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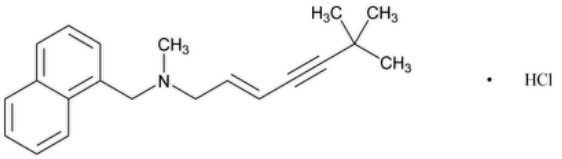
Terbinafine Hydrochloride



$C_{21}H_{25}N \cdot HCl$ 327.90

1-Naphthalenemethanamine, *N*-(6,6-dimethyl-2-hepten-4-ynyl)-*N*-methyl-, (*E*)-, hydrochloride;

(*E*)-*N*-(6,6-Dimethyl-2-hepten-4-ynyl)-*N*-methyl-1-naphthalenemethylamine, hydrochloride;

(2*E*)-*N*,6,6-Trimethyl-*N*-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine hydrochloride CAS RN®: 78628-80-5; UNII: 012C11ZU6G.

DEFINITION

Terbinafine Hydrochloride contains NLT 98.0% and NMT 102.0% of terbinafine hydrochloride ($C_{21}H_{25}N \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **B.** **Identification Tests—General**, *Chloride* ⟨191⟩**:** Meets the requirements of the test when using dehydrated alcohol as a solvent

ASSAY

• **Procedure**

Protect all solutions containing Terbinafine Hydrochloride from light.

Buffer: Prepare a solution in water containing 2.0 mL/L of triethylamine. Adjust with diluted acetic acid to a pH of 7.5.

Solution A: *Solution C* and *Buffer* (7:3)

Solution B: *Solution C* and *Buffer* (95:5)

Solution C: Methanol and acetonitrile (3:2)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
4	100	0
25	0	100
30	0	100
30.1	100	0
38	100	0

Diluent: Acetonitrile and water (1:1)

System suitability solution: 1 mg/mL of USP Terbinafine Hydrochloride RS and 5 µg/mL of USP Terbinafine Related Compound B RS in *Diluent*

Standard solution: 0.5 mg/mL of USP Terbinafine Hydrochloride RS in *Diluent*

Sample solution: 0.5 mg/mL of Terbinafine Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 3.0-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 0.8 mL/min

Injection volume: 20 µL

System suitability

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

[NOTE—The relative retention times for terbinafine related compound B and terbinafine are 0.94 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between terbinafine related compound B and terbinafine, *System suitability solution*

Tailing factor: NLT 0.8 and NMT 1.5 for terbinafine, *Standard solution*

Relative standard deviation: NMT 2.0% for terbinafine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of terbinafine hydrochloride ($C_{21}H_{25}N \cdot HCl$) in the portion of Terbinafine Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%

• **ORGANIC IMPURITIES**

Protect all solutions containing Terbinafine Hydrochloride from light.

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

Standard solution: 0.5 µg/mL each of USP Terbinafine Hydrochloride RS, USP Terbinafine Related Compound A RS, USP Terbinafine Related Compound B RS, USP Terbinafine Related Compound C RS, and USP Terbinafine Related Compound D RS in *Diluent*

Sample solution: 0.5 mg/mL of Terbinafine Hydrochloride in *Diluent*

Sensitivity solution: 0.25 µg/mL of USP Terbinafine Hydrochloride RS in *Diluent* from the *Standard solution*

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between terbinafine related compound B and terbinafine, *System suitability solution*

Relative standard deviation: NMT 10% for terbinafine, *Standard solution*

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

Calculate the signal-to-noise ratio:

$$\text{Result} = (2H)/h$$

H = measured height of the terbinafine peak

h = amplitude of the average measured baseline noise

Analysis

Samples: *Standard solution* and *Sample solution*

Identify the peaks based on their relative retention times as given in *Table 2*.

Calculate the percentage of terbinafine related compound A, terbinafine related compound B, terbinafine related compound C, and terbinafine related compound D in the portion of Terbinafine Hydrochloride taken:

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

r_U = peak response of terbinafine related compound A, terbinafine related compound B, terbinafine related compound C, or terbinafine related compound D from the *Sample solution*

r_S = peak response of terbinafine related compound A, terbinafine related compound B, terbinafine related compound C, or terbinafine related compound D from the *Standard solution*

C_S = concentration of USP Terbinafine Related Compound A RS, USP Terbinafine Related Compound B RS, USP Terbinafine Related Compound C RS, or USP Terbinafine Related Compound D RS in the *Standard solution* (µg/mL)

C_U = concentration of Terbinafine Hydrochloride in the *Sample solution* (µg/mL)

Calculate the percentage of terbinafine dimer or any other individual impurity in the portion of Terbinafine Hydrochloride taken:

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

r_U = peak response of terbinafine dimer or any other individual impurity from the *Sample solution*

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

C_S = concentration of USP Terbinafine Hydrochloride RS in the *Standard solution* (µg/mL)

C_U = concentration of Terbinafine Hydrochloride in the *Sample solution* (µg/mL)

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

Acceptance criteria: See *Table 2*. Disregard any peak observed in the blank, and any peak less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Terbinafine related compound A[a]	0.1	—	0.1
Terbinafine related compound C[b]	0.92	—	0.1
Terbinafine related compound B[c]	0.94	—	0.1
Terbinafine	1.0	—	—
Terbinafine related compound D[d]	1.1	—	0.1
Terbinafine dimer[e]	1.7	2.5	0.05
Any other individual impurity	—	1.0	0.1
Total impurities	—	—	0.3

[a] *N*-Methyl-1-(naphthalen-1-yl)methanamine, also known as *N*-methyl-*C*-(naphthalen-1-yl)methanamine.

[b] *trans*-Isoterbinafine or (2*E*)-*N*,6,6-Trimethyl-*N*-(naphthalen-2-ylmethyl)hept-2-en-4-yn-1-amine.

[c] *cis*-Terbinafine or (2*Z*)-*N*,6,6-Trimethyl-*N*-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine.

[d] 4-Methylterbinafine or (2*E*)-*N*,6,6-Trimethyl-*N*-((4-methylnaphthalen-1-yl)methyl)hept-2-en-4-yn-1-amine.

[e] (2*E*,4*E*)-4-(4,4-Dimethylpent-2-ynylidene)-N^1,N^5-dimethyl-N^1,N^5-bis(naphthalen-1-ylmethyl)pent-2-ene-1,5-diamine.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° to constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, protected from light. Store at room temperature.

• **USP Reference Standards ⟨11⟩**

USP Terbinafine Hydrochloride RS

USP Terbinafine Related Compound A RS

N-Methyl-*C*-(naphthalen-1-yl)methanamine hydrochloride.

$C_{12}H_{13}N \cdot HCl$ 207.70

USP Terbinafine Related Compound B RS

(2*Z*)-*N*,6,6-Trimethyl-*N*-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine hydrochloride.

$C_{21}H_{25}N \cdot HCl$ 327.89

USP Terbinafine Related Compound C RS

(2*E*)-*N*,6,6-Trimethyl-*N*-(naphthalen-2-ylmethyl)hept-2-en-4-yn-1-amine hydrochloride.

$C_{21}H_{25}N \cdot HCl$ 327.89

USP Terbinafine Related Compound D RS

(2*E*)-*N*,6,6-Trimethyl-*N*-[(4-methylnaphthalen-1-yl)methyl]hept-2-en-4-yn-1-amine hydrochloride.

$C_{22}H_{27}N \cdot HCl$ 341.92

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

Topic/Question	Contact	Expert Committee
TERBINAFINE HYDROCHLORIDE	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

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