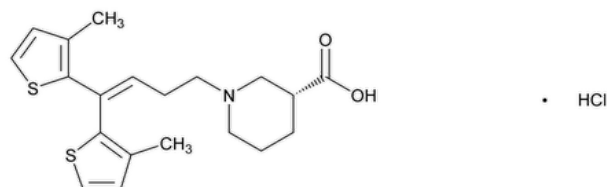


Status: Currently Official on 17-Feb-2025
 Official Date: Official as of 01-Nov-2021
 Document Type: USP Monographs
 DocId: GUID-817E607A-2C4B-4C14-8623-96CC1982E47C_9_en-US
 DOI: https://doi.org/10.31003/USPNF_M83490_09_01
 DOI Ref: edk4o

© 2025 USPC
 Do not distribute

Tiagabine Hydrochloride



$C_{20}H_{25}NO_2S_2 \cdot HCl$ 412.00

3-Piperidinecarboxylic acid, 1-[4,4-bis(3-methyl-2-thienyl)-3-butenyl]-, hydrochloride, (R)-;

(-)-(R)-1-[4,4-Bis(3-methyl-2-thienyl)-3-butenyl]nipecotic acid, hydrochloride CAS RN®: 145821-59-6; UNII: DQH6T6D8OY.

Free base

$C_{20}H_{25}NO_2S_2$ 375.55 CAS RN®: 115103-54-3; UNII: Z80I64HMNP.

Monohydrate

$C_{20}H_{25}NO_2S_2 \cdot HCl \cdot H_2O$ 430.02 CAS RN®: 145821-57-4.

DEFINITION

Tiagabine Hydrochloride contains NLT 97.5% and NMT 102.5% of tiagabine hydrochloride ($C_{20}H_{25}NO_2S_2 \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K

Sample: Transfer about 5 mg of Tiagabine Hydrochloride to a test tube. Add 4 mL of [2-propanol](#), and sonicate to dissolve, if necessary. Evaporate the solvent under inert atmosphere at 50°, using a nitrogen evaporator, for 2 h.

Analysis: The IR spectrum of the *Sample* corresponds to that of a similarly prepared [USP Tiagabine Hydrochloride RS](#).

Acceptance criteria: Meets the requirements

- **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

PROCEDURE

Solution A: 1.38 g/L of [monobasic sodium phosphate](#). Adjust with [phosphoric acid](#) to a pH of 2.0.

Mobile phase: [Acetonitrile](#) and *Solution A* (35:65)

Diluent: [Methanol](#) and [water](#) (50:50)

Internal standard solution: 0.4 mg/mL of [butylparaben](#) in *Diluent*

Standard stock solution: 1 mg/mL of [USP Tiagabine Hydrochloride RS](#) in *Diluent*

Standard solution: 0.1 mg/mL of [USP Tiagabine Hydrochloride RS](#) and 0.04 mg/mL of [butylparaben](#) in *Diluent* prepared as follows. Transfer suitable volumes of the *Standard stock solution* and *Internal standard solution* into a suitable volumetric flask and dilute with *Diluent* to volume.

Sample stock solution: 1 mg/mL of Tiagabine Hydrochloride in *Diluent*

Sample solution: 0.1 mg/mL of Tiagabine Hydrochloride and 0.04 mg/mL of [butylparaben](#) in *Diluent* prepared as follows. Transfer suitable volumes of the *Sample stock solution* and *Internal standard solution* into a suitable volumetric flask and dilute with *Diluent* to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-μm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 3.5 times the retention time of tiagabine

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 5.5 between tiagabine and butylparaben

Relative standard deviation: NMT 1.5% for the peak response ratios

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tiagabine hydrochloride ($C_{20}H_{25}NO_2S_2 \cdot HCl$) in the portion of Tiagabine Hydrochloride taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak area ratio of tiagabine hydrochloride to the internal standard from the *Sample solution*

R_S = peak area ratio of tiagabine hydrochloride to the internal standard from the *Standard solution*

C_S = concentration of [USP Tiagabine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Tiagabine Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 97.5%–102.5% on the anhydrous basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%

• **LIMIT OF (S)-(+)** ISOMER

Mobile phase: [n-Hexane](#), [isopropyl alcohol](#), [alcohol](#), and [trifluoroacetic acid](#) (80: 14: 6: 0.5). [NOTE—Increase or decrease the percentage of *n*-hexane or alcohol, but keep the percentage of isopropyl alcohol constant. Make other adjustments, if necessary (see [Chromatography \(621\), System Suitability](#)).]

Standard solution: 0.1 mg/mL of [USP Racemic Tiagabine Hydrochloride Mixture RS](#) prepared as follows. Transfer a suitable quantity of [USP Racemic Tiagabine Hydrochloride Mixture RS](#) into a suitable volumetric flask, dissolve in a few drops of [methanol](#), and dilute with [isopropyl alcohol](#) to volume.

Sample solution: 2 mg/mL of Tiagabine Hydrochloride prepared as follows. Transfer a suitable quantity of Tiagabine Hydrochloride in a suitable volumetric flask, dissolve in a few drops of [methanol](#), and dilute with [isopropyl alcohol](#) to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 25-cm; 10-µm packing [L40](#)

Flow rate: 0.8 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention of the (R)-(-) isomer

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times of the (S)-(+) isomer and the (R)-(-) isomer are about 0.76 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the (S)-(+) and (R)-(-) isomers

Analysis

Sample: *Sample solution*

Calculate the percentage of the (S)-(+) isomer in the portion of Tiagabine Hydrochloride taken:

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

r_U = peak response of the (S)-(+) isomer from the *Sample solution*

r_T = sum of the peak responses of the (S)-(+) isomer and (R)-(-) isomer from the *Sample solution*

Acceptance criteria: NMT 0.5%

• **ORGANIC IMPURITIES**