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Gonadorelin Hydrochloride

5-OxoP H W S Y G L R P G —NH₂ • x HCl

C₅₅H₇₅N₁₇O₁₃ × HCl 1182.30 (free base)

Gonadorelin hydrochloride;

5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosylglycyl-L-leucyl-L-arginyl-L-prolylglycinamide hydrochloride salt CAS RN®: 51952-41-1; UNII: 3PFC574ITA.

DEFINITION

Gonadorelin Hydrochloride is a synthetic polypeptide hormone having the property of stimulating the release of the luteinizing hormone from the hypothalamus. It contains NLT 95.0% and NMT 102.0% of gonadorelin (C₅₅H₇₅N₁₇O₁₃), calculated on the anhydrous and hydrochloride-free basis.

[CAUTION—Gonadorelin Hydrochloride is extremely hygroscopic. Protect from exposure to moisture, and store in a desiccator.]

IDENTIFICATION

• **A.** The monoisotopic mass by [Mass Spectrometry \(736\)](#) is 1181.6 ± 1 mass units.

[NOTE—This quantity corresponds to $m/z = 1182.6 \pm 1$ for $(M + H)^+$ or $m/z = 591.8 \pm 0.5$ for $(M + 2H)^{2+}$.]

• **B. HPLC**

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

Identity sample solution: Mix equal volumes of the *Standard solution* and the *Sample solution*.

Analysis

Samples: *Standard solution*, *Sample solution*, and *Identity sample solution*

Examine the chromatograms of the *Standard solution*, the *Sample solution*, and the *Identity sample solution*.

Acceptance criteria: The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, and the major peak of the *Identity sample solution* elutes as a single peak.

ASSAY

• **PROCEDURE**

[NOTE—Perform all manipulations involving the weighing of the gonadorelin hydrochloride and the Reference Standard in a low-humidity glove box.]

Buffer: Dissolve 6.8 g of monobasic potassium phosphate in water and dilute to 1 L. Adjust with 1 N potassium hydroxide to a pH of 6.5.

Mobile phase: Acetonitrile and *Buffer* (18:82)

Standard solution: 0.10 mg/mL of [USP Gonadorelin Hydrochloride RS](#) in *Mobile phase*

[NOTE—*Standard solution* may be stored in a refrigerator for 2 months. Remove suitable portions and warm to room temperature before use.]

Sample solution: 0.10 mg/mL of Gonadorelin Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 5-μm packing L1

Flow rate: 1.5 mL/min

[NOTE—Condition the column with *Mobile phase* until a stable baseline is obtained.]

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Retention time: 8–11 min for the gonadorelin peak

Tailing factor: NMT 2.5

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of gonadorelin ($C_{55}H_{75}N_{17}O_{13}$) in the portion of Gonadorelin Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times F \times [100/(100 - W - \text{HCl})] \times 100$$

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

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

C_S = concentration of [USP Gonadorelin Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

F = conversion factor, (1182.3/1255.2)

W = water content in Gonadorelin Hydrochloride sample (%)

HCl = hydrochloride content in Gonadorelin Hydrochloride sample (%) [NOTE—%HC = %Cl $\times$ (36.46/35.45).]

Acceptance criteria: 95.0–102.0% on the anhydrous and hydrochloride-free basis

OTHER COMPONENTS

• COUNTER ION: CHLORIDE

Sample: 25 mg of Gonadorelin Hydrochloride

Titrimetric system

(See [Titrimetry \(541\)](#).)

Mode: Direct titration

Titrant: 0.01 N silver nitrate VS

Blank: To 1 mL of methanol, add 10 mL of water and 1 drop of glacial acetic acid.

Endpoint detection: Potentiometric

Analysis: Dissolve the *Sample* in 1 mL of methanol, and add 10 mL of water and 1 drop of glacial acetic acid. Titrate with *Titrant* and perform a blank determination.

Calculate the percentage of chloride (Cl^-) in the portion of Gonadorelin Hydrochloride taken:

$$\text{Result} = [(V_S - V_B) \times N \times F \times 100]/W$$

V_S = *Titrant* volume consumed by the *Sample* (mL)

V_B = *Titrant* volume consumed by the *Blank* (mL)

N = actual normality of the *Titrant* (Eq/L = mEq/mL)

F = equivalency factor for chloride, 35.45 mg/mEq

W = *Sample* weight (mg)

Acceptance criteria: 4.0%–6.0%

IMPURITIES

• GONADORELIN RELATED IMPURITIES

[NOTE—The *Sample solution* may be stored at room temperature for up to 20 min or at 4° for up to 8 h.]

Solution A: Dissolve 6.8 g of monobasic potassium phosphate in water and dilute to 1 L. Adjust with 1 N potassium hydroxide to a pH of 6.5.

Solution B: Acetonitrile

Mobile phase: See [Table 1](#).

Table 1