For the treatment of iron deficiency anemia in chronic hemodialysis patients undergoing epoetin therapy

Available in a Vial
• Convenient administration of regular low doses of IV iron with 62.5-mg single-dose vials

AB-Rated by the FDA
• Nulecit™ is therapeutically equivalent to branded sodium ferric gluconate complex in sucrose injection

Optimized ESA Usage and Hospital Spending
• Sodium ferric gluconate complex in sucrose injection showed a mean reduction in ESA requirements by up to 60.2%
• Sodium ferric gluconate complex in sucrose injection provided significant cost savings when used with ESA therapy
  – $1390 net cost savings per g/dL Hb increase over 12 weeks compared to ESA alone

Stability Data Available
• Data supports its stability in syringes and saline bags
  – Stability testing with syringes was conducted at room temperature for up to 2 days and at refrigerated conditions for up to 7 days
  – Stability testing with intravenous infusion bags containing 0.9% sodium chloride solution was conducted at room temperature for up to 1 day and at refrigerated conditions for up to 7 days

More Than 10 Years of Clinical Use
• Sodium ferric gluconate complex in sucrose injection is safe and effective

*Studies used Ferrlecit®. Nulecit™ is bioequivalent to Ferrlecit®.
† In anemic patients with high ferritin (500-1200 ng/mL), low TSAT (<25%), and receiving adequate ESA therapy.
‡ Economic model only included drugs and hospitalizations due to serious adverse events. In DRIVE (Dialysis Patients’ Response to IV Iron with Elevated Ferritin), patients were either given no iron (control group) or Ferrlecit® (sodium ferric gluconate in sucrose injection; 125 mg x 8); ESA dosage was raised 25% in each group at randomization with no further dose adjustments. DRIVE-II was a 6-week, observational extension of the DRIVE study designed to evaluate the sustained effects of IV iron administration on epoetin requirements, hemoglobin (Hb), and iron parameters under usual anemia clinical management. Investigators were not restricted in the type of iron product administered.

For more information, please visit Nulecit.com.

Important Safety Information
• Sodium ferric gluconate complex in sucrose is contraindicated in non iron-deficient anemias, in patients hypersensitive to sodium ferric gluconate complex in sucrose or its inactive components, or with evidence of iron overload
• Hypersensitivity reactions have been reported with injectable iron products
• Hypotension has been reported with rapid administration of IV iron
• In a single-dose, placebo-controlled safety study (n=1097), the most frequent adverse events occurring after sodium ferric gluconate complex in sucrose administration were hypotension, nausea, and vomiting and/or diarrhea
• In multiple-dose studies (n=126), the most frequent adverse events, whether or not related to sodium ferric gluconate complex in sucrose administration were nausea, vomiting and/or diarrhea, injection site pain, hypotension, cramps, hypertension, dizziness, dyspnea, and chest pain

Please see next page for references and brief summary of full Prescribing Information.
Evidence of iron overload.

enteral iron will cause excess storage of iron with consequent possibility of iatrogenic hemosiderosis. Iron overload
ated hypersensitivity events in Study A resulting in premature study discontinuation occurred in three out of a total
In multiple dose Studies A and B, no fatal hypersensitivity reactions occurred among the 126 patients who received
flushing immediately on sodium ferric gluconate complex in sucrose injection exposure. No hypotension occurred and
incidences of both drug intolerance or suspected allergic events following first dose sodium ferric gluconate complex
controlled studies in pregnant women. Nulecit™ should be used during pregnancy only if the potential benefit justifies
All anemias not associated with iron deficiency. Hypersensitivity to Nulecit ™ or any of its inactive components.

WARNINGS

Hypersensitivity reactions have been reported with injectable iron products. See PRECAUTIONS.

PRECAUTIONS

General: Iron is not easily eliminated from the body and accumulation can be toxic. Unnecessary therapy with par-
enteral iron with iron overload is particularly apt to occur in patients with hemoglobinopathies and other refractory anemias. Nulecit™ should not be administered to patients who may have iron overload. See OVERDOSAGE.

Hypersensitivity: One case of a life-threatening hypersensitivity reaction was observed in 1,097 patients who received a single dose of sodium ferric gluconate complex in sucrose injection in a post-marketing safety study. In the post-gluconate complex in sucrose injection in patients receiving sodium ferric gluconate complex in sucrose injection. See ADVERSE REACTIONS.

Hypersensitivity: Hypersensitivity associated with iron deficiency anemia in adult patients and in pediatric patients age 6 to 15 years (refer to CLINICAL STUDIES section). Safety and effectiveness in pediatric patients younger than 6 years of age have not been established.

Nulecit™ contains benzyl alcohol and therefore should not be used in neonates.

Geriatric Use: Clinical studies of sodium ferric gluconate complex in sucrose injection did not include sufficient numbers of patients aged 65 years and older; therefore, it is unknown whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In particular, 0.1% (1/683) of reports were from patients aged 65 years and over. Among all patients included in the studies, differences in safety or efficacy as a result of age were identified. In general, dose selection for an elderly patient should be based on age-related changes in drug disposition such as decreased renal or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

Exposure to sodium ferric gluconate complex in sucrose injection has been documented in over 1,400 patients on hemodialysis. This population included 1,097 sodium ferric gluconate complex injection in a placebo-controlled, cross-over, post-marketing safety study. Undiluted sodium ferric gluconate complex in sucrose injection was administered within ten minutes (125 mg of elemental iron at 12.5 mg/min). No test dose was used. From a total of 1,498 sodium ferric gluconate complex in sucrose injection-treated patients in medical reports, North American trials, and post-marketing surveillance reports, ten adverse reaction episodes were reported in patients receiving sodium ferric gluconate complex in sucrose injection. Of these episodes, nine were reported in patients receiving sodium ferric gluconate complex in sucrose injection treatment prior to the test dose of sodium ferric gluconate complex in sucrose injection (23%), tachycardia (17%), vomiting (11%), fever (9%), nausea (9%), abdominal pain (9%), pharyngitis (9%), conjunctivitis, abnormal vision, ear disorder.

Other Adverse Reactions Observed During Clinical Trials: In the single-dose post-marketing safety study in 1,097 sodium ferric gluconate complex in sucrose injection-treated patients, the following adverse events were reported in two or more patients: hypotension, tachycardia, heart failure, peripheral edema, and urticaria. In the single-dose post-marketing safety study, the following additional adverse events were reported in patients receiving sodium ferric gluconate complex in sucrose injection: injection site reaction (33%), chest pain (19%), pain (10%), headache (7%), rash (6%), abdominal pain (6%), fatigue (6%), fever (5%), malaise, injection, abscess, back pain, chills, rashes, arm pain, fascia, flu-like syndrome, sporadic adverse event, fatal adverse reaction, absence of any adverse events included in the pooled safety data. In the single-dose, post-marketing, safety study one patient experienced a "red blotchy rash" following the first dose of sodium ferric gluconate complex in sucrose injection. The first patient withdrawn after the development of pruritus and chest pain following the test dose of sodium ferric gluconate complex in sucrose injection.

The second patient, in the high dose group, experienced nausea, abdominal and flank pain, fatigue and rash following the first dose of sodium ferric gluconate complex in sucrose injection. Nixon et al. in the patient with the low dose group experienced a "red rash" following the first dose of sodium ferric gluconate complex in sucrose injection. Of the 38 patients exposed to sodium ferric gluconate complex in sucrose injection in Study B, none reported hypersensitivity reactions.

Many chronic renal failure patients experience cramps, pain, nausea, rash, flushing, and pruritus. In the postmarketing spontaneous reporting system, life-threatening hypersensitivity reactions have been reported rarely following sodium ferric gluconate complex in sucrose injection.

Hypotension: See PRECAUTIONS. In the single-dose post-marketing safety study, hypotensive adverse events were observed in 229 patients (2%) following sodium ferric gluconate complex in sucrose injection administration. Hypotension was also reported following administration of sodium ferric gluconate complex in sucrose injection in European case reports. Of the 226 renal dialysis patients exposed to sodium ferric gluconate complex in sucrose injection and reported in the literature, 3 (1.3%) patients experienced hypotensive events, which were accompanied by symptoms such as headache, dizziness, hypotension, and drowsiness. All patients recovered within one hour without sequelae. Hypotension may occur during dialysis. Administration of Nulecit™ may augment hypotension caused by dialysis.

Anticipate 32 patients who received sodium ferric gluconate complex in sucrose injection in Studies A and B, one patient experienced a transient decreased level of consciousness without hypotension. Another patient discontinued treatment prematurely because of dizziness, light-headedness, diplopia, malaise, and weakness without hypotension that resulted in a 3 to 4 hour hospitalization for observation following drug administration. The syndrome resolved spontaneously.

Adverse Laboratory Changes: No differences in laboratory findings associated with sodium ferric gluconate complex in sucrose injection were reported in North American clinical trials when normalized against a National Institute of Health database on laboratory findings in 1,100 hemodialysis patients.

Most Frequent Adverse Reactions: In the single-dose, post-marketing safety study, 11% of patients who received sodium ferric gluconate complex in sucrose injection and 94% of patients who received placebo reported adverse reactions. The most frequent adverse reactions following sodium ferric gluconate complex in sucrose injection were: hypotension (15%), nausea, vomiting and/or diarrhea (13%), headache (9%), dizziness (9%), chest pain (8.5%), pruritus (8.5%), and back pain (0.4%). Similar adverse reactions were seen following placebo administration. However, because of the baseline incidence of adverse events in placebo population, insufficient number of exposed patients, and limitations inherent to the cross-over, single dose design, no comparison of event rates between sodium ferric gluconate complex in sucrose injection and placebo study design can be made.

In multiple-dose Studies A and B, the most frequent adverse reactions following sodium ferric gluconate complex in sucrose injection were:

Hypersensitivity reaction (injection site reaction (33%), chest pain (19%), pain (10%), headache (7%), rash (6%), abdominal pain (6%), fatigue (6%), fever (5%), malaise, injection, abscess, back pain, chills, rashes, arm pain, fascia, flu-like syndrome, sporadic adverse event, fatal adverse reaction, absence of any adverse events included in the pooled safety data. In the single-dose, post-marketing, safety study one patient experienced a "red blotchy rash" following the first dose of sodium ferric gluconate complex in sucrose injection. The first patient withdrawn after the development of pruritus and chest pain following the test dose of sodium ferric gluconate complex in sucrose injection.

The second patient, in the high dose group, experienced nausea, abdominal and flank pain, fatigue and rash following the first dose of sodium ferric gluconate complex in sucrose injection. Nixon et al. in the patient with the low dose group experienced a "red rash" following the first dose of sodium ferric gluconate complex in sucrose injection.