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Somatropin for Injection

DEFINITION

Somatropin for Injection is a sterile, lyophilized mixture of Somatropin with one or more suitable buffering and stabilizing agents.

Manufacturers must demonstrate a correlation between the *Assay* and a validated and approved growth-promotion-based bioassay.

[NOTE—One mg of anhydrous Somatropin is equivalent to 3.0 USP Somatropin Units.]

IDENTIFICATION

• **A.** The retention time of the somatropin peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Chromatographic Purity*, except that a *Standard solution* is also chromatographed and prepared by reconstituting a vial of USP Somatropin RS with *Diluent* to obtain a known concentration of about 2 mg/mL.

Change to read:

• **B.** ▲Somatropin Bioidentity Test ⟨126⟩▲ (CN 1-May-2023) **:** Meets the requirements

[NOTE—The bioidentity test may be performed either on the Somatropin bulk drug substance or on the finished pharmaceutical product.]

ASSAY

• **Somatropin Content**

Buffer solution: 5.18 g of dibasic sodium phosphate and 3.65 g of monobasic sodium phosphate in 950 mL of water. Adjust with phosphoric acid or sodium hydroxide solution to a pH of 7.0. Dilute with water to 1000 mL.

Mobile phase: Isopropyl alcohol and *Buffer solution* (3:97). Filter and degas.

Diluent: *Buffer solution* and water (1:1.5)

System suitability solution: Place 1 vial of USP Somatropin RS in an oven at 50° for 12–24 h. Remove from the oven, and dissolve the contents of the vial in *Diluent* to obtain a solution with a known concentration of about 1 mg/mL and a dimer content of 1%–2%.

Standard solution: Known concentration of about 1 mg/mL of USP Somatropin RS in *Diluent*

Sample solution: Dissolve the contents of a suitable number of containers in *Diluent* to obtain a concentration of 1 mg/mL of somatropin.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 214 nm

Column: 7.8-mm × 30-cm; packing L33

Column temperature: Ambient

Flow rate: 0.6 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NMT 0.4 for the ratio of the valley height, between the dimer and the monomer, and the dimer peak height

Tailing factor: NMT 1.7 for the monomer (major) peak

Analysis

Samples: *Standard solution* and *Sample solution*, separately injected

Record the chromatograms for NLT twice the retention time of the somatropin monomer (major) peak, and measure the peak responses for the monomer.

Calculate the percentage of somatropin per container:

$$\text{Result} = (r_U/r_S) \times C_S \times (V/N) \times 100$$

r_U = peak response of the monomer from the *Sample solution*

r_S = peak response of the monomer from the *Standard solution*

C_S = concentration of USP Somatropin RS in the *Standard solution* (mg/mL)

V = total volume of the *Sample solution* (mL)

N = number of containers used to obtain the *Sample solution*

Acceptance criteria: 89.0%–110.0%

IMPURITIES

• **Chromatographic Purity**

Diluent: 0.05 M tris(hydroxymethyl)aminomethane in water. Adjust with hydrochloric acid to a pH of 7.5.

Mobile phase: *n*-Propyl alcohol and degassed *Diluent* (29:71). Filter.

System suitability solution: 2.0 mg/mL of somatropin in *Diluent*. Pass through a filter to sterilize or add sodium azide to a final concentration of 0.01%, and allow to stand at room temperature for 24 h. [Note—Use within 48 h of preparation, or store the solution in a refrigerator until ready to use.]

Sample solution: 2.0 mg/mL of somatropin in *Diluent*. [Note—Maintain the solutions between 2° and 8°, and use within 24 h. If an automatic injector is used, maintain the temperature between 2° and 8°.]

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; packing L26

Column temperature: 45°

Flow rate: 0.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.0 between somatropin and its adjacent peak

Tailing factor: 0.9–1.8 for the somatropin (major) peak

Analysis

Sample: *Sample solution*

Calculate the percentage of impurities in the portion of Injection taken:

$$\text{Result} = [A_U/(A_U + A_S)] \times 100$$

A_U = sum of all the peak responses other than the somatropin (major) peak, disregarding any peak due to the solvent

A_S = peak response of somatropin

Acceptance criteria: NMT 12% of total impurities

• **Limit of High Molecular Weight Proteins**

Buffer solution, Mobile phase, Diluent, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Samples: *System suitability solution* and *Sample solution*

Measure the areas of the main peak and of the peaks eluting before the main peak, excluding the solvent peaks.

Calculate the percentage of high molecular weight proteins in the portion of Injection taken:

$$\text{Result} = [A_H/(A_H + A_M)] \times 100$$

A_H = sum of the areas of the high molecular weight peaks

A_M = peak area of the monomer from the *Sample solution*

Acceptance criteria: NMT 6% of high molecular weight proteins

SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 20 USP Endotoxin Units/mg of Somatropin

• **Sterility Tests ⟨71⟩,** *Test for Sterility of the Product to Be Examined, Membrane Filtration*: Meets the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store between 2° and 8°.

• **Labeling:** The labeling states that the material is of recombinant DNA origin.

• **USP Reference Standards ⟨11⟩**
USP Somatropin RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
SOMATROPIN FOR INJECTION	Rebecca C. Potts Associate Scientific Liaison	BIO2 Biologics Monographs 2 - Proteins
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	BIO2 Biologics Monographs 2 - Proteins

Chromatographic Database Information: Chromatographic Database

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