INFeD® Product Information

MARKETING SPECIFICATIONS

<table>
<thead>
<tr>
<th>Strength</th>
<th>Size</th>
<th>NDC #</th>
<th>Color</th>
<th>Shape</th>
<th>Imprint</th>
<th>UPC Code</th>
<th>WAC</th>
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<tbody>
<tr>
<td>50 mg/mL</td>
<td>10 x 2 mL</td>
<td>52544-0931-02</td>
<td>Dark Brown</td>
<td>Liquid</td>
<td>N/A</td>
<td>3-5254493102-0</td>
<td>$240.55*</td>
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</tbody>
</table>

*Contract Price May Apply

DISTRIBUTION SPECIFICATIONS

| Master Case Pack | 24 | 9.50" | 7.25" | 3.75" | 5.30 lbs. | 225 Cases |
| Inner Case Pack  | N/A | N/A   | N/A   | N/A   | N/A       | N/A       |
| Item Dimensions | 1  | 1.50" | 3.50" | 1.75" | 0.20 lbs. | 5400 Boxes |

NDA#: 17-441
OB Rating: BP
Temperature Information: 20°-25°C (68°-77°F)
Distributed by: Watson Pharma, Inc.

All of us at Watson appreciate your business. Provided above is the Wholesale Acquisition Cost (WAC) price. If you have any questions regarding the meaning or usage of any pricing term contained in this announcement or if we can provide you with any additional information, please do not hesitate to contact your National Account Manager or the Watson Customer Service Department. To place an order, contact our Watson Customer Service Department at 800-272-5525.

Please see reverse for Important Safety Information.
Please see accompanying full Prescribing Information.
In the treatment of patients with documented iron deficiency in whom oral administration is unsatisfactory or impossible

Making the Case for INFeD®

Broad usage

- For treating iron deficiency anemia that is not amenable to oral iron therapy
- Allows FDA-approved treatment of a wide range of patients with iron deficiency anemia

Optimized the erythropoietic response with ESA therapy

- INFeD® improved the hemoglobin response to erythropoietic therapy in patients with documented iron deficiency

Proven safety profile of iron dextran

- In a retrospective analysis of 841,252 doses, dyspnea, hypotension, and neurological symptoms were the most common major adverse drug events (ADEs)
  - The most common minor ADEs were nausea, vomiting, flushing, and pruritus

Important Safety Information

The parenteral use of complexes of iron and carbohydrates has resulted in anaphylactic-type reactions. Deaths associated with such administration have been reported. Therefore, INFeD® should be used only in those patients in whom the indications have been clearly established and laboratory investigations confirm an iron deficient state not amenable to oral iron therapy. Because fatal anaphylactic reactions have been reported after administration of iron dextran injection, the drug should be given only when resuscitation techniques and treatment of anaphylactic and anaphylactoid shock are readily available. Test dose is required. INFeD® should be used with caution in individuals with histories of significant allergies and/or asthma, and is contraindicated in patients with hypersensitivity to the product and patients with all anemias not associated with iron deficiency. Allergic reactions may potentially still occur in patients who have previously tolerated test or therapeutic doses of INFeD®, so administration of subsequent test doses during therapy should be considered. INFeD® should be used with extreme care in patients with serious impairment of liver function, and should not be used during the acute phase of infectious kidney disease. Unwarranted therapy with parenteral iron will cause excess storage of iron with the consequent possibility of exogenous hemosiderosis, which is particularly apt to occur in patients with hemoglobinopathies and other refractory anemias.

Please see accompanying full Prescribing Information.

References:

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Information For Patients: Patients should be advised of the potential adverse reactions associated with the use of INFeD.

Drug/Laboratory Test Interactions: Large doses of iron dextran (5 mL or more) have been reported to give a brown color to serum from a blood sample drawn 4 hours after administration. The drug may cause falsely elevated values of serum bilirubin and falsely decreased values of serum calcium. Serum iron determinations (especially by colorimetric assays) may not be meaningful for 3 weeks following the administration of iron dextran.

Ref: Serum ferritin peaks approximately 7 to 9 days after an intravenous dose of INFeD and slowly returns to baseline in 2 to 3 weeks. Examination of the bone marrow for iron stores may not be meaningful for prolonged periods following iron dextran therapy because residual iron stores may remain in the reticuloendothelial cells. Bone scans involving 99mTc-diphosphonate have been reported to show a dense, crescentic area of activity in the buttocks, following the contour of the iliac crest, 1 to 6 days after intramuscular injections of iron dextran. Iron scans with 99mTc-labeled bone seeking agents, in the presence of high serum ferritin levels or following iron dextran infusions, have been reported to show reduction of bony uptake, marked renal activity, and excessive blood pool and soft tissue accumulation.

Carcinogenesis, Mutagenesis, Impairment Of Fertility: See WARNINGS.

Pregnancy: Pregnancy Category C: Iron dextran has been shown to be teratogenic and embryocidal in mice, rats, rabbits, dogs, and monkeys when given in doses of about 3 times the maximum human dose. No consistent adverse fetal effects were observed in mice, rats, rabbits, dogs and monkeys at doses of 50 mg iron/kg or less. Fetal and maternal toxicity has been reported in monkeys at a total intravenous dose of 30 mg iron/kg or over a 14 day period. Similar effects were observed in mice and rats on administration of a single dose of 125 mg iron/kg. Fetal abnormalities in rats and dogs were observed at doses of 250 mg iron/kg and higher. The animals used in these tests were not iron deficient. There are no adequate and well-controlled studies in pregnant women. INFeD should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Placental Transfer: Various animal studies and studies in pregnant humans have demonstrated inconclusive results with respect to the placental transfer of iron dextran as iron dextran. It appears that some iron does reach the fetus, but the form in which it crosses the placenta is not clear.

Nursing Mothers: Caution should be exercised when INFeD is administered to a nursing woman. Traces of unmetabolized iron dextran are excreted in human milk.

Pediatric Use: Not recommended for use in infants under 4 months of age (See DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS: Severe/Fatal: Anaphylactic reactions have been reported after the use of iron dextran injection, on occasions these reactions have been fatal. Such reactions, which occur most often within the first few minutes, have been generally characterized by sudden onset of respiratory difficulty and/or cardiovascular collapse. Because fatal anaphylactic reactions have been reported after administration of iron dextran injection, the drug should be given only when resuscitation techniques and treatment of anaphylactic and anaphylactoid shock are readily available. (See boxed WARNING and PRECAUTIONS: General, pertaining to immediate availability of epinephrine.)

Cardiovascular: Chest pain, chest tightness, shock, cardiac arrest, hypotension, hypertension, tachycardia, bradycardia, flushing, arrhythmias. (Flushing and hypotension may occur from too rapid injections by the intravenous route.)

Dermatologic: Urticaria, pruritus, purpura, rash, cyanosis.

Gastrointestinal: Abdominal pain, nausea, vomiting, diarrhea.

Hematologic/Lymphatic: Leucocytosis, lymphopenopathy.

Musculoskeletal/soft tissue: Arthritis, arthralgia, arthritis may represent reaction in patients with quiescent rheumatoid arthritis - See PRECAUTIONS: General, myalgia, backache, sterile abscess, atrophy/abrosis (granulomatous tissue site), brown skin and underlying tissue discoloration (staining), soreness or pain at or near intramuscular injection site; cellulitis; swelling; inflammation; local phlebitis at an intravenous injection site.

Neurologic: Convulsions, seizures, syncope, headache, weakness, unresponsiveness, paresthesia, febrile episodes, chills, dizziness, disorientation, numbness, unconsciousness.

Respiratory: Respiratory arrest, dyspnea, bronchospasms, wheezing.

Urologic: Hematuria.

Delayed reactions: Arthralgia, backache, chills, dizziness, fever, headache, malaise, myalgia, nausea, vomiting (See WARNINGS).

Miscellaneous: Febrile episodes, sweating, shivering, chills, malaise, altered taste.

OVERDOSAGE: Overdose with iron dextran is unlikely to be associated with any acute manifestations. Doses of iron dextran in excess of the requirements for restoration of hemoglobin and replenishment of iron stores may lead to hemosiderosis. Periodic monitoring of serum ferritin levels may be helpful in recognizing a deleterious progressive accumulation of iron resulting from impaired uptake of iron from the reticuloendothelial system in concurrent medical conditions such as chronic renal failure, Hodgkin’s disease, and rheumatoid arthritis. The LD₅₀ of iron dextran is not less than 500 mg/kg in the mouse.

DOSAGE AND ADMINISTRATION: Oral iron should be discontinued prior to administration of INFeD.

Dosage:

1. Iron Deficiency Anemia: Periodic hematologic determination (hemoglobin and hematocrit) is a simple and accurate technique for monitoring hematologic response, and should be used as a guide in therapy. It should be first ensured that iron storage status is below the appearance of normal blood morphology. Serum iron, total iron binding capacity (TIBC) and percent saturation of transferrin are other important tests for detecting and monitoring the iron deficient state.

After administration of iron dextran complex, evidence of a therapeutic response can be seen in a few days. In the case of iron deficiency anemia the response is more rapid. The response is usually apparent in patients with pernicious anemia. It may need to be corrected over a longer period of time. It is advisable to continue monitoring the patient’s state of iron deficiency anemia with periodic hematologic determination (hemoglobin and hematocrit) during therapy.

Although serum ferritin is usually a good guide to body iron stores, the correlation of body iron stores and serum ferritin may not be valid in patients on chronic renal dialysis who are also receiving iron dextran complex.

Although there are significant variations in body build and weight distribution among males and females, women may have a lower body iron requirement due to the menstrual phase and formula replentish in premenstrual phases for estimating the total iron required. This total iron requirement reflects the amount of iron needed to restore hemoglobin concentration to normal or near normal levels plus an additional allowance to provide adequate replenishment of iron stores in most individuals with moderately or severely reduced levels of hemoglobin. It should be remembered that iron deficiency anemia will not appear until essentially all iron stores have been depleted. Therapy, thus, should aim at not only replenishment of hemoglobin iron but iron stores as well.
Factors contributing to the formula are shown below.

\[
\text{mg blood iron} = \text{ml blood} \times \frac{\text{g hemoglobin}}{1000} \times \frac{\text{mg iron}}{1000} \\
\text{lb body weight} \times \frac{\text{ml blood}}{1000} \times \frac{\text{g hemoglobin}}{1000} \\
\text{a) Blood volume} = 65 \text{ml/kg of body weight} \\
\text{b) Normal hemoglobin (males and females) over 15 kg} = 14.8 \text{g/dl} \\
15 \text{kg (33 lbs) or less} = 12.0 \text{g/dl} \\
\text{c) Iron content of hemoglobin} = 0.34% \\
\text{d) Hemoglobin deficit} \\
\text{e) Weight} \\
\text{Based on the above factors, individuals with normal hemoglobin levels will have approximately 33 mg of}
\text{blood iron per kilogram of body weight (15 mg/kg).} \\
\text{Note: The table and accompanying formula are applicable for dosage determinations only in patients}
\text{with iron deficiency anemia; they are not to be used for dosage determinations in patients requiring}
\text{iron replacement for blood loss.}

### TOTAL INFeD REQUIREMENT FOR HEMOGLOBIN RESTORATION AND IRON STORES REPLACEMENT*

<table>
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<th>PATIENT LEAN BODY WEIGHT</th>
<th>Milliliter Requirement of INFeD Based On Observed Hemoglobin of</th>
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<tbody>
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<td>kg</td>
<td>lb</td>
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*Table values were calculated based on a normal adult hemoglobin of 14.8 g/dl for weights greater than
15 kg (33 lbs) and a hemoglobin of 12.0 g/dl for weights less than or equal to 15 kg (33 lbs).

The total amount of INFeD in ml required to treat the anemia or replenish iron stores may be approximated as follows:

**Adults and Children over 15 kg (33 lbs)**: See Dosage Table. Alternatively the total dose may be calculated:

**Children 5 - 15 kg (11 - 33 lbs)**: See Dosage Table. INFeD should normally be given in the first four months of life.

(See PRECAUTIONS: Pediatric Use)

### II. Iron Replacement for Blood Loss:

Some individuals sustain blood losses on an intermittent or repetitive basis. Such blood losses may occur periodically in patients with hemorrhagic diatheses (familial telangiectasia; hemophilia; gastrointestinal bleeding) and on a repetitive basis from procedures such as renal hemodialysis.

Iron therapy in these patients should be directed toward replacement of the equivalent amount of iron reported in the blood loss. The table and formula described under I. Iron Deficiency Anemia are not applicable for simple iron replacement.

Quantitative estimates of the individual's periodic blood loss and hematocrit during the bleeding episode provide a convenient method for the calculation of the required iron dose.

The formula shown below is based on the approximation that 1 mL of normocytic, normochromic red cells contains 1 mg of elemental iron:

\[
\text{Replacement iron (in mg)} = \text{Blood loss (in mL)} \times \text{hematocrit}
\]

**Example:** Blood loss of 500 mL with 20% hematocrit

\[
\text{Replacement iron} = 500 \times 0.20 = 100 \text{mg}
\]

INFeD dose = 100 mg + 2 mL

50

**Administration:** The total amount of INFeD required for the treatment of iron deficiency anemia or iron replacement for blood loss is determined from the table or appropriate formula (See Dosage).

**I. Intravenous Injection - PREVIOUS TO RECEIVING THEIR FIRST INFeD THERAPEUTIC DOSE, ALL PATIENTS SHOULD BE GIVEN AN INTRAVENOUS TEST DOSE OF 0.5 mL. (See PRECAUTIONS: General.) THE TEST DOSE SHOULD BE ADMINISTERED AT A GRADUAL RATE OVER AT LEAST 30 SECONDS.**

Some anaphylactic reactions known to occur following INFeD administration are usually evident within a few minutes, or sooner, it is recommended that a period of an hour or longer elapse before the remainder of the initial therapeutic dose is given.

Individual doses of 2 mL or less may be given on a daily basis until the calculated total amount required has been reached. INFeD is given undiluted at a slow gradual rate to not exceed 50 mg (1 mL) per minute.

**2. Intramuscular Injection - PREVIOUS TO RECEIVING THEIR FIRST INFeD THERAPEUTIC DOSE, ALL PATIENTS SHOULD BE GIVEN AN INTRAMUSCULAR TEST DOSE OF 0.5 mL.**

The test dose should be administered in the same recommended test site and by the same technique as described in the last paragraph of this section. Although anaphylactic reactions known to occur following INFeD administration are usually evident within a few minutes, or sooner, it is recommended that a period of an hour or longer elapse before the remainder of the initial therapeutic dose is given.

If no adverse reactions are observed, INFeD can be given according to the following schedule until the calculated total amount required has been reached. Each day's dose should ordinarily not exceed 0.5 mL (25 mg of iron) for infants under 5 kg (11 lbs); 1.0 mL (50 mg of iron) for children under 10 kg (22 lbs); and 2.0 mL (100 mg of iron) for other patients.

INFeD should be injected only into the muscle mass of the outer quadrant of the buttock - never into the arm or other exposed areas - and should be injected deepy, with a 2-inch or 3-inch 19 or 20 gauge needle. If the patient is standing, he/she should be bearing his/her weight on the leg opposite the injection site, or in bed, he/she should be in the lateral position with injection site uppermost. To avoid injection or leakage into the subcutaneous tissue, a Z-track technique (displacement of the skin laterally prior to injection) is recommended.

Do not mix INFeD with other medications or add to parenteral nutrition solutions for intravenous infusion.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever the solution and container are intact.

**HOW SUPPLIED:** INFeD (Iron Dextran Injection USP) containing 50 mg of elemental iron per mL, is available in 2 mL single dose amber vials (for intramuscular or intravenous use) in cartons of 10 (NDC 5254-931-02).

Store at 20°-25°C (68°-77°F) (See USP Controlled Room Temperature). Rx Only

**REFERENCES:**


Revised: August 2008

Product No.: 1001-02

**Manufactured:**

Watson Pharmaceuticals, Inc.

Corona, CA 92880 USA

Manufactured by:

Patenon Italia S.p.A.

Ferentino, Italy 00173

251261

58080

Watson.