic
NEWHEM
CHO-A PHARM.CO.,LTD.
10mL X 20Amps.
NEWHEM


■ Composition : 10mL contains
Iron (as Ferrous Gluconate) 23.17mg
Manganese (as Manganese Gluconate) 2.47mg
Copper (as Copper Gluconate) 0.14mg
■ Description : Dark brown liquid with a sweet, acidulous taste and characteristic odor
■ Package : 10mL / Ampoule, 20 Ampoules / Box
■ Dosage and Administration
Adults : 2 to 3 ampoules per day, for 2 to 3 weeks
Child : 1 to 2 ampoules per day, for 2 to 3 weeks
Infant : 1 ampoule every other day, for 2 to 3 weeks
8 806446 001326

- Ferrous sulfate (20% & 32% for time released)
  - 325 mg tablet (contains 65 mg elemental iron per tablet)
  - 220 mg/5 mL oral elixir (contains 44 mg elemental iron per 5 mL)
  - 75 mg/mL oral solution (contains 15 mg elemental iron per mL)
  - SR: 150 mg capsules (contains 48 mg elemental iron per tablet)

Polysaccharide-iron complex



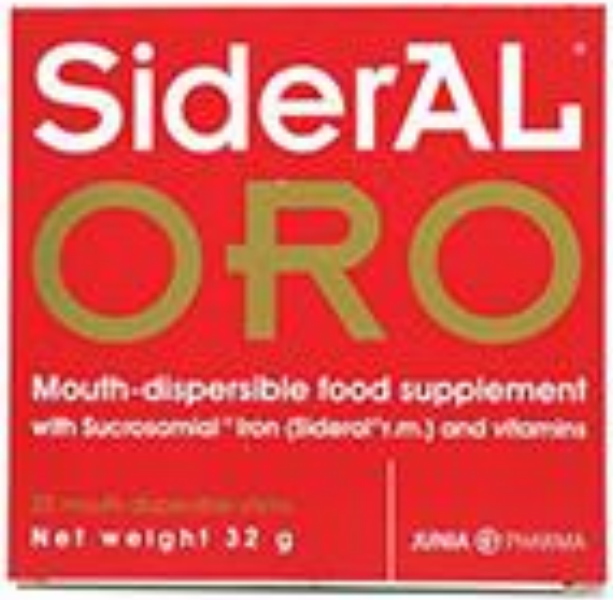
po


BioSyent
FeraMAX
100
HEMATINIC
Polysaccharide-iron complex
30 Capsules
ANTIANÉMIQUE
Complexe polysaccharide-fer
30 gélules

carbonyl iron

Carbonyl Iron is metallic iron – not a salt. It's fine particle size and the particle's huge surface area allows for a much slower but more successful absorption. With an absorption rate of 69% doses per capsule can be lower but very little iron is left behind compared to iron salt forms

Liposomal iron

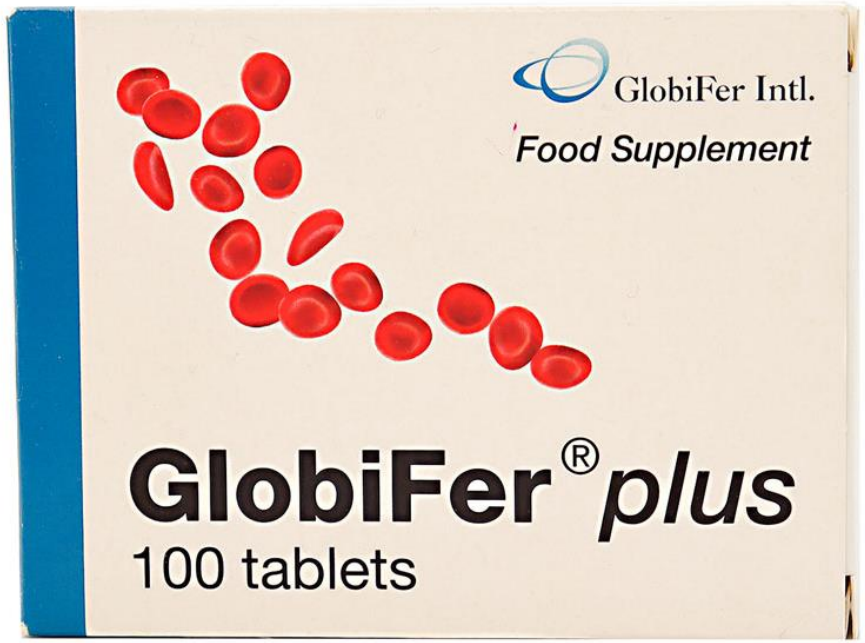


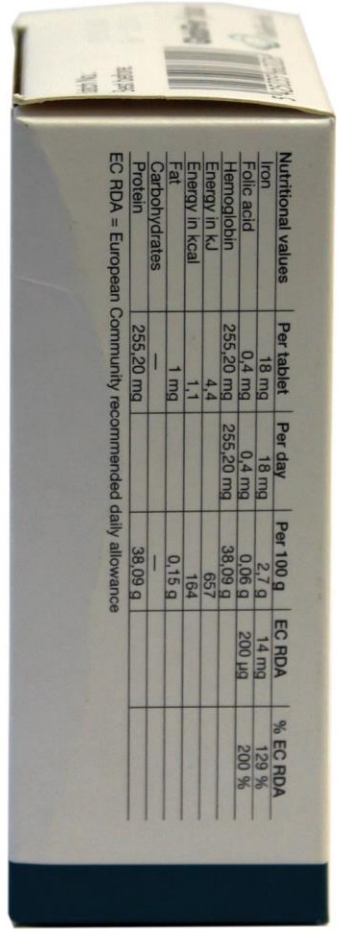

SideralGOCCE
Ferrosomal
liposofer
CAPTOSIDER
Drop
30ml bottle

مقایسه قطره های آهن لیپوزومال در یک نگاه

نام قطره آهن	مقدار آهن در هر میلی لیتر	ترکیبات دیگر	مدت نگه داری
سیدرال گوچه SiderAL Gocce	۷ میلی گرم	-	بعد از آماده سازی در یخچال به مدت یک ماه قابل نگهداری
فری نون Ferrinon (طعم پرتقال)	۸ میلی گرم	ویتامین B2 ویتامین A	تا ۳ ماه بعد از باز شدن قابل مصرف
کپتوسیدر Captosider	۱۰ میلی گرم	-	تا ۱ ماه بعد از باز شدن قابل مصرف
لیپوزوفر Liposofer (طعم تافی)	۷ میلی گرم (قرمز) ۱۴ میلی گرم (آبی)	-	تا ۱ ماه بعد از باز شدن قابل مصرف
آیروفیکس Irofix	۷ میلی گرم	ویتامین D3	تا ۱ ماه بعد از باز شدن قابل مصرف
لیپیفر Lipiferr	۷ میلی گرم	ویتامین B12 فولیک اسید	تا ۱ ماه بعد از باز شدن قابل مصرف
فروزومال Ferrosomal	۷ میلی گرم	-	تا ۱ ماه بعد از باز شدن قابل مصرف
فولیزومال Folisomal (طعم سیب)	۷ میلی گرم	-	تا ۱ ماه بعد از باز شدن قابل مصرف

Heme Iron


GlobiFer Intl.
Food Supplement
GlobiFer® plus
100 tablets


Nutritional values
Per tablet
Per day
Per 100 g
EC RDA
% EC RDA
Iron 18 mg 18 mg 2,7 g 14 mg 129 %
Folic acid 0,4 mg 0,4 mg 0,06 g 200 µg 200 %
Hemoglobin 255,20 mg 255,20 mg 38,09 g
Energy in kJ 4,4 657
Energy in kcal 1,1 164
Fat 1 mg 0,15 g
Carbohydrates — —
Protein 255,20 mg 38,09 g
EC RDA = European Community recommended daily allowance

Salt Form	Elemental Iron, % (w/w)
Ferrous gluconate	12
Ferrous bis-glycinate	20
Ferrous sulfate heptahydrate	20
Ferrous glycinate sulfate	23
Ferrous sulfate monohydrate, dried	30
Ferrous fumarate	33
Polysaccharide complex	100
Heme iron	100
Sucrosomial or liposomal Iron	100

over-the-counter preparations

- iron polypeptide
- carbonyl iron
- ferric citrate
- ferrous ascorbate
- ferrous succinate

Among these, there is no evidence that one is more effective than another or has fewer side effects than another. All are relatively inexpensive.

daily versus alternate-day dosing

- We typically advise our patients to take their dose every other day as long as they can manage the schedule appropriately; a reasonable variation on the schedule that is easier to follow is to give the dose on Monday, Wednesday, and Friday.

- As noted above, evidence suggests that alternate-day dosing (taking the iron every other day rather than every day) appears to result in equivalent or **better** iron absorption than daily dosing, usually with fewer adverse effects!!!

Number & Amount of doses per day

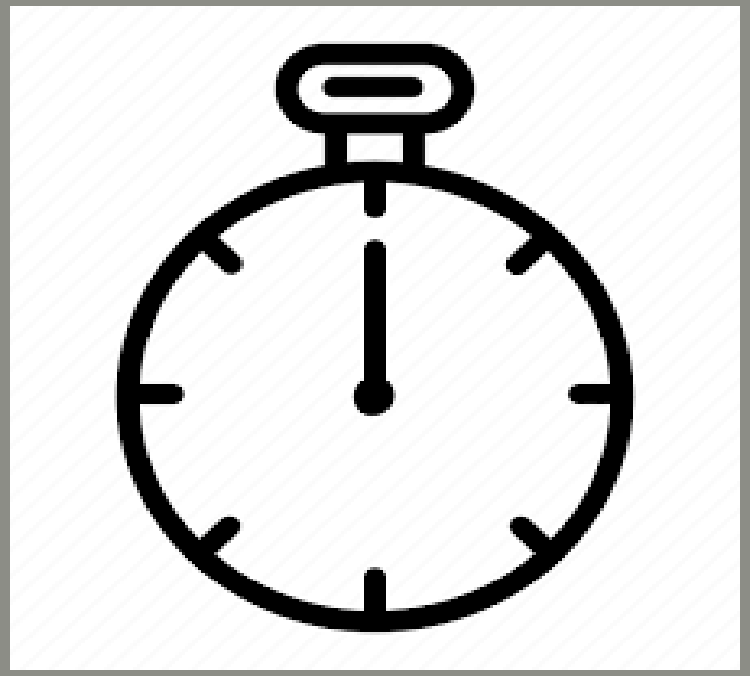
- There is no reason to give more than one dose per day.

- The amount of iron in the every-other-day dose or the Monday-Wednesday-Friday dose is also not well established. However, there is not a reason to think higher doses improve absorption, and adverse effects are generally dose related. Thus, we typically use one tablet per dose.

enteric-coated or sustained-release capsules

- enteric-coated or sustained-release capsules are less efficient for oral absorption because they release iron too far distally in the intestine (or not at all). As a result, we avoid these formulations.

The duration of treatment



- The duration of treatment differs among experts and in different settings. Some stop treatment when the hemoglobin level normalizes because this allows early detection of recurrent anemia from further blood loss (following therapy for a gastric lesion). Others treat for at least six months after the hemoglobin has normalized in order to completely replenish iron stores (following delivery for a multigravid woman). Treatment with oral iron may take as long as six to eight weeks in order to fully ameliorate the anemia, and as long as six months to replete iron stores

Side effects (oral iron)

- Gastrointestinal side effects are extremely common with oral iron administration.
- These include metallic taste, nausea, flatulence, constipation, diarrhea, epigastric distress, and/or vomiting. Patients may also be bothered by itching and by black/green or tarry stools that stain clothing or cause anxiety about bleeding.
- Additional concerns with oral iron administration include a possible role for oral iron in altering colonic microflora and/or promoting carcinogenesis; however, no clinically significant association has been demonstrated

Strategies to improve tolerability

- every other day
- (taking iron with food or milk
- Switching to a formulation with a lower amount of elemental iron
- Switching from a tablet to a liquid, for which it is easier to titrate the dose
- Use of a stool softener or bulk-forming laxative
- switching to IV iron

Intravenous iron

- Side effects
- Monitoring (test dose, rate of infusion, premedication, infusion reaction)
- Inflammatory state
- Infection
- Comparison
- equally effective & similar safety profile

premedication

- We do not use routine premedication prior to IV iron and we avoid diphenhydramine.
- For patients with asthma or more than one drug allergy, who are at slightly increased risk of an allergic or infusion reaction, we routinely premedicate with 125 mg of methylprednisolone and an H2 blocker (eg, 10 mg of famotidine) given intravenously prior to administration of any IV iron product.
- For patients with a history of inflammatory arthritis, we administer methylprednisolone, 125 mg intravenously, and prescribe a short course of prednisone (1 mg/kg per day orally for four days).

Routes we do not use (IM, transdermal)

- Intramuscular – Intramuscular (IM) iron is available and will raise the iron level, but this route of administration is painful, stains the buttocks, and has variable absorption . Case reports have also described development of sarcoma following IM iron administration.

- Transdermal – Transdermal iron delivery systems are being studied in animal models. However, there is no clinical evidence in humans that the transdermal route is effective or safe.

dosing

- We often give a fixed dose of approximately **1000 mg**, which is generally sufficient to treat anemia (typical red blood cell iron deficit between 500 and 1000 mg) and provide additional storage iron without causing iron overload. Whether this dose can be administered as a single (total dose) infusion or requires multiple infusions depends on the specific product.

LMW iron dextran

Ferric gluconate

- Elemental iron: 125 mg
- Each dose of 10 to 15 mL can be administered as a two-minute bolus (in patients undergoing hemodialysis)
- diluted in normal saline and infused over 20 to 30 minutes.
- 125 mg diluted in 100 mL of normal saline and infused over 30 to 60 minutes

Iron sucrose

- Elemental iron: 100 mg
- Doses of 10 mL (200 mg elemental iron) are routinely given over 2 to 15 minutes in dialysis centers.
- For patients with cancer receiving ESAs, 10 mL may be infused over 60 minutes every two to three weeks. Larger doses (ie,doses above 300 mg) are not recommended.

Ferumoxytol

- Elemental iron: 510/1020 mg

- Many patients are treated with two doses of ferumoxytol (510 mg elemental iron per dose) administered three to eight days apart, or a single total dose infusion of 1020 mg given over approximately 30 minutes.
- The infusion rate of ferumoxytol was revised from initial product labeling (1 mL per second of the undiluted solution), to a 15-minute infusion requiring dilution in 50 to 250 mL of normal saline or glucose solution.
- Ferumoxytol can cause a brighter signal on magnetic resonance imaging (MRI) scans, which is important to be aware of but does not negatively affect interpretation of the scan. If an MRI is planned within three months of administration, the radiologist should be notified that the patient has received ferumoxytol.

Ferric carboxymaltose

- Elemental iron: 500 mg
- Doses of FCM may be given over a 15-minute infusion.
- Hypophosphatemia: Serum phosphate levels may need to be monitored in selected populations such as those with borderline phosphate levels at baseline or those receiving repeated doses of FCM.

Iron isomaltoside/ ferric derisomaltose

Thanks for your attention...