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Terbutaline Sulfate Injection

DEFINITION

Terbutaline Sulfate Injection is a sterile solution of Terbutaline Sulfate in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of terbutaline sulfate $[(C_{12}H_{19}NO_3)_2 \cdot H_2SO_4]$.

[**Caution—**Do not use the Injection if it is discolored.]

IDENTIFICATION

Delete the following:

▲• **A. Thin Layer Chromatography**▲ (USP 1-Dec-2023)

Add the following:

▲• **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2023)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

• **Procedure**

Buffer: 3.15 g/L of ammonium formate and 5.49 g/L of sodium 1-hexanesulfonate in water prepared as follows. Transfer 3.15 g of ammonium formate to a 1000-mL volumetric flask, dissolve in 900 mL of water, adjust the solution with formic acid to a pH of 3.0, add 5.49 g of sodium 1-hexanesulfonate, and dilute with water to volume.

Mobile phase: Methanol and *Buffer* (23:77)

System suitability solution: 1.0 mg/mL of USP Terbutaline Sulfate RS and 0.4 mg/mL of USP Terbutaline Related Compound A RS in *Mobile phase*

Standard solution: 1.0 mg/mL of USP Terbutaline Sulfate RS in *Mobile phase*

Sample solution: Nominally 1.0 mg/mL from a volume of Injection. If necessary, dilute with water.

Chromatographic system

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

Mode: LC

Detector: UV 276 nm. ▲For *Identification A*, use a diode array detector in the range of 240–400 nm.▲ (USP 1-Dec-2023)

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 terbutaline▲ (USP 1-Dec-2023)

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for terbutaline related compound A and terbutaline are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between terbutaline related compound A and terbutaline

▲▲ (USP 1-Dec-2023)

Tailing factor: NMT 2.0 for terbutaline

Relative standard deviation: NMT ▲1.0%▲ (USP 1-Dec-2023) for terbutaline

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of terbutaline sulfate $[(C_{12}H_{19}NO_3)_2 \cdot H_2SO_4]$ in the portion of Injection taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

Add the following:

▲IMPURITIES

• **Organic Impurities**

Buffer: 3.15 g/L of ammonium formate and 5.49 g/L of sodium 1-hexanesulfonate in water prepared as follows. Transfer 3.15 g of ammonium formate to a 1000-mL volumetric flask, dissolve in 900 mL of water, adjust the solution with formic acid to a pH of 3.0, add 5.49 g of sodium 1-hexanesulfonate, and dilute with water to volume.

Solution A: Methanol and *Buffer* (23:77)

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	100	0
35	80	20
40	80	20
42	100	0
45	100	0

System suitability solution: 0.2 mg/mL of USP Terbutaline Sulfate RS and 0.08 mg/mL of USP Terbutaline Related Compound A RS in *Solution A*

Sensitivity solution: 0.0003 mg/mL of USP Terbutaline Sulfate RS in *Solution A*

Standard solution: 0.0006 mg/mL each of USP Terbutaline Sulfate RS and USP Terbutaline Related Compound A RS in *Solution A*

Sample solution: Nominally 0.3 mg/mL of terbutaline sulfate, from the pooled content of Injection from vials (NLT 5), in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 276 nm

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

Flow rate: 1 mL/min

Injection volume: 100 µL

System suitability

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

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between terbutaline related compound A and terbutaline, *System suitability solution*

Relative standard deviation: NMT 5.0% from terbutaline and terbutaline related compound A, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of terbutaline related compound A in the portion of Injection taken:

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

r_U = peak response of terbutaline related compound A from the *Sample solution*

r_S = peak response of terbutaline related compound A from the *Standard solution*

C_S = concentration of USP Terbutaline Related Compound A RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified degradation product in the portion of Injection taken:

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

r_U = peak response of any unspecified degradation product from the *Sample solution*

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

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

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

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

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Terbutaline related compound A	0.86	0.2
Terbutaline	1.0	—
Any unspecified degradation product	—	0.2
Total degradation products	—	1.0▲ (USP 1-Dec-2023)

SPECIFIC TESTS

Change to read:

• **Bacterial Endotoxins Test ⟨85⟩:** ▲Meets the requirements▲ (USP 1-Dec-2023)

Add the following:

▲• **Sterility Tests ⟨71⟩:** Meets the requirements▲ (USP 1-Dec-2023)

• **pH ⟨791⟩:** 3.0–5.0

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose containers, preferably of Type I glass, protected from light. Store at controlled room temperature.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Terbutaline Sulfate RS

USP Terbutaline Related Compound A RS

▲2-(*tert*-Butylamino)-1-(3,5-dihydroxyphenyl)ethan-1-one sulfate.

$(C_{12}H_{17}NO_3)_2 \cdot H_2SO_4$ 544.62▲ (USP 1-Dec-2023)

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

Topic/Question	Contact	Expert Committee
TERBUTALINE SULFATE 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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