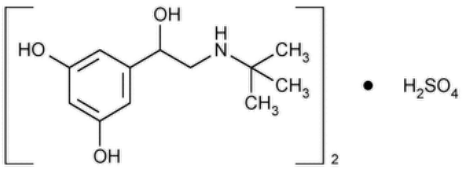
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Dec-2023
Document Type: USP Monographs
DocId: GUID-5D475B1E-ECC5-4CE9-80B6-70AD1DF547D8_5_en-US
DOI: https://doi.org/10.31003/USPNF_M80850_05_01
DOI Ref: h05ft

Terbutaline Sulfate

Change to read:



$(C_{12}H_{19}NO_3)_2 \cdot H_2SO_4$ 548.65

1,3-Benzenediol, 5-[2-[(1,1-dimethylethyl)amino]-1-hydroxyethyl]-, sulfate (2:1) (salt);

(±)-α-[(*tert*-Butylamino)methyl]-3,5-dihydroxybenzyl alcohol sulfate (2:1) (salt)

▲5-[2-(*tert*-Butylamino)-1-hydroxyethyl]benzene-1,3-diol sulfate▲ (USP 1-Dec-2023) CAS RN®: 23031-32-5; UNII: 576PU70Y8E.

Change to read:

DEFINITION

Terbutaline Sulfate contains NLT 98.0% and NMT ▲102.0%▲ (USP 1-Dec-2023) of terbutaline sulfate $[(C_{12}H_{19}NO_3)_2 \cdot H_2SO_4]$, calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (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*.

Add the following:

▲• **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sulfate*:** Meets the requirements▲ (USP 1-Dec-2023)

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: 1.0 mg/mL of Terbutaline Sulfate in *Mobile phase*

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: 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 ▲0.73%▲ (USP 1-Dec-2023) for terbutaline

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of terbutaline sulfate $[(C_{12}H_{19}NO_3)_2 \cdot H_2SO_4]$ in the portion of Terbutaline Sulfate 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 = concentration of Terbutaline Sulfate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–▲102.0%▲ (USP 1-Dec-2023) on the dried basis

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.2%

Change to read:

• **ORGANIC IMPURITIES**

Buffer and **System suitability solution:** Prepare as directed in the *Assay*.

▲**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

Sensitivity solution: 0.75 µg/mL of USP Terbutaline Sulfate RS in *Solution A*

Standard solution: 0.003 mg/mL each of USP Terbutaline Sulfate RS, USP Terbutaline Related Compound A RS, and USP Terbutaline Related Compound D RS in *Solution A*

Sample solution: 1.5 mg/mL of Terbutaline Sulfate 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: 20 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 2.0 between terbutaline related compound A and terbutaline, *System suitability solution*

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

Relative standard deviation: NMT 5.0% for terbutaline, terbutaline related compound A, and terbutaline related compound D, *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 Terbutaline Sulfate 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 = concentration of Terbutaline Sulfate in the *Sample solution* (mg/mL)

Calculate the percentage of terbutaline related compound D in the portion of Terbutaline Sulfate taken:

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

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

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

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

C_U = concentration of Terbutaline Sulfate in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of terbutaline related compound D sulfate salt (2:1), 724.87

M_{r2} = molecular weight of terbutaline related compound D free base times 2, 626.80

Calculate the percentage of any unspecified impurity in the portion of Terbutaline Sulfate taken:

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

r_U = peak response of any unspecified impurity 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 = concentration of Terbutaline Sulfate in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Terbutaline related compound A	0.86	0.2
Terbutaline	1.0	—
Terbutaline related compound D	3.4	0.2
Any unspecified impurity	—	0.10
Total impurities[a]	—	0.4

[a] Excluding terbutaline related compound A.

▲ (USP 1-Dec-2023)

SPECIFIC TESTS

Change to read:

• **Acidity**

Sample solution: 20 mg/mL in carbon dioxide-free water

Analysis: Titrate 10 mL of the *Sample solution* with ▲0.02 N sodium hydroxide VS▲ (USP 1-Dec-2023) from a microburet to a pH of 6, determining the endpoint potentiometrically, using a calomel-glass electrode system.

Acceptance criteria: NMT 0.50 mL of ▲0.02 N sodium hydroxide VS▲ (USP 1-Dec-2023) is required (0.3% as acetic acid).

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers. 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 Terbutaline Related Compound D RS

2-[Benzyl(*tert*-butyl)amino]-1-(3,5-dihydroxyphenyl)ethan-1-one.
$C_{19}H_{23}NO_3$ 313.40▲ (USP 1-Dec-2023)

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

Topic/Question	Contact	Expert Committee
TERBUTALINE SULFATE	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(5)

Current DocID: GUID-5D475B1E-ECC5-4CE9-80B6-70AD1DF547D8_5_en-US

DOI: https://doi.org/10.31003/USPNF_M80850_05_01

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