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*Add the following:*

# ▲Sildenafil Injection

**DEFINITION**

Sildenafil Injection is a sterile solution of Sildenafil Citrate in Water for Injection. It contains NLT 95.0% and NMT 105.0% of the labeled amount of sildenafil ($C_{22}H_{30}N_6O_4S$). It also contains dextrose.

**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.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

**ASSAY**

- **Procedure**

**Solution A:** 15.4 g/L of ammonium acetate in water

**Mobile phase:** Acetonitrile and *Solution A* (50:50)

**Standard solution:** 0.11 mg/mL of USP Sildenafil Citrate RS in *Mobile phase*. Sonicate to dissolve if necessary.

**Sample solution:** Nominally 0.08 mg/mL of sildenafil prepared as follows. Transfer 5 mL of Injection to a 50-mL volumetric flask and dilute with *Mobile phase* to volume.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 245 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

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

**Flow rate:** 1 mL/min

**Injection volume:** 20 µL

**Run time:** NLT 1.6 times the retention time of sildenafil

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 1.0%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sildenafil ($C_{22}H_{30}N_6O_4S$) 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 response of sildenafil from the *Sample solution*

$r_S$ = peak response of sildenafil from the *Standard solution*

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

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

$M_{r1}$ = molecular weight of sildenafil, 474.58

$M_{r2}$ = molecular weight of sildenafil citrate, 666.70

**Acceptance criteria:** 95.0%–105.0%

## IMPURITIES

• **Organic Impurities**

**Dilute phosphoric acid:** 10% (v/v) phosphoric acid in water

**Buffer:** 3.5 g/L of potassium phosphate, dibasic in water. Adjust with *Dilute phosphoric acid* to a pH of 7.0.

**Solution A:** Acetonitrile and *Buffer* (14:86)

**Solution B:** Acetonitrile and *Buffer* (74:26)

**Mobile phase:** See *Table 1*.

**Table 1**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 78 | 22 |
| 5 | 78 | 22 |
| 20 | 50 | 50 |
| 30 | 40 | 60 |
| 35 | 78 | 22 |
| 40 | 78 | 22 |

**Diluent:** Methanol and water (50:50)

**Standard stock solution:** 0.46 mg/mL of USP Sildenafil Citrate RS in methanol. Sonicate to dissolve if necessary.

**Standard solution:** 1.15 µg/mL of USP Sildenafil Citrate RS from the *Standard stock solution* in *Diluent*

**Sensitivity solution:** 0.575 µg/mL of USP Sildenafil Citrate RS from the *Standard solution* in *Diluent*

**Sample solution:** Nominally 0.4 mg/mL of sildenafil prepared as follows. Transfer 5 mL of Injection to a 10-mL volumetric flask and dilute with methanol to volume.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 240 nm

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

**Column temperature:** 30°

**Flow rate:** 1 mL/min

**Injection volume:** 20 µL

**System suitability**

**Samples:** *Standard solution* and *Sensitivity solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0, *Standard solution*

**Relative standard deviation:** NMT 5.0%, *Standard solution*

**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of sildenafil *N*-oxide and any unspecified degradation product in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

$r_U$ = peak response of each degradation product from the *Sample solution*

$r_S$ = peak response of sildenafil from the *Standard solution*

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

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

$M_{r1}$ = molecular weight of sildenafil, 474.58

$M_{r2}$ = molecular weight of sildenafil citrate, 666.70

$F$ = relative response factor (see *Table 2*)

**Acceptance criteria:** See *Table 2*. The reporting threshold is 0.1%.

**Table 2**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Sildenafil *N*-oxide[a] | 0.44 | 0.95 | 0.2 |
| Sildenafil | 1.0 | — | — |
| Any unspecified degradation product | — | 1.00 | 0.2 |
| Total degradation products | — | — | 0.5 |

[a] 4-[(4-Ethoxy-3-(1-methyl-7-oxo-3-propyl-6,7-dihydro-1*H*-pyrazolo[4,3-*d*]pyrimidin-5-yl)phenyl)sulfonyl]-1-methylpiperazine 1-oxide.

## SPECIFIC TESTS

- **pH ⟨791⟩:** 3.5–4.5
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements
- **Sterility Tests ⟨71⟩:** Meets the requirements
- **Bacterial Endotoxins Test ⟨85⟩:** Meets the requirements

## ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose glass containers. Store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**

USP 5-Hydroxymethylfurfural RS

5-(Hydroxymethyl)furan-2-carbaldehyde.

$C_6H_6O_3$ 126.11

USP Sildenafil Citrate RS▲ (USP 1-Aug-2023)

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| SILDENAFIL INJECTION | Documentary Standards Support | SM52020 Small Molecules 5 |
| REFERENCE STANDARD SUPPORT | RS Technical Services RSTECH@usp.org | SM52020 Small Molecules 5 |

**Chromatographic Database Information:** Chromatographic Database

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