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Glucagon for Injection

DEFINITION

Glucagon for Injection is a sterile lyophilized mixture of the hydrochloride of glucagon with one or more suitable buffering and stabilizing agents. It contains NLT 65% and NMT 110% of the labeled amount of glucagon.

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. Glucagon Bioidentity Tests ⟨123⟩:** Meets the requirements

ASSAY

Change to read:

- **Procedure**

Solution A: Dissolve 16.3 g of monobasic potassium phosphate in 750 mL of water, adjust with phosphoric acid to a pH of 2.7 (±0.05), add water to 800 mL, add 200 mL of acetonitrile, and degas.

Solution B: Prepare a degassed solution of acetonitrile and water (4:6).

Mobile phase: See *Table 1*. [Note—The ratio of *Solution A* to *Solution B* can be adjusted to obtain a retention time of about 21 min for the main peak.]

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	61	39
25[a]	61	39
29	12	88
30	12	88
31	61	39
▲45▲ (USP 1-Aug-2022)	61	39

[a] The end time of the isocratic elution can be adjusted so that the gradient begins after the fourth desamido peak elutes (relative retention time about 1.4). The rest of the program is then adjusted accordingly with this offset.

System suitability solution: Reconstitute a vial of ▲USP Glucagon (Human) RS▲ (USP 1-Aug-2022) in 0.01 N hydrochloric acid to obtain a solution with a concentration of about 0.5 mg/mL. Let stand at 50° for 48 h. At least 7% total of all four desamido glucagons should be present in the solution.

Standard solution: Reconstitute a vial of ▲USP Glucagon (Human) RS▲ (USP 1-Aug-2022) in 0.01 N hydrochloric acid to obtain a solution with a concentration of about 0.5 mg/mL.

Sample solution: Dissolve the substance to be examined in 0.01 N hydrochloric acid in order to obtain a concentration of 0.5 mg/mL of glucagon.

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 3-mm × 15-cm; 3-µm or less packing L1

Column temperature: 45°

Flow rate: 0.5 mL/min

Injection volume: 15 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between the main peak and the first eluting desamido peak. Four peaks eluting after the glucagon peak that correspond to the desamido glucagons are clearly visible, *System suitability solution*.

Tailing factor: NMT 1.8 for the glucagon peak, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of glucagon ($C_{153}H_{225}N_{43}O_{49}S$) in the portion of Glucagon for Injection taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

C_U = concentration of the *Sample solution* (mg/mL)

Acceptance criteria: 65%–110%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A, Solution B, Mobile phase, System suitability solution, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Sample solution: Dissolve the substance to be examined in ▲0.01 N hydrochloric acid▲ (USP 1-Aug-2022) in order to obtain a concentration of 0.5 mg/mL of glucagon.

Analysis

Sample: *Sample solution*

Calculate separately the percentage of each impurity in the portion of Glucagon for Injection taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity

r_T = sum of all the peak responses

Acceptance criteria: NMT 14% total of all four desamido glucagons is found, and NMT 31% of total impurities and related compounds is found.

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I, Method Ic*:** NMT 4.0%

• **pH and Clarity of Solution:** Dissolve it in the solvent and in the concentration recommended in the labeling: the pH of the solution is between 1.7 and 3.5, and the solution is clear.

Change to read:

• **Bacterial Endotoxins Test ⟨85⟩:** ▲Meets the requirements▲ (USP 1-Aug-2022)

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **Constituted Solution:** At the time of use, it meets the requirements for *Injections and Implanted Drug Products ⟨1⟩, Product Quality Tests Common to Parenteral Dosage Forms, Specific Tests, Completeness and Clarity of Solutions*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for Constitution*.

Change to read:

• **Labeling:** The labeling states that the material is ▲synthetic or of recombinant DNA origin.▲ (USP 1-Aug-2022)

Change to read:

• **USP Reference Standards ⟨11⟩**

▲USP Glucagon (Human) RS▲ (USP 1-Aug-2022)

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

Topic/Question	Contact	Expert Committee
GLUCAGON FOR INJECTION	Julie Zhang Associate Science & Standards Liaison	BIO12020 Biologics Monographs 1 - Peptides

Chromatographic Database Information: Chromatographic Database

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