IRON SUPPLEMENTS (Systemic)

VA CLASSIFICATION (Primary)¾TN401

Commonly used brand name(s):Apo-Ferrous Gluconate2; Apo-Ferrous Sulfate3; DexFerrum4; DexIron4; Femiron1; Feosol3; Feostat1; Feostat Drops1; Fer-In-Sol Capsules3; Fer-In-Sol Drops3; Fer-In-Sol Syrup3; Fer-Iron Drops3; Fer-gen-sol3; Feratab3; Fergon2; Fero-Gradumet3; Ferospace3; Ferra-TD3; Ferralet2; Ferralet Slow Release2; Ferralyn Lanacaps3; Ferretts1; Ferrlecit8; Fertinic2; Fumasorb1; Fumerin1; Hemocyte1; Hytinic5; InFeD4; Ircon1; Jectofer6; Mol-Iron3; Neo-Fer1; Nephro-Fer1; Niferex5; Niferex-1505; Novoferrogluc2; Novoferrosulfa3; Novofumar1; Nu-Iron5; Nu-Iron 1505; PMS-Ferrous Sulfate3; Palafer1; Simron2; Slow Fe3; Span-FF1; Venofer7.
Other commonly used names are:
Ferric hydroxide sucrose complex [Iron sucrose]
Ferrous sulfate exsiccated [Ferrous Sulfate]
Iron saccharate [Iron sucrose]
Iron sucrose complex [Iron sucrose]
Iron sugar [Iron sucrose]
Saccharated ferric oxide [Iron sucrose]

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms
Antianemic; nutritional supplement (mineral).

Indications

Accepted

Iron deficiency anemia, hemodialysis-induced (treatment)¾Sodium ferric gluconate complex injection and iron sucrose injection are indicated for the treatment of iron deficiency anemia in patients undergoing chronic hemodialysis who are receiving supplemental erythropoietin therapy. 148, 149

Iron deficiency anemia (prophylaxis and treatment)¾Iron supplements are indicated in the prevention and treatment of iron deficiency anemia, which may result from inadequate diet, malabsorption, pregnancy, rapid growth during childhood, and/or blood loss. 105

Iron dextran and iron sorbitol are recommended for patients in whom iron deficiency has been determined, only after the cause has been corrected, if possible, and only when oral administration has been found unsatisfactory or impossible. 1, 43, 105

Note: The cause of iron deficiency states should always be determined, as it may relate to a serious condition. 105

Deficiency of iron may lead to fatigue, 105 shortness of breath, 105 decreased physical performance, impaired learning in children and adults, 4, 5, 9, 11, 76, 77, 103, 130 altered body temperature, and altered immune function. 10, 52, 53, 54

Requirements may be increased and/or supplementation may be necessary in the following persons or conditions (based on documented iron deficiency):
Achlorhydria 31, 104, 105

Blood loss, excessive 55

Burns
Gastrectomy 105

Hemodialysis 43

Hemorrhage 55

Infants¾full-term infants after 4 months of age and 106, 107 preterm infants after 2 months of age, 55 especially those receiving breast milk or low-iron formulas 10, 127

Intestinal diseases¾celiac, 55 Crohn's, 76 diarrhea, 104 inflammatory bowel disease, 81, 115 malabsorption 104

In addition, individuals with conditions that cause chronic blood loss (e.g., peptic ulcer, hemorrhoids, hookworms) may be at risk for iron deficiency anemia. 105

Some unusual diets (e.g., reducing diets that drastically restrict food selection) may not supply minimum

Precautions to Consider

Carcinogenicity/Tumorigenicity

For iron dextran¾Tumors at the injection site have been reported in humans who had previously received intramuscular injections of iron-carbohydrate complexes. However, the actual risk of such tumors is unknown because of the long latency period between injection and appearance of a tumor. Animal studies have shown the production of sarcoma in rodents injected repeatedly at the same site with large doses of iron-carbohydrate complexes. However, the rodent tumors were a different type than those reported in humans. 1

For iron sorbitol¾There was no evidence of lymphatic obstruction or tumors at the injection site in mice receiving iron sorbitol subcutaneously at doses of 1 mg a week for seven months. 43

For iron sucrose¾Long-term carcinogenicity studies in animals have not been performed. 149

For sodium ferric gluconate¾Long-term carcinogenicity studies in animals have not been performed 148.

Mutagenicity

For iron sucrose¾There was no evidence of mutagenicity in the Ames test, mouse lymphoma cell forward mutation test, human lymphocyte chromosome aberration test, or the mouse micronucleus test. 149

For sodium ferric gluconate¾There was no evidence of mutagenicity in the Ames test and the rat micronucleus test. Sodium ferric gluconate produced a clastogenic effect in an in vitro chromosomal aberration assay in Chinese hamster ovary cells. 148

Pregnancy/Reproduction

Fertility¾For iron sucrose¾

Intravenous doses up to 15 mg iron per kg of body weight (mg/kg) per day (1.2 times the recommended maximum human dose on a body surface area basis) did not result in any effects on fertility or reproductive performance in male or female rats. 149

For sodium ferric gluconate¾

Studies to assess the effects on fertility were not performed. 148

Pregnancy¾For ferrous fumarate, ferrous gluconate, ferrous sulfate, and iron-polysaccharide ¾

In the first trimester of pregnancy, adequate iron intake is usually obtained from a proper diet; however, in the second and third trimesters, when iron deficiency is more prevalent because of greatly increased requirements, iron supplements may be recommended. However, some clinicians prefer to evaluate the patient before giving routine iron supplementation. 117, 118

Studies in humans have not been done, and problems in humans have not been documented with intake of normal daily recommended amounts.

Studies in animals have not been done.

For iron dextran¾

Iron dextran crosses the placenta. Studies in humans have not been done. 1

Iron dextran has been shown to be teratogenic and embryocidal in mice, rats, rabbits, dogs, and monkeys when given in doses three times the maximum human dose. 1

FDA Pregnancy Category C.

For iron sucrose¾

Studies in humans have not been done. Studies in rats and rabbits at doses of 13 mg/kg/day (0.5 times the recommended human dose on a body surface area (BSA) basis and 1 time the recommended human dose on a BSA basis, respectively) have shown no evidence of fetal harm. 149

FDA Pregnancy Category B. 149

For iron sorbitol¾

Although no adequate and well-controlled studies have been done in humans, there have been a few reports of abortion after use of iron sorbitol in early pregnancy. Use is not recommended in the first 3 to 4 months of pregnancy. 43

Studies in animals have not been done. 43

For sodium ferric gluconate¾

Adequate and well-controlled studies in humans have not been done. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus 148.

Sodium ferric gluconate was not teratogenic in mice and rats at doses of 300 milligram per square meter of body surface area (mg/m 2) per day and 120 mg/m2 per day (1.3 and 3.4 times the recommended human dose), respectively. 148

FDA Pregnancy Category B.

Breast-feeding

For ferrous fumarate, ferrous gluconate, ferrous sulfate, and iron-polysaccharide ¾
Problems in humans have not been documented with intake of normal daily recommended amounts. 1

For iron dextran¾
Only traces of unmetabolized iron dextran are distributed into breast milk. 1

For iron sucrose¾
It is not known whether this drug is distributed into human breast milk. However, it has been shown to distribute into the milk of rats. Because many drugs are distributed into human milk, caution should be exercised when this drug is administered to a nursing woman. 149

For sodium ferric gluconate¾
It is not known whether this drug is distributed into human milk. Because many drugs are distributed into human milk, caution should be exercised when this drug is administered to a nursing woman 148.

Pediatrics

The American Academy of Pediatrics recommends that iron supplementation (as iron-fortified formula or cereal or as iron-containing drops) 127 be given to preterm infants after 2 months of age and to full-term infants after 4 months of age, whether breast or formula fed. 106

Problems in pediatrics have not been documented with intake of normal daily recommended amounts. Iron dextran is not normally given to infants under 4 months of age. 20 There have been reports from other countries of increased gram-negative sepsis in neonates given iron dextran, probably due to Escherichia coli , after intramuscular injection. 1

No information is available on the relationship of age to the effects of sodium ferric gluconate in the pediatric population. Safety and efficacy have not been established. The sodium ferric gluconate complex in sucrose injection contains benzyl alcohol and therefore should not be used in neonates 148.

No information is available on the relationship of age to the effects of iron sucrose in the pediatric population. Safety and efficacy have not been established. 149.

Geriatrics

Problems in geriatrics have not been documented with intake of normal daily recommended amounts. Some geriatric patients may require a larger than usual daily ingestion of bioavailable 77 iron to correct

an iron deficiency, because their ability to absorb iron has been diminished by reduced gastric secretions and achlorhydria.
Appropriate studies on the relationship of age to the effects of iron sucrose and sodium ferric gluconate have not been performed in the geriatric population. However, no geriatrics-specific problems have been documented to date. In general, dose selection for an elderly patient should be cautious , usually starting at the low end of the dosing range 148.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following, depending on the amount present, may also interact with this iron supplement.
>> Acetohydroxamic acid 7

(iron, and possibly other heavy metals, when taken orally, are chelated by acetohydroxamic acid; this may result in reduced intestinal absorption of both acetohydroxamic acid and oral iron supplements; if iron therapy is indicated during treatment with acetohydroxamic acid, parenteral administration of iron is recommended 7)

Alcohol

(concurrent use with ferric iron for a prolonged period may result in toxicity since absorption and hepatic storage of iron are increased, especially if alcohol usage is high 37, 61)

>> Antacids or 21, 23, 38

Calcium supplements (calcium carbonate or phosphate) or 35, 36

Coffee or 50, 61

Eggs or 46

Foods or medications containing bicarbonates, 108 carbonates, 120 oxalates, 108 or phosphates or 60, 104, 129

Milk or milk products or 31

Tea containing tannic acid or 31

Whole-grain breads and cereals (contain phytic acid) and dietary fiber 31, 47, 61

(concurrent use with iron may 78 decrease iron absorption because of the formation of less soluble or insoluble complexes; iron supplements should not be taken within 1 hour before or 2 hours after ingestion of any of the above)

Cimetidine

(the decrease in gastric acid caused by cimetidine may decrease the absorption of nonheme iron; concurrent use with iron supplements is not recommended; iron supplements should be taken at least 2 hours before or after cimetidine 82, 83, 84)

Deferoxamine, and possibly other chelating agents

(deferoxamine chelates iron and is used in the treatment of iron overdose and other iron overload conditions; iron may be necessary in patients receiving other chelating agents; however, it should be given at least 2 hours after the chelating agent 79)

>> Dimercaprol 23, 32

(concurrent administration of medicinal iron with dimercaprol results in the formation of a toxic complex; if iron deficiency is present, its treatment should be postponed until therapy with dimercaprol has been discontinued for at least 24 hours; severe iron deficiency anemia occurring during dimercaprol therapy should be managed with blood transfusion)

>> Etidronate 33

(concurrent use may prevent absorption of oral etidronate; patients should be advised to avoid using iron supplements within 2 hours of etidronate)

>> Fluoroquinolones

(iron may reduce absorption of fluoroquinolones by chelation, resulting in lower serum and urine concentrations of fluoroquinolones; fluoroquinolones should be taken at least 2 hours before or 2 hours after iron supplements 12, 13, 44, 45, 100, 131)

Pancreatin or 21

Pancrelipase 21

(concurrent use of these medications with iron supplements may decrease iron absorption)

Penicillamine 19, 22 or

Trientine 34

(concurrent use with iron supplements may decrease the therapeutic effects of these medications; if necessary, iron may be administered in short courses, but a period of 2 hours should elapse between administration of penicillamine or trientine and iron)

>> Tetracyclines, oral 21, 23, 38

(concurrent use with iron reduces absorbability and resultant therapeutic effects of oral tetracyclines; patients should be advised to take iron supplements 2 hours after tetracycline)

Zinc supplements, oral

(large doses of iron supplements have been found to inhibit the intestinal absorption of zinc; 39, 40, 41, 42 this may be a problem in individuals taking commercial multivitamin-mineral preparations or infant formulas that have a high iron-to-zinc ratio; 40, 42 however, most firms in the U.S. have reformulated their products; zinc supplements should be taken at least 2 hours after iron supplements)