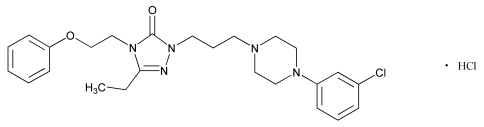
Nefazodone Hydrochloride



$C_{25}H_{32}ClN_5O_2 \cdot HCl$ 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 [*82752-99-6*].

» Nefazodone Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{25}H_{32}ClN_5O_2 \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers. Store at a temperature between 15° and 30°.

USP Reference standards ⟨11⟩**—***USP Nefazodone Hydrochloride RS. USP Nefazodone Related Compound A RS. USP Nefazodone Related Compound B RS.*

Completeness of solution ⟨641⟩**—**A 25 mg per mL solution in methanol meets the requirements.

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: A solution of 10 mg per mL meets the requirements of the test for *Chloride* ⟨191⟩.

Loss on drying ⟨731⟩**—**Dry it in vacuum at 105° for 3 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Heavy metals, *Method II* ⟨231⟩**:** 0.001%.

Organic volatile impurities, *Method I* ⟨467⟩**:** meets the requirements.

(Official until July 1, 2008)

Related compounds—

Diluent—Prepare a solution of water and acetonitrile (50 : 50).

Solution A—Dissolve 0.77 g of ammonium acetate in about 950 mL of water. Adjust with triethylamine to a pH of 7.10 ± 0.05. Dilute with water to 1 L. Filter and degas.

Solution B—Use filtered and degassed acetonitrile.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard stock solution—Dissolve an accurately weighed amount of USP Nefazodone Hydrochloride RS in *Diluent* to obtain a solution containing 0.1 mg of nefazodone hydrochloride per mL.

Impurities stock solution—Dissolve accurately weighed quantities of USP Nefazodone Related Compound A RS and USP Nefazodone Related Compound B RS in *Diluent* to obtain a final solution having a known concentration of about 0.1 mg per mL of each compound.

Resolution solution—Dilute a suitable volume of the *Impurities stock solution* with the *Standard stock solution* to obtain a solution having a concentration of about 5 µg per mL each of nefazodone related compounds A and B.

Standard solution—Dilute accurately measured volumes of the *Impurities stock solution* and the *Standard stock solution* quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 1 µg per mL each of nefazodone hydrochloride, nefazodone related compound A, and nefazodone related compound B.

Test solution—Transfer about 100 mg of Nefazodone Hydrochloride, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 250-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.7 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0	50	50	equilbration
0–10	50→45	50→55	linear gradient
10–16	45→35	55→65	linear gradient
16–25	35	65	isocratic
25–26	35→50	65→50	linear gradient
26–35	50	50	re-equilbration

Chromatograph the *Resolution solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between nefazodone related compound A and nefazodone hydrochloride is not less than 4.0 and is not less than 1.5 between nefazodone hydrochloride and nefazodone related compound B. Chromatograph the *Standard solution,* and measure the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 5.0% for nefazodone related compound A and nefazodone related compound B. [NOTE—For identification purposes, the relative retention times are about 1.2 for nefazodone related compound A, 1.0 for nefazodone hydrochloride, and 0.94 for nefazodone related compound B.]

Procedure—Inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of each nefazodone related compound in the portion of Nefazodone Hydrochloride taken by the formula:

$$100(C_S / C_T)(r_U / r_S)$$

in which C_S is the concentration, in mg per mL, of the relevant USP Reference Standard in the *Standard solution;* C_T is the concentration of Nefazodone Hydrochloride, in mg per mL, in the *Test solution;* and r_U and r_S are the peak areas of the corresponding nefazodone related compound obtained from the *Test solution* and the *Standard solution,* respectively: not more than 0.2% of nefazodone related compound A is found; not more than 0.2% of nefazodone related compound B is found; not more than 0.1% of any unknown impurity is found; and not more than 0.5% of total impurities is found. [NOTE—Use the peak area for nefazodone hydrochloride in the *Standard solution* as r_S to calculate any unknown impurity.]

Assay—Dissolve about 800 mg of Nefazodone Hydrochloride, accurately weighed, in 50 mL of glacial acetic acid, and add 15 mL of 3% (v/v) mercuric acetate in glacial acetic acid. Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid VS is equivalent to 50.65 mg of $C_{25}H_{32}ClN_5O_2 \cdot HCl$.