• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Ofloxacin RS

Hydrophilic Ointment

DEFINITION
Prepare Hydrophilic Ointment as follows.

Methylparaben	0.25 g
Propylparaben	0.15 g
Sodium Lauryl Sulfate	10 g
Propylene Glycol	120 g
Stearyl Alcohol	250 g
White Petrolatum	250 g
Purified Water	370 g
To make about	1000 g

Melt the *Stearyl Alcohol* and the *White Petrolatum* on a steam bath, and warm to about 75°. Add the other ingredients, previously dissolved in *Purified Water* and warmed to 75°, and stir the mixture until it congeals.

ADDITIONAL REQUIREMENTS
• **PACKAGING AND STORAGE:** Package in tight containers.

White Ointment

DEFINITION
Prepare White Ointment as follows.

White Wax	50 g
White Petrolatum	950 g
To make	1000 g

Melt the *White Wax* in a suitable dish on a water bath, add the *White Petrolatum*, warm until liquefied, then discontinue the heating, and stir the mixture until it begins to congeal.

ADDITIONAL REQUIREMENTS
• **PACKAGING AND STORAGE:** Package in well-closed containers.

Yellow Ointment

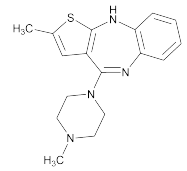
DEFINITION
Prepare Yellow Ointment as follows.

Yellow Wax	50 g
Petrolatum	950 g
To make	1000 g

Melt the *Yellow Wax* in a suitable dish on a steam bath, add the *Petrolatum*, warm until liquefied, then discontinue the heating, and stir the mixture until it begins to congeal.

ADDITIONAL REQUIREMENTS
• **PACKAGING AND STORAGE:** Package in well-closed containers.

Olanzapine



$C_{17}H_{20}N_4S$ 312.43
10*H*-Thieno[2,3-*b*][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-;
2-Methyl-4-(4-methyl-1-piperazinyl)-10*H*-thieno[2,3-*b*][1,5]benzodiazepine [132539-06-1].

DEFINITION
Olanzapine contains NLT 98.0% and NMT 102.0% of olanzapine ($C_{17}H_{20}N_4S$), calculated on the anhydrous, solvent-free basis.

IDENTIFICATION
• **A. INFRARED ABSORPTION** ⟨**197K**⟩
• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **PROCEDURE**
Buffer: Dissolve 6.9 g of monobasic sodium phosphate in 1 L of water. Adjust with phosphoric acid to a pH of 2.5, and dissolve 12 g of sodium dodecyl sulfate in the resulting solution.
Mobile phase: Acetonitrile and *Buffer* (47:53)
System suitability solution: 0.1 mg/mL of USP Olanzapine RS and 0.01 mg/mL of USP Olanzapine Related Compound A RS in *Mobile phase*
Standard solution: 0.1 mg/mL of USP Olanzapine RS in *Mobile phase*
Sample solution: 0.1 mg/mL of Olanzapine in *Mobile phase*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 260 nm
Column: 4.6-mm × 15-cm; 5-µm packing L7
Flow rate: 1.5 mL/min
Injection volume: 20 µL
System suitability
Sample: *System suitability solution*
[NOTE—The relative retention times for olanzapine related compound A and olanzapine are 0.8 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 2.0 between olanzapine related compound A and olanzapine
Tailing factor: 0.8–1.5 for the olanzapine peak
Relative standard deviation: NMT 1.0% for the olanzapine peak
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of olanzapine ($C_{17}H_{20}N_4S$) in the portion of Olanzapine 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 USP Olanzapine RS in the *Standard solution* (mg/mL)
C_U = concentration of Olanzapine in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous, solvent-free basis

IMPURITIES

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

Delete the following:

•• **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 10 ppm•• (Official 1-Jan-2018)

• **ORGANIC IMPURITIES**

Buffer: Dissolve 13 g of sodium dodecyl sulfate in 1500 mL of water. Add 5 mL of phosphoric acid, and adjust with a sodium hydroxide solution to a pH of 2.5.
Solution A: Acetonitrile and *Buffer* (48:52)
Solution B: Acetonitrile and *Buffer* (70:30)
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0
20	0	100
25	0	100
27	100	0
35	100	0

Edetate disodium solution: 37 mg/L of edetate disodium in *Buffer*
Diluent: Acetonitrile and *Edetate disodium solution* (40:60)
System suitability solution: 20 µg/mL of USP Olanzapine RS and 2 µg/mL each of USP Olanzapine Related Compound A RS and USP Olanzapine Related Compound B RS in *Diluent*
Standard solution: 2 µg/mL of USP Olanzapine RS in *Diluent*
Sample solution: 0.4 mg/mL of Olanzapine in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 25-cm; 5-µm packing L7
Temperatures
Column: 35°
Sample: 5°
Flow rate: 1.5 mL/min
Injection volume: 20 µL
System suitability
Sample: *System suitability solution*
[NOTE—Identify the peaks using the *Relative Retention Time* values given in *Table 2*.]
Suitability requirements
Resolution: NLT 3.0 between olanzapine related compound A and olanzapine
Tailing factor: NMT 1.5 for the olanzapine peak
Relative standard deviation: NMT 2.0% from four replicate injections for the olanzapine peak
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Olanzapine 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 olanzapine from the *Standard solution*
C_S = concentration of USP Olanzapine RS in the *Standard solution* (mg/mL)
C_U = concentration of Olanzapine in the *Sample solution* (mg/mL)
F = relative response factor for each impurity from *Table 2*
Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Olanzapine related compound B[a]	0.3	2.3	0.10
Olanzapine related compound A[b]	0.8	2.3	0.10
Olanzapine	1.0	—	—
Chloromethyl olanzapinium chloride[c] (if present)	1.1	1.0	0.15
Any individual, unspecified impurity	—	—	0.10
Total impurities	—	—	0.4

[a] 2-Methyl-10*H*-thieno-[2,3-*b*][1,5]benzodiazepin-4[5*H*]-one.
[b] 5-Methyl-2-((2-nitrophenyl)amino)-3-thiophenecarbonitrile.
[c] 1-Chloromethyl-1-methyl-4-(2-methyl-10*H*-benzo[*b*]thieno[2,3-*e*][1,4]diazepin-4-yl)piperazin-1-ium chloride.

SPECIFIC TESTS

• **WATER DETERMINATION,** *Method I* ⟨**921**⟩
[NOTE—A suitable solvent system for water determination in ketones and aldehydes (e.g., Hydranal composite 5K-working medium K or Aquastar composite 5K-solvent KC or equivalent) is recommended.]
Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at room temperature.
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Olanzapine RS
USP Olanzapine Related Compound A RS
5-Methyl-2-((2-nitrophenyl)amino)-3-thiophenecarbonitrile.
$C_{12}H_9N_3O_2S$ 259.28
USP Olanzapine Related Compound B RS
2-Methyl-10*H*-thieno-[2,3-*b*][1,5]benzodiazepin-4[5*H*]-one.
$C_{12}H_{10}N_2OS$ 230.29

Olanzapine Tablets

DEFINITION

Olanzapine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of olanzapine ($C_{17}H_{20}N_4S$).

IDENTIFICATION

• **INFRARED ABSORPTION** ⟨**197K**⟩
Standard: Dissolve 10 mg of USP Olanzapine RS in 10 mL of chloroform. Evaporate to dryness on a water bath maintained at 55°. Use about 2 mg of the residue to prepare a potassium bromide pellet.
Sample: Crush NLT 5 Tablets, and transfer the powder equivalent to 30 mg of olanzapine to a suitable container. Add 30 mL of chloroform, and sonicate for 15 min to dissolve. Pass through a suitable filter, and evaporate the filtrate to dryness on a water bath maintained at 55°. Use about 2 mg of the residue to prepare a potassium bromide pellet.