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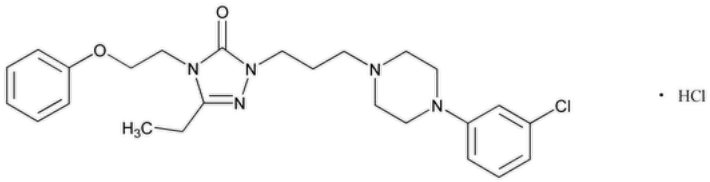
Nefazodone Hydrochloride



$C_{25}H_{32}ClN_5O_2 \cdot HCl$ 506.47

3*H*-1,2,4-Triazol-3-one, 2-[3-[4-(3-chlorophenyl)-1-piperazinyl)]propyl]-5-ethyl-2,4-dihydro-4-(2-phenoxyethyl)-, monohydrochloride; 1-[3-[4-(*m*-Chlorophenyl)-1-piperazinyl]propyl]-3-ethyl-4-(2-phenoxyethyl)-Δ^2-1,2,4-triazolin-5-one monohydrochloride 2-{3-[4-(3-Chlorophenyl)piperazin-1-yl]propyl}-5-ethyl-4-(2-phenoxyethyl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one CAS RN®: 82752-99-6; UNII: 27X63J94GR.

DEFINITION

Change to read:

Nefazodone Hydrochloride contains NLT 98.0% and NMT 102.0% of ▲nefazodone hydrochloride▲ (USP 1-May-2021) ($C_{25}H_{32}ClN_5O_2 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K
- **B. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride***

  Sample solution: 10 mg/mL in methanol

  Acceptance criteria: Meets the requirements

Add the following:

▲- **C.** 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-May-2021)

ASSAY

Change to read:

- **Procedure**

  ▲**Solution A:** 0.77 g/L of ammonium acetate in water. Adjust with triethylamine to a pH of 7.10 ± 0.05, and degas.

  Solution B: Acetonitrile (degassed)

  Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	50	50
10	45	55
16	35	65
25	35	65
26	50	50
35	50	50

Diluent: Acetonitrile and water (50:50)

Impurities stock solution: 0.1 mg/mL of USP Nefazodone Related Compound A RS and USP Nefazodone Related Compound B RS in *Diluent*

System suitability stock solution: 0.1 mg/mL of USP Nefazodone Hydrochloride RS in *Diluent*

System suitability solution: 5 µg/mL each of USP Nefazodone Related Compound A RS and USP Nefazodone Related Compound B RS from the *Impurities stock solution* in the *System suitability stock solution*

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

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

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

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

Flow rate: 1.7 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 4.0 between nefazodone related compound A and nefazodone; NLT 1.5 between nefazodone and nefazodone related compound B, *System suitability solution*

Relative standard deviation: NMT 0.73% for nefazodone, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nefazodone hydrochloride ($C_{25}H_{32}ClN_5O_2 \cdot HCl$) in the portion of Nefazodone Hydrochloride taken:

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

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

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

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

C_U = concentration of Nefazodone Hydrochloride in the *Sample solution* (mg/mL)▲ (USP 1-May-2021)

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

IMPURITIES

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

Change to read:

• **ORGANIC IMPURITIES**

▲**Solution A, Solution B, Mobile phase, Diluent, Impurities stock solution,** and **Chromatographic system:** Proceed as directed in the *Assay*.▲ (USP 1-May-2021)

Standard stock solution: 0.1 mg/mL of USP Nefazodone Hydrochloride RS in *Diluent*

System suitability solution: 5 µg/mL each of USP Nefazodone Related Compound A RS and USP Nefazodone Related Compound B RS from the *Impurities stock solution* in the *Standard stock solution*

Standard solution: ▲0.001 mg/mL▲ (USP 1-May-2021) each of ▲USP Nefazodone Hydrochloride RS,▲ (USP 1-May-2021) USP Nefazodone Related Compound A RS, and USP Nefazodone Related Compound B RS from the *Standard stock solution* and the *Impurities stock solution* in *Diluent*

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

▲▲ (USP 1-May-2021)

System suitability

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

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 4.0 between nefazodone related compound A and nefazodone; ▲▲ (USP 1-May-2021) NLT 1.5 between nefazodone ▲▲ (USP 1-May-2021) and nefazodone related compound B, *System suitability solution*

Relative standard deviation: NMT 5.0% for nefazodone related compound A and nefazodone related compound B, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each nefazodone related compound in the portion of Nefazodone Hydrochloride taken:

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

r_U = peak area of the corresponding nefazodone related compound from the *Sample solution*

r_S = peak area of the corresponding nefazodone related compound from the *Standard solution*

C_S = concentration of the ▲corresponding▲ (USP 1-May-2021) USP Reference Standard in the *Standard solution* (mg/mL)

C_U = concentration of ▲Nefazodone Hydrochloride in▲ (USP 1-May-2021) the *Sample solution* (mg/mL)

▲Calculate the percentage of any unspecified impurity in the portion of Nefazodone Hydrochloride taken:

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

r_U = peak area of any unspecified impurity from the *Sample solution*

r_S = peak area of nefazodone from the *Standard solution*

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

C_U = concentration of Nefazodone Hydrochloride in the *Sample solution* (mg/mL)▲ (USP 1-May-2021)

Acceptance criteria: See ▲*Table 2*.

Table 2▲ (USP 1-May-2021)

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
▲▲ (USP 1-May-2021)	▲▲ (USP 1-May-2021)	▲▲ (USP 1-May-2021)
Nefazodone related compound B	0.94	0.2
Nefazodone	1.0	—
▲Nefazodone related compound A	1.2	0.2▲ (USP 1-May-2021)
Any ▲unspecified▲ (USP 1-May-2021) impurity	—	0.1
Total impurities	—	0.5

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry under vacuum at 105° for 3 h.

Acceptance criteria: NMT 0.5%

• **Completeness of Solution ⟨641⟩**

Sample solution: 25 mg/mL in methanol

Acceptance criteria: Meets the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store between 15° and 30°.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Nefazodone Hydrochloride RS

USP Nefazodone Related Compound A RS

1-(3-Chloropropyl)-4-(▲3-▲ (USP 1-May-2021) chlorophenyl)piperazine ▲hydrochloride.▲ (USP 1-May-2021)

$C_{13}H_{18}Cl_2N_2$▲ · HCl 309.66▲ (USP 1-May-2021)

USP Nefazodone Related Compound B RS

2-{3-(4-(▲4-▲ (USP 1-May-2021) Chlorophenyl)-1-piperazinyl)propyl}-5-ethyl-2,4-dihydro-4-(2-phenoxyethyl)-3*H*-1,2,4-triazol-3-one ▲hydrochloride.▲ (USP 1-May-2021)

$C_{25}H_{32}ClN_5O_2$▲ · HCl 506.47▲ (USP 1-May-2021)

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

Topic/Question	Contact	Expert Committee
NEFAZODONE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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