Iron Dextran Injection

Type of Posting	Notice of Intent to Revise
Posting Date	28-Apr-2023
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 2

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 2 Expert Committee intends to revise the Iron Dextran Injection monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to remove the test for *Acute Toxicity* from the monograph.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.[1]

Should you have any questions, please contact V. Durga Prasad, Scientific Liaison (+91-40-4448-8723 or durgaprasad.v@usp.org).

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the *USP–NF*.

Notice of Intent to Revise
Official: To Be Determined

Iron Dextran Injection

DEFINITION

Iron Dextran Injection is a sterile, colloidal solution of ferric hydroxide in complex with partially hydrolyzed Dextran of low molecular weight, in Water for Injection. It contains NLT 95.0% and NMT 105.0% of the labeled amount of iron. It may contain NMT 0.5% of phenol as a preservative.

IDENTIFICATION

● **A.** To 1 mL of Injection on a watch glass add 2 drops of ammonium hydroxide. No precipitate is formed. Add 2 mL of hydrochloric acid, and add 2 mL of ammonium hydroxide. A brown precipitate is formed.

ASSAY

● **Procedure for Iron**

Solution A: Transfer 2.64 g of calcium chloride dihydrate to a 1000-mL volumetric flask. Add 500 mL of water, and swirl to dissolve. Add 5.0 mL of hydrochloric acid, and dilute with *water* to volume.

Standard stock solution: 50 µg/mL of iron prepared as follows. Transfer 350 mg of ferrous ammonium sulfate hexahydrate to a 1000-mL volumetric flask. Add water to dissolve, dilute with water to volume, and mix.

Standard solutions: 1.0, 2.0, 3.0, 4.0, and 5.0 µg/mL of iron from *Standard stock solution* prepared as follows. To separate 100-mL volumetric flasks transfer 2.0, 4.0, 6.0, 8.0, and 10.0 mL, respectively, of *Standard stock solution*. Dilute the contents in each flask with *Solution A* to volume, and mix.

Sample stock solution: Nominally equivalent to 0.5 mg/mL of iron prepared as follows. Using a "to contain" pipet, transfer a volume of Injection, nominally equivalent to 100 mg of iron, to a 200-mL volumetric flask. Dilute with *Solution A* to volume, and mix.

Sample solution: Nominally equivalent to 4 µg/mL of iron in *Solution A* from *Sample stock solution* prepared as follows. Transfer 2.0 mL of *Sample stock solution* to a 250-mL volumetric flask, and dilute with *Solution A* to volume.

Instrumental conditions

(See *Atomic Absorption Spectroscopy* ⟨852⟩.)

Mode: Atomic absorption

Analytical wavelength: Iron emission line of 248.3 nm

Lamp: Iron hollow-cathode

Flame: Air–acetylene

Blank: *Solution A*

Analysis

Samples: *Standard solutions* and *Sample solution*

Plot the absorbance of each of the *Standard solutions* versus concentration, in µg/mL, of iron, and draw the straight line best fitting the five plotted points. From the graph so obtained, determine the concentration of iron, in µg/mL, in the *Sample solution*, C_A.

Calculate the percentage of the labeled amount of iron in the portion of Injection taken:

$$\text{Result} = (C_A/C_T) \times 100$$

C_A = concentration of iron in the *Sample solution*, determined from the standard calibration graph (µg/mL)

C_T = nominal concentration of the *Sample solution* (µg/mL)

Acceptance criteria: 95.0%–105.0%

OTHER COMPONENTS

- **Antimicrobial Agents—Content, *Phenol* ⟨341⟩:** NMT 0.5%

IMPURITIES

- **Content of Chloride**

Sample: Using a "to contain" pipet, transfer 10.0 mL of Injection to a 150-mL beaker, rinsing the pipet into the beaker with several small portions of water. Add 50 mL of water and 2 mL of nitric acid.

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N silver nitrate VS

Endpoint detection: Potentiometric

Analysis: Titrate with *Titrant* determining the endpoint potentiometrically using silver–glass electrodes. Each mL of *Titrant* consumed is equivalent to 3.545 mg of chloride (Cl).

Acceptance criteria

For products labeled to contain 50 mg/mL of iron: 0.48%–0.68%

For products labeled to contain 75 or 100 mg/mL of iron: 0.8%–1.1%

- **Nonvolatile Residue**

Sample solution: Using a "to contain" pipet, transfer 1.0 mL of Injection onto 3–5 g of sand spread in a shallow layer in a stainless steel dish, the dish and sand having been previously dried and weighed. Rinse the pipet, with several small portions of water, onto the sand.

Analysis: Evaporate the *Sample solution* on a steam bath to dryness, continue the drying in an oven at 105° for 15 h, and weigh.

Acceptance criteria

For products labeled to contain 50 mg/mL of iron: 28.0%–32.0%

For products labeled to contain 75 mg/mL of iron: 35.0%–40.0%

For products labeled to contain 100 mg/mL of iron: 37.0%–43.0%

SPECIFIC TESTS

- **pH ⟨791⟩:** 4.5–7.0
- **Bacterial Endotoxins Test ⟨85⟩:** NMT 0.50 USP Endotoxin Units/mg of iron

Delete the following:

▲● **Acute Toxicity** ▲(TBD)

- **Absorption from Injection Site**

Analysis: Prepare a site over the semitendinosus muscle of one leg of each of two rabbits by clipping the fur and disinfecting the exposed skin. Inject each site with a dose of 0.4 mL/kg of body weight in the following manner. Place the needle in the distal end of the semitendinosus muscle at an angle such as to ensure that the full length of the needle is used, then pass it through the sartorius and vastus medialis muscles. House the rabbits separately. Seven days after the injection, sacrifice the rabbits, and dissect the treated legs to examine the muscles.

Acceptance criteria: No heavy black deposit of unabsorbed iron compounds is observed, and the tissue is only lightly colored.

- **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products* ⟨1⟩

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I or Type II glass.

Page Information:

Not Applicable

Current DocID: