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Mitoxantrone Injection

DEFINITION

Mitoxantrone Injection is a sterile solution of Mitoxantrone Hydrochloride in Water for Injection. It contains the equivalent of NLT 90.0% and NMT 105.0% of the labeled amount of mitoxantrone ($C_{22}H_{28}N_4O_6$).

IDENTIFICATION

Change to read:

• ▲▲**A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: **197U**▲ (CN 1-May-2020) ▲ (USP 1-May-2019)

Standard solution: 0.01 mg/mL of USP Mitoxantrone Hydrochloride RS (equivalent to 0.01 mg/mL of mitoxantrone) prepared as follows. Transfer a suitable amount of USP Mitoxantrone Hydrochloride RS to an appropriate volumetric flask. Add 50% of the flask volume of water and 10% of the flask volume of 1 N hydrochloric acid VS. Dilute with water to volume.

Sample solution: Nominally 0.01 mg/mL of mitoxantrone from Injection prepared as follows. Transfer a volume of Injection equivalent to 2 mg of mitoxantrone to a 200-mL volumetric flask containing about 50% of the flask volume of water and 10% of the flask volume of 1 N hydrochloric acid VS. Dilute with water to volume.

Acceptance criteria: ▲Meets the requirements▲ (USP 1-May-2019)

Add the following:

▲• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2019)

ASSAY

Change to read:

• **Procedure**

Solution A: 0.09 mg/mL of sodium 1-heptanesulfonate prepared as follows. Dissolve 22.0 g of sodium 1-heptanesulfonate in 150 mL of water. Pass through a filter of NMT 0.5-µm pore size and transfer the filtrate to a 250-mL volumetric flask. Wash the filter with 50 mL of water and add the ▲washings▲ (USP 1-May-2019) to the flask. Add 32.0 mL of glacial acetic acid to the flask, and dilute with water to volume.

Mobile phase: Acetonitrile, *Solution A*, and water▲(10:1:30)▲ (USP 1-May-2019)

System suitability solution: 0.2 mg/mL of ▲monoalkyl mitoxantrone hydrochloride▲ (USP 1-May-2019) and 0.1 mg/mL of mitoxantrone hydrochloride from USP Mitoxantrone System Suitability Mixture RS in *Mobile phase*

Standard solution: 0.46 mg/mL of USP Mitoxantrone Hydrochloride RS (equivalent to 0.4 mg/mL of mitoxantrone) prepared as follows. Transfer a suitable amount of USP Mitoxantrone Hydrochloride RS to an appropriate volumetric flask. Add 80% of the flask volume of *Mobile phase*. Sonicate for about 5 min to dissolve. Cool to room temperature and dilute with *Mobile phase* to volume.

Sample solution: Nominally 0.4 mg/mL of mitoxantrone from Injection, in *Mobile phase*

Chromatographic system

Chromatography ⟨621⟩, *System Suitability*

Mode: LC

Detector: UV 254 nm

Column: 3.9 mm × 30 cm; ▲10-µm▲ (USP 1-May-2019) packing L11

[Note—After use, wash the column with a mixture of acetonitrile and water (50:50), and store in this mixture.]

Flow rate: 3 mL/min

Injection volume: 50 µL

System suitability

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

[Note—The relative retention times for mitoxantrone and ▲monoalkyl mitoxantrone hydrochloride▲ (USP 1-May-2019) are about ▲1.0 and 1.4,▲ (USP 1-May-2019) respectively.]

Suitability requirements

Resolution: NLT 3.0 between mitoxantrone and ▲monoalkyl mitoxantrone hydrochloride,▲ (USP 1-May-2019) *System suitability solution*

Tailing factor: NMT 2.0 for mitoxantrone, *System suitability solution*

Capacity factor, *k'*: NLT 3.5 for mitoxantrone, *Standard solution*

Relative standard deviation: NMT ▲1.0%,▲ (USP 1-May-2019) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mitoxantrone ($C_{22}H_{28}N_4O_6$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak area of mitoxantrone from the *Sample solution*

r_S = peak area of mitoxantrone from the *Standard solution*

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

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

M_{r1} = molecular weight of mitoxantrone, 444.49

M_{r2} = molecular weight of mitoxantrone hydrochloride, 517.40

Acceptance criteria: 90.0%–105.0%

IMPURITIES

• **Organic Impurities**

Analysis: Using the chromatogram of the *Sample solution* obtained as directed in the *Assay*, calculate the percentage of each impurity in the portion of Injection taken:

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

r_U = peak response of each impurity

r_T = sum of all peak responses

Acceptance criteria

Individual impurities: NMT 1.5%

Total impurities: NMT 3.0%

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 3.0–4.5

Change to read:

• **Bacterial Endotoxins Test** ⟨85⟩**:** ▲Meets the requirements▲ (USP 1-May-2019)

Change to read:

• **Sterility Tests** ⟨71⟩**:** Meets the requirements ▲▲ (USP 1-May-2019)

• **Other Requirements:** It meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩.

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass. ▲Do not freeze. Store at controlled room temperature.▲ (USP 1-May-2019)

Change to read:

• **Labeling:** Label Injection to state both the content of the active moiety and the name of the salt used in formulating the article. Label Injection to indicate that it is to be diluted to appropriate ▲volume with▲ (USP 1-May-2019) suitable fluid before administration.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Mitoxantrone Hydrochloride RS

USP Mitoxantrone System Suitability Mixture RS

▲0.2 mg of 1-Amino-5,8-dihydroxy-4-({2-[(2-hydroxyethyl)amino]ethyl}amino)anthracene-9,10-dione hydrochloride [monoalkyl mitoxantrone hydrochloride ($C_{18}H_{19}N_3O_5 \cdot HCl$, 393.82)] and 0.1 mg of USP Mitoxantrone Hydrochloride RS▲ (USP 1-May-2019)

Topic/Question	Contact	Expert Committee
MITOXANTRONE INJECTION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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