

BRIEFING

Iron Sucrose Injection. On the basis of comments received and supporting validation data, a pending revision is proposed to revise the tests for *Limit of Fe II* and *Absence of Low-Molecular Weight Fe(II) and Fe(III) Complexes*. Currently there is an official USP–NF monograph for this product which uses a nonspecific polarographic test method for determining the limit of Fe(II) and low-molecular weight Fe(II) and Fe(III) complexes. This proposal therefore includes revised procedures for these two tests only, which are specific to determining the limit of Fe II and absence of low-molecular weight Fe(II) and Fe(III) complexes. These procedures may later be adopted into USP–NF once the product is approved by FDA.

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Iron Sucrose Injection

Draft 1

IMPURITIES

Change to read:

Inorganic Impurities

• **LIMIT OF Fe(II)**

~~Supplementary electrolyte solution: 150 mg/mL of sodium acetate in water, adjusted with 0.1 N acetic acid to a pH of 7.0~~

~~Sample solution: Volume of Iron Sucrose Injection equivalent to 20–120 µg of elemental iron/mL of water~~

~~Analysis: Transfer a suitable amount of Supplementary electrolyte solution to a polarographic cell equipped with a mercury drop electrode. With the electrode submerged in the liquid, bubble nitrogen through the liquid for 5 min. Avoiding any undue exposure to air, immediately transfer the Sample solution to the polarographic cell. [NOTE—The sample must be analyzed immediately upon opening the container.] Record the polarogram from 0 mV and –1700 mV. The Fe(III)/Fe(II) peak is detected at –750 ± 50 mV and the Fe(II)/Fe(0) peak is detected at –1400 ± 50 mV. Measure the Fe(II)/Fe(III) peak responses of the polarogram, and perform a blank determination. Calculate the Fe(II) content, in % w/v, in the volume of Iron Sucrose Injection taken:~~

$$\text{Result} = [1 - (2/R)] \times C_T$$

R = peak response ratio of Fe(II) to Fe(III)
C_T = total iron concentration of the Iron Sucrose Injection (% w/v)

~~Sample solution: Prepare a solution of 2 g each of sodium bicarbonate and potassium iodide in 20 mL of water. Slowly add 7 mL of concentrated hydrochloric acid, and swirl to dissolve the salts. Using a volumetric pipette, add 2.0 mL of Injection, and rinse the pipette with 5–10 mL of water into the same flask. Cover the flask, and let the solution stand for 15 min.~~

~~Blank solution: Prepare a solution similar to the Sample solution except for the addition of the iron sucrose sample.~~

~~Analysis: Add 1.0 mL of starch indicator, and titrate with 0.1 N sodium thiosulfate VS.~~

~~Samples: Sample solution and Blank solution Calculate the Fe(II) content, in percentage, in the volume of Iron Sucrose Injection taken:~~

$$\text{Result} = T_1 - \text{Fe(III)} \times (F)100$$

T₁ = Total iron as determined from the Assay for Iron (mg/mL)
F = 1 g/1000 mg
Calculate Fe(III) (mg/mL) as follows:

$$\text{Result} = (V_1 - V_2) \times N \times W_1/V$$

V₁ = titer values of Sample solution (mL)
V₂ = titer values of Blank solution (mL)
N = normality of the sodium thiosulfate VS
W₁ = equivalent weight of iron, equal to 55.85
V = volume of sample (mL)

◀ (1-May-2010)

Acceptance criteria: NMT 0.4%

SPECIFIC TESTS

Change to read:

• **ABSENCE OF LOW-MOLECULAR WEIGHT Fe(II) AND Fe(III) COMPLEXES** In the polarograms obtained in the test for *Limit of Fe(II)*, no additional peaks are found:

▶ **Ascorbic acid solution:** 100 mg/mL of ascorbic acid in water

Dipyridine reagent solution: 3 mg/mL of 2,2'-dipyridine in 5% acetic acid solution

Ammonium acetate solution: 5 M aqueous ammonium acetate

Sodium chloride solution: 9 mg/mL of sodium chloride in water

Standard stock solution: 50 µg/mL of iron prepared from 350 mg/L of ferrous ammonium sulfate in water

Standard solution: Pipet 6 mL of the Standard stock solution into a 200-mL volumetric flask, add 1 mL of concentrated hydrochloric acid, and wait for 15 min. Add 10 mL of Ascorbic acid solution, and wait for 15 min. Then add 5 mL of Ammonium acetate solution followed by 4 mL of the Dipyridine reagent solution. Allow the solution to stand for 15 min at ambient temperature, and dilute with water to volume.

Sample solution: Transfer 3.0 mL of Iron Sucrose Injection into a 12,000–14,000 dialysis bag and dialyze against 100 mL of Sodium chloride solution for 18 h. Transfer 100 mL of the dialysate into a 200-mL volumetric flask, add 1 mL of concentrated hydrochloric acid, and wait for 15 min. Add 10 mL of Ascorbic acid solution, and wait for 15 min. Then add 5 mL of Ammonium acetate solution followed by 4 mL of the Dipyridine reagent solution. Allow the solution to stand for 15 min at ambient temperature, and dilute with water to volume.

Analysis

Samples: Standard solution and Sample solution Set the wavelength of the spectrophotometer at 523 nm and measure the absorbance readings of the samples. Calculate the iron (µg/mL) in the low-molecular weight fraction from the sample taken.

$$\text{Result} = (A_S/A_U) \times C_S \times D$$

A_S = absorbance of the Standard solution
A_U = absorbance of the Sample solution
C_S = concentration of iron in the Standard solution (µg/mL)
D = dilution factor

Acceptance criteria: NMT 100 ppm ◀ (1-May-2010)