

# New easy-to-read monographs— Designed to make your job easier!

## HIGHLIGHTS INCLUDE

**New Format:** Tests and procedures are now clearly designated and have been arranged in a logical flow; a modern font throughout *USP 33–NF 28* makes it easier to locate information; tables have been edited to facilitate lab use

*Streamlined layout and new font make it easier to find and interpret the information you need!*

**Reorganized Content:** Tests have been reprioritized and arranged by major headings; sub-headings have been reordered and renamed to meet ICH specifications; acceptance criteria have been moved to the assay test

*No more time wasted on searching for acceptance criteria*

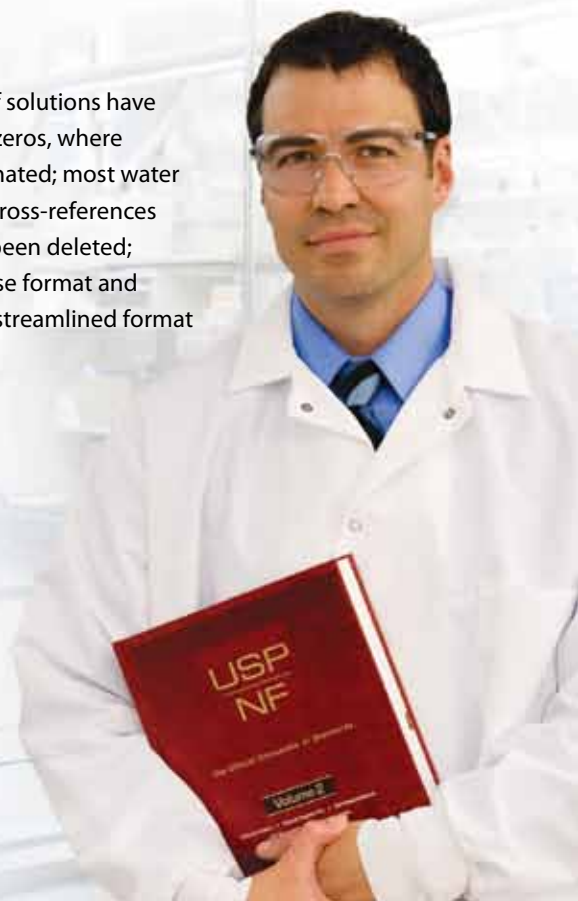
**Additions:** Calculations have been expanded to provide more details; heavy metal units updated to ppm; additional impurity tables; new harmonized ICH sub-heads

*New details, measurements, and tables*

**Deletions:** Preparation of solutions have been abbreviated; leading zeros, where confusing, have been eliminated; most water references are gone; most cross-references among monographs have been deleted; superfluous and wordy prose format and language replaced by new streamlined format

*No more paragraphs to review—data is clearly presented and to the point!*

See next page for sample monograph.



**Chromatographic system**  
(See *Chromatography* (621),  
**Mode:** LC  
**Detector:** UV 295 nm  
**Column:** 4.6-mm x 25-cm  
**Column temperature:** 30°  
**Flow rate:** 1.0 mL/min  
**Injection size:** 5 µL  
**System suitability**  
**Sample:** System suitability  
[NOTE—The relative retention  
times of paroxetine  
related compound C and paroxetine]

the Sample solution (mg/mL)  
**Acceptance criteria:** NMT 0.1% of paroxetine related compound C  
**PROCEDURE 2: LIMIT OF 1-METHYL-4-(p-FLUOROPHENYL)-1,2,3,6-TETRAHYDROPYRIDINE**  
**Solution A:** Dissolve 30 g of sodium perchlorate in 100 mL of water. Add 3.5 mL of phosphoric acid.

**Impurity Table 1**

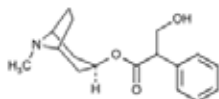
Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Paroxetine related compound A	0.66	—	0.1
Paroxetine related compound B	0.73	—	0.3
Paroxetine			
Any unspecified impurity			
Total impurities			

**Result =  $(r_u/r_s) \times (C_s/C_u) \times I \times 100$**

$r_u$  = peak response from the Sample solution  
 $r_s$  = peak response from the Standard solution  
 $C_s$  = concentration of USP Paroxetine Related Compound E Mixture RS in the Standard solution (mg/mL)  
 $C_u$  = concentration of paroxetine in the Sample solution (mg/mL)  
 $I$  = fraction by weight of 1-methyl-4-(p-fluorophenyl)-1,2,3,6-tetrahydropyridine in the USP Paroxetine Related Compound E Mixture

**Standard solution:** Prepare a solution containing the following in Diluent: 4 mg/mL of USP Paroxetine Hydrochloride RS, 10 µg/mL of USP Paroxetine Related Compound B RS, 10 µg/mL of USP Paroxetine Related Compound F RS, and 4 µg/mL of USP Paroxetine Related Compound G RS.  
**Sample solution:** 0.5 mg/mL of Paroxetine Hydrochloride in Diluent  
**Mobile phase:** See the gradient table below.

## Atropine



$C_{17}H_{23}NO_3$  289.37  
Benzeneacetic acid,  $\alpha$ -(hydroxymethyl)-8-methyl-8-azabicyclo  
[3.2.1]oct-3-yl ester, *endo*-( $\pm$ );  
1 $\alpha$ H,5 $\alpha$ H-Tropan-3 $\alpha$ -ol ( $\pm$ )-tropate (ester) [51-55-8].

### DEFINITION

Atropine contains NLT 99.0% and NMT 100.5% of  $C_{17}H_{23}NO_3$ , calculated on the anhydrous basis.

[CAUTION—Handle Atropine with exceptional care, since it is highly potent.]

### IDENTIFICATION

#### A. PROCEDURE

Standard: 36 mg of USP Atropine Sulfate RS

Sample: 30 mg

Analysis: Dissolve *Standard* and *Sample* in individual 60-mL separators with the aid of 5-mL portions of water. To each separator, add 1.5 mL of 1 N sodium hydroxide solution and 10 mL of chloroform. Shake for 1 min, allow the layers to separate, and pass the chloroform extracts through separate filters of 2 g of anhydrous granular sodium sulfate supported on pledgets of glass wool. Extract each aqueous layer with two additional 10-mL portions of chloroform, filtering and combining with the respective main extracts. Evaporate the chloroform solutions under reduced pressure to dryness, and dissolve each residue in 10 mL of carbon disulfide.

Acceptance criteria: The IR absorption spectrum, determined in a 1-mm cell, of the solution of the *Sample* exhibits maxima only at the same wavelengths as that of the solution of the *Standard*.

#### B. PROCEDURE

Sample solution: A solution (1 in 50) in 3 N hydrochloric acid

Analysis: Add gold chloride TS to the *Sample solution*.

Acceptance criteria: A lusterless precipitate is formed (distinction from hyoscyamine, which, similarly treated, yields a lustrous precipitate).

### ASSAY

#### PROCEDURE

Sample: 400 mg of Atropine

Analysis: Dissolve in 50 mL of glacial acetic acid. Titrate with 0.1 N perchloric acid VS to a green endpoint, using 1 drop of crystal violet TS. Perform a blank determination (see *Titrimetry* (541)). Each mL of 0.1 N perchloric acid is equivalent to 28.94 mg of  $C_{17}H_{23}NO_3$ .

Acceptance criteria: 99.0%–100.5% on the anhydrous basis

### IMPURITIES

#### Inorganic Impurities

- RESIDUE ON IGNITION (281): NMT 0.1%

#### Organic Impurities

- PROCEDURE 1: LIMIT OF FOREIGN ALKALOIDS AND OTHER

##### IMPURITIES

Standard solution: 24 mg/mL of USP Atropine Sulfate RS in methanol

Sample solution A: 20 mg/mL of Atropine in methanol

Sample solution B: 1 mg/mL of Atropine from *Sample solution A* diluted with methanol

##### Chromatographic system

(See *Chromatography* (621), *Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.5-mm layer of chromatographic silica gel

##### Application volume

Standard solution: 5  $\mu$ L

Sample solution A: 25  $\mu$ L

Sample solution B: 1  $\mu$ L

Developing solvent system: Chloroform, acetone, and diethylamine (5:4:1)

Spray reagent: Potassium iodoplatinate TS

Analysis: Proceed as directed under General Chapter. Allow the spots to dry, and develop the chromatogram in a solvent system, until the solvent front has moved three-fourths of the length of the plate. Locate the spots on the plate by spraying with *Spray reagent*.

Acceptance criteria: The  $R_f$  value of the principal spot of each *Sample solution* corresponds to that of the *Standard solution*; no secondary spot of the *Sample solution A* exhibits intensity equal to or greater than the principal spot of the *Sample solution B* (NMT 0.2%).

- PROCEDURE 2: READILY CARBONIZABLE SUBSTANCES TEST (271)

Sample solution: 200 mg in 5 mL of 2 N sulfuric acid

Acceptance criteria: The solution has no more color than *Matching Fluid A*, and the solution is colored no more than light yellow upon the addition of 0.2 mL of nitric acid.

### SPECIFIC TESTS

- OPTICAL ROTATION, *Angular Rotation* (781A):  $-0.70^\circ$  to  $+0.05^\circ$  (limit of hyoscyamine)

Sample solution: 1 g, previously dried at  $105^\circ$  for 1 h, in sufficient 50% alcohol (w/w) to obtain a volume of 20 mL at  $25^\circ$  (200-mm tube being used)

- MELTING RANGE OR TEMPERATURE (741):  $114^\circ$ – $118^\circ$

- WATER DETERMINATION, *Method I* (921): NMT 0.2%

### ADDITIONAL REQUIREMENTS

- PACKAGING AND STORAGE: Preserve in tight, light-resistant containers.

- USP REFERENCE STANDARDS (11)

USP Atropine Sulfate RS