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Methadone Hydrochloride Injection

DEFINITION

Methadone Hydrochloride Injection is a sterile solution of Methadone Hydrochloride in Water for Injection. It contains, in each mL, NLT 9.5 mg and NMT 10.5 mg of methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$).

IDENTIFICATION

- **A. [IDENTIFICATION—ORGANIC NITROGENOUS BASES \(181\)](#):** Meets the requirements

ASSAY

Change to read:

• PROCEDURE

Internal standard solution: 5 mg/mL of procaine in methylene chloride

Standard solution: Transfer 10 mg of [USP Methadone Hydrochloride RS](#) to a 60-mL separator. Add 1 mL of water and 2 mL of 0.5 N sodium hydroxide, and extract with three 10-mL portions of methylene chloride, combining the extracts in a vessel containing about 3 g of anhydrous sodium sulfate. Transfer 2.0 mL of *Internal standard solution* to the vessel containing the extracts, insert the stopper, and mix. Decant 15 mL of the methylene chloride solution to a test tube, and evaporate to a volume of 2–3 mL using vacuum or a stream of nitrogen.

Sample solution: Transfer 1.0 mL of Injection, equivalent to 10 mg of methadone hydrochloride, to a 60-mL separator. Add 2 mL of 0.5 N sodium hydroxide, and extract with three 10-mL portions of methylene chloride, combining the extracts in a vessel containing about 3 g of anhydrous sodium sulfate. Transfer 2.0 mL of *Internal standard solution* to the vessel containing the extracts, insert the stopper, and mix. Decant 15 mL of the methylene chloride solution to a test tube, and evaporate to a volume of 2–3 mL using vacuum or a stream of nitrogen.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: Glass column, 1.2-m long and 4-mm in diameter; packed with 3% phase G2 on 100- to 200-mesh support S1A

Temperatures

Column: 170°

Injection port: 225°

Detector: 240°

Carrier gas: Dry helium

Flow rate: 55 mL/min

Injection volume: Containing 5 µg of methadone

System suitability

Sample: *Standard solution* (six replicate injections)

Suitability requirements

Resolution: NLT 5.0 between methadone and procaine

Coefficient of variation: NMT 1% in the ratios of the peak areas of methadone to the peak area of procaine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in mg, of methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$) in each mL of Injection taken:

$$\text{Result} = (R_U/R_S) \times W \blacktriangle (\text{ERR 1-Oct-2018})$$

R_U = peak area ratio of methadone to procaine from the *Sample solution*

R_S = peak area ratio of methadone to procaine from the *Standard solution*

W = weight, in mg, of [USP Methadone Hydrochloride RS](#) in the *Standard solution*

Acceptance criteria: 9.5–10.5 mg/mL

SPECIFIC TESTS

- **[pH \(791\)](#):** 3.0–6.5

- **BACTERIAL ENDOTOXINS TEST (85):** NMT 8.8 USP Endotoxin Units/mg of methadone hydrochloride
- **OTHER REQUIREMENTS:** It meets the requirements in [Injections and Implanted Drug Products \(1\)](#).

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in single-dose or multiple-dose, light-resistant containers, preferably of Type I glass.

Change to read:

- **USP REFERENCE STANDARDS (11).**

▲▲ (CN 1-May-2018)
[USP Methadone Hydrochloride RS](#)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
METHADONE HYDROCHLORIDE INJECTION	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

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