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Fondaparinux Sodium Injection

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DEFINITION

Fondaparinux Sodium Injection is a sterile solution of Fondaparinux Sodium in Water for Injection with sodium chloride added for isotonicity. It is a clear, colorless to slightly yellow solution.

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **B.** [IDENTIFICATION TESTS—GENERAL, Chloride \(191\)](#): Proceed as directed in the chapter. Meets the requirements of the [Chloride and Sulfate \(221\)](#) test.

ASSAY

• **PROCEDURE**

5 mM phosphate solution: 0.210 g of [monobasic sodium phosphate dihydrate](#) and 0.650 g of [dibasic sodium phosphate dihydrate](#). Dissolve in and dilute with [water](#) to 1000 mL. pH is approximately 7.3.

Solution A: 15 ± 10 ppm of [dimethylsulfoxide \(DMSO\)](#) in 5 mM phosphate solution (1 in 67000, v/v)

Solution B: 2.0 M [sodium chloride](#) solution in 5 mM phosphate solution

Mobile phase: See [Table 1](#). [NOTE—Make adjustments to *Solution A* as necessary, and degas the *Mobile phase* before use. Dissolved gas in the injected solution may lead to baseline interference. Degassing of the *Mobile phase* is critical to obtain a suitable signal-to-noise ratio and higher sensitivity. An eluant generator¹ installed between the injector and the column may reduce the baseline interference.]

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	50	50
5	50	50
25	5	95
30	5	95
35	50	50
50	50	50

System suitability solution: 5.0 mg/mL of [USP Fondaparinux Sodium System Suitability Mixture B RS](#)

Standard solution: 5.0 mg/mL of [USP Fondaparinux Sodium for Assay RS](#) in [water](#). Prepare in duplicate.

Sensitivity check solution: 0.01 mg/mL of [USP Fondaparinux Sodium for Assay RS](#) in [water](#) from the *Standard solution*

Sample solution: Transfer the contents of prefilled syringes to a suitable container, and mix well. Dilute with [water](#), if needed, to obtain a 5.0-mg/mL solution of fondaparinux sodium.

Blank:

[water](#)

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4-mm × 25-cm; packing [L46](#)

Column temperature: 25°

Flow rate: 1.0 mL/min

Injection volume: 100 µL

System suitability

Samples: *System suitability solution, Standard solution, Sensitivity check solution, and Blank*

Inject the *Blank* in duplicate, the *Sensitivity check solution*, and the *System suitability solution*. Inject the *Standard solution* at least six times consecutively.

Suitability requirements

Specificity and baseline drift: The chromatogram of a second *Blank* injection shows a baseline drift between 0.00 and 0.02 AU over 30 min. If necessary, adjust the DMSO content of the *Mobile phase* until an acceptable baseline is achieved. The chromatogram of a second *Blank* injection does not contain peaks between 3.00 and 30.00 min.

Chromatogram similarity: The chromatogram of the *System suitability solution* corresponds to that of the reference chromatogram provided with [USP Fondaparinux Sodium System Suitability Mixture B RS](#).

Signal-to-noise ratio: NLT 10 for the fondaparinux peak in the chromatogram of the *Sensitivity check solution*

Resolution: NLT 1.2 between fondaparinux related compound C and fondaparinux related compound D, *System suitability solution*; NLT 1.1 between fondaparinux related compound F and fondaparinux related compound G (see [Table 2](#)), *System suitability solution*

Standard agreement: The difference in the mean response factors for each *Standard solution* is NMT 2.0%.

Relative standard deviation: For six consecutive injections of the *Standard solution* the calculated % RSD of the area of the fondaparinux peak is NMT 2.0%. The retention time of the fondaparinux peak should be ±5% of the mean value. The calculated % RSD of the response factors for six consecutive injections of the *Standard solution* is NMT 2.0%. The calculated % RSD of the pooled response factors for all injections of the *Standard solution* is NMT 2.0%. The % RSD of the mean response factors for the duplicate preparations of the duplicate *Standard solutions* is NMT 2.0%.

Analysis

Samples: *Standard solution and Sample solution*

Inject the *Standard solution* at least six times consecutively. Inject duplicate preparations of the *Sample solution*. Record the chromatograms, and measure the retention times and areas for the major peaks (excluding peaks before 3.00 and after 30.00 min).

Calculations: For each injection of the *Standard solution* calculate a response factor (F_R):

$$F_R = (C_S / r_S)$$

C_S = concentration of fondaparinux sodium in the *Standard solution* (mg/mL)

r_S = peak response of fondaparinux sodium from the *Standard solution*

Relative retention times (RRT) are calculated by dividing the retention time of the peak by the retention time of fondaparinux established by the *Standard solution*. Using the mean response factor (F_M), calculate the concentration (mg/mL) of fondaparinux sodium in each injection of the *Sample solution*:

$$\text{Result} = F_M \times r_U \times D_U$$

F_M = mean response factor from the *Standard solution*

r_U = peak response of fondaparinux sodium in the *Sample solution*

D_U = dilution factor for the *Sample solution*, if needed

Acceptance criteria: 90%–105% (for the 2.5-mg/0.5-mL injection) or 95%–105% (for the 5.0-mg/0.4-mL, 7.5-mg/0.6-mL, and 10-mg/0.8-mL injections)

IMPURITIES

• FREE SULFATE DETERMINATION

[NOTE—Regenerate the anion-exchange column for 15 min with 0.1 M [sodium hydroxide](#) after each injection of fondaparinux sample, followed by equilibration with *Mobile phase* for 21 min.]

Mobile phase: 3 mM carbonate solution using 0.106 g of [sodium carbonate](#) and 0.168 g of [sodium hydrogen carbonate](#) in 1000 mL of [water](#)

Standard solution 1: Prepare a 1000-ppm sulfate solution, using [anhydrous sodium sulfate](#) in [water](#).

Standard solution 2: Prepare a 10-ppm sulfate solution by diluting *Standard solution 1* in [water](#).

Sensitivity check solution: Dilute 1.0 mL of *Standard solution 2* with [water](#) to 5.0 mL.

Resolution solution: 0.100 g of [anhydrous sodium sulfate](#) and 0.100 g of [sodium chloride](#). Dissolve in and dilute with [water](#) to 100.0 mL.

Dilute 1.0 mL with [water](#) to 100.0 mL.

Sample solution: In triplicate, combine and mix the contents of a suitable number of syringes. Dilute 0.8 mL (strengths of 5.0 mg/0.4 mL, 7.5 mg/0.6 mL, and 10.0 mg/0.8 mL) or 2.0 mL (strengths of 1.5 mg/0.3 mL and 2.5 mg/0.5 mL) with [water](#) to 5.0 mL.

Blank: A sample of the [water](#) used to prepare other solutions

Chromatographic system

(See [Chromatography \(621\), System Suitability](#)).

Mode: LC