Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Aug-2022
Document Type: USP Monographs
DocId: GUID-38F658BD-EC86-4ABC-8B7A-8D40C2E291A8_2_en-US
DOI: https://doi.org/10.31003/USPNF_M83990_02_01
DOI Ref: n8jnb

Tolbutamide Tablets

DEFINITION
Tolbutamide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of tolbutamide ($C_{12}H_{18}N_2O_3S$).

IDENTIFICATION

Delete the following:

▲• **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M

Sample solution: Triturate a quantity of finely powdered Tablets, equivalent to 500 mg of tolbutamide, with 50 mL of chloroform, and filter. Evaporate the clear filtrate on a steam bath to dryness.▲ (USP 1-Aug-2022)

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-Aug-2022)

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-Aug-2022)

ASSAY

Change to read:

• **Procedure**

▲**Buffer:** 1.36 g/L of potassium phosphate, monobasic in water. Adjust with phosphoric acid to a pH of 3.5.

Mobile phase: Acetonitrile and *Buffer* (35:65)

Diluent: Acetonitrile and *Buffer* (70:30)

System suitability solution: 1 mg/mL of USP Tolbutamide RS and 10 µg/mL of USP Tolazamide RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Tolbutamide RS in *Diluent*

Sample stock solution: Nominally 0.2 mg/mL of tolbutamide from Tablets in *Diluent* prepared as follows. Transfer a quantity equivalent to 50 mg of tolbutamide, from finely powdered Tablets (NLT 5), to a 250-mL volumetric flask containing 150 mL of *Diluent*. Shake by mechanical means for NLT 30 min, and dilute with *Diluent* to volume.

Sample solution: Nominally 0.1 mg/mL of tolbutamide from the *Sample stock solution* in *Diluent*. Let stand for NLT 10 min and analyze the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm. For *Identification A*, use a diode array detector in the range of 210–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L1

Autosampler temperature: 4°

Flow rate: 1.5 mL/min

Injection volume: 30 µL

Run time: NLT 1.5 times the retention time of tolbutamide

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between tolbutamide and tolazamide, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tolbutamide ($C_{12}H_{18}N_2O_3S$) in the portion of Tablets taken:

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

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

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

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

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

▲ (USP 1-Aug-2022)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: pH 7.4 phosphate buffer; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Standard solution: USP Tolbutamide RS prepared in a similar manner as the *Sample solution*

[Note—An amount of alcohol not to exceed 1% of the total volume of the *Standard solution* may be used to bring the Reference Standard into solution before dilution with *Medium*.]

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with water as needed.

▲**Instrumental conditions**

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis▲ (USP 1-Aug-2022)

Analytical wavelength: UV 226 nm

▲**Analysis**

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tolbutamide ($C_{12}H_{18}N_2O_3S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times D \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

D = dilution factor of the *Sample solution*, as needed

▲ (USP 1-Aug-2022)

Tolerances: NLT 70% (Q) of the labeled amount of tolbutamide ($C_{12}H_{18}N_2O_3S$) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

Add the following:

▲**IMPURITIES**

• **Organic Impurities**

Buffer, Mobile phase, Diluent, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.002 mg/mL of USP Tolbutamide RS in *Diluent*

Sensitivity solution: 0.5 µg/mL of USP Tolbutamide RS in *Diluent* from the *Standard solution*

Sample solution: Nominally 1 mg/mL of tolbutamide from Tablets in *Diluent* as follows. Transfer a quantity equivalent to 250 mg of tolbutamide, from finely powdered Tablets (NLT 5), to a 250-mL volumetric flask containing 150 mL of *Diluent*. Shake by mechanical means for NLT 30 min, and dilute with *Diluent* to volume. Let stand for NLT 10 min and analyze the clear supernatant.

System suitability

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

[NOTE—The relative retention times for tosylurea, tolbutamide, and tolazamide are 0.21, 1.00, and 1.14, respectively.]

Suitability requirements

Resolution: NLT 2.0 between tolbutamide and tolazamide, *System suitability solution*

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 each degradation product in the portion of Tablets taken:

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

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

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

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

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Tosylamide[a]	0.26	1.3	0.2
Any unspecified degradation products	—	—	0.10
Total degradation products	—	—	0.5

[a] 4-Methylbenzenesulfonamide.

▲ (USP 1-Aug-2022)

ADDITIONAL REQUIREMENTS

Change to read:

• **PACKAGING AND STORAGE:** Preserve in well-closed containers. ▲Store at controlled room temperature and protect from light.▲ (USP 1-Aug-2022)

Change to read:

• **USP REFERENCE STANDARDS** ⟨11⟩

▲ USP Tolazamide RS▲ (USP 1-Aug-2022)

USP Tolbutamide RS

Topic/Question	Contact	Expert Committee
TOLBUTAMIDE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(2)

Current DocID: GUID-38F658BD-EC86-4ABC-8B7A-8D40C2E291A8_2_en-US
DOI: https://doi.org/10.31003/USPNF_M83990_02_01
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