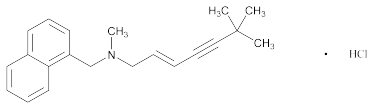
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Naproxen RS
USP Terazosin Hydrochloride RS

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 [78628-80-5].

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

IDENTIFICATION
• **A. INFRARED ABSORPTION** ⟨**197K**⟩
• **B. IDENTIFICATION TESTS—GENERAL,** *Chloride* ⟨**191**⟩**:** Meets the requirements of the test when using dehydrated alcohol as a solvent.

ASSAY
• **PROCEDURE**
[NOTE—Protect all solutions containing Terbinafine Hydrochloride from light.]
Buffer, Solution A, Solution B, Solution C, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the test for *Organic Impurities*.
Standard solution: 0.5 mg/mL of USP Terbinafine Hydrochloride RS in *Diluent*
System suitability solution: 1 mg/mL of USP Terbinafine Hydrochloride RS in *Diluent*. Expose to UV light at 254 nm for 1 h.
Sample solution: 0.5 mg/mL of Terbinafine Hydrochloride in *Diluent*
System suitability
Samples: *Standard solution* and *System suitability solution*
[NOTE—The relative retention times for *cis*-terbinafine and terbinafine are 0.94 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 2.0 between *cis*-terbinafine 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 $C_{21}H_{25}N \cdot HCl$ 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
Inorganic Impurities
• **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%
Organic Impurities
• **PROCEDURE**
[NOTE—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 the gradient table below.

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)
Standard solution: 0.5 µg/mL of USP Terbinafine Hydrochloride RS in *Diluent*
Sample solution: 0.5 mg/mL of Terbinafine Hydrochloride in *Diluent*
System suitability solution: 1 mg/mL of USP Terbinafine Hydrochloride RS in *Diluent*. Expose to UV light at 254 nm for 1 h.
Sensitivity solution: 0.25 µg/mL of terbinafine hydrochloride in *Diluent* from the *Standard solution*
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 size: 20 µL
System suitability
Samples: *Standard solution*, *System suitability solution*, and *Sensitivity solution*
Suitability requirements
Resolution: NLT 2.0 between *cis*-terbinafine and terbinafine, *System suitability solution*
Relative standard deviation: NMT 10%, *Standard solution*
Signal-to-noise ratio: NLT 10, *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 *Impurity Table 1*.
Calculate the percentage of each 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 each 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 *Impurity Table 1*)

[NOTE—Disregard any peak observed in the blank, and any peak less than 0.05%.]

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.3%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
N-Methyl-*C*-(naphthalen-1-yl)methanamine	0.1	1.7	0.1
trans-Isoterbinafine[a]	0.92	1.0	0.1
cis-Terbinafine[b]	0.94	1.0	0.1
Terbinafine	1.0	—	—
4-Methylterbinafine[c]	1.1	1.0	0.1
Terbinafine dimer[d]	1.7	2.5	0.05
Any other individual impurity	—	1.0	0.1

[a] (2*E*)-*N*,6,6-Trimethyl-*N*-(naphthalen-2-ylmethyl)hept-2-en-4-yn-1-amine.
[b] (2*Z*)-*N*,6,6-Trimethyl-*N*-(naphthalen-1-ylmethyl)hept-2-en-4-yn-1-amine.
[c] (2*E*)-*N*,6,6-Trimethyl-*N*-[(4-methylnaphthalen-1-yl)methyl]hept-2-en-4-yn-1-amine.
[d] (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⟩:** Dry a sample at 105° to constant weight: it loses NMT 0.5% of its weight.

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

Terbinafine Oral Suspension

DEFINITION

Terbinafine Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled content of terbinafine hydrochloride ($C_{21}H_{25}N \cdot HCl$). Prepare Terbinafine Oral Suspension (28.1 mg/mL as hydrochloride) equivalent to 25 mg of Terbinafine per mL as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Terbinafine (as Hydrochloride)	2500 mg (2810 mg)
Vehicle: A mixture of Vehicle for Oral Solution, *NF*, and Vehicle for Oral Suspension, *NF*, (1:1), a sufficient quantity to make	100 mL

Calculate the required quantity of each ingredient for the total amount to be prepared. If using tablets, place the required number of tablets in a suitable mortar, and comminute the tablets to a fine powder or add *Terbinafine Hydrochloride* powder. Add the *Vehicle* in small portions, and triturate to make a smooth paste. Add increasing volumes of the *Vehicle* to make a terbinafine suspension that is pourable. Transfer the contents of the mortar, stepwise and quantitatively, to a calibrated bottle. Add enough of the *Vehicle* to bring to final volume, and mix well.

ASSAY

- **PROCEDURE**

Mobile phase: Acetonitrile and water (2:3), with 0.15% triethylamine and 0.15% phosphoric acid. Make adjustments if necessary.

Standard stock solution: 1.0 mg/mL USP Terbinafine Hydrochloride RS in methanol

Standard solution: Transfer 0.5 mL of *Standard stock solution* to a 100-mL volumetric flask, dilute with *Mobile phase* to volume to obtain a solution containing 5 µg/mL of terbinafine hydrochloride, and pass through a suitable filter of 0.22-µm pore size.

Sample solution: Shake thoroughly by hand each bottle of Oral Suspension. Accurately pipet 1.0 mL to a 25-mL volumetric flask. Dilute with methanol to volume to obtain a nominal concentration of 1 mg/mL of terbinafine hydrochloride. Mix the sample again. Accurately pipet 1.0 mL of the diluted terbinafine hydrochloride solution to a 10-mL volumetric flask, and dilute with *Mobile phase* to volume to obtain a nominal concentration of 5 µg/mL of terbinafine hydrochloride.

Chromatographic system

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

Mode: LC

Detector: UV 224 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Flow rate: 0.4 mL/min

Injection size: 10 µL

System suitability

Sample: *Standard solution*

[NOTE—The retention time of the terbinafine peak is 5.1 min.]

Suitability requirements

Relative standard deviation: NMT 5.8%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of $C_{21}H_{25}N \cdot HCl$ in the volume of Oral Suspension taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of terbinafine hydrochloride in the *Standard solution* (µg/mL)
C_U = nominal concentration of terbinafine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

- **pH ⟨791⟩:** 5.3–5.7

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Package in tight, light-resistant containers. Store at controlled room temperature or controlled cold temperature.
- **LABELING:** Label it to state that it is to be well shaken before use, and to state the *Beyond-Use Date*.
- **BEYOND-USE DATE:** NMT 30 days after the date on which it was compounded when stored at controlled room temperature or at controlled cold temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Terbinafine Hydrochloride RS

Terbinafine Tablets

DEFINITION

Terbinafine Tablets contain Terbinafine Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of terbinafine ($C_{21}H_{25}N$).