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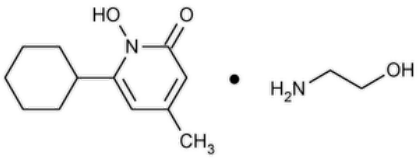
Ciclopirox Olamine



$C_{12}H_{17}NO_2 \cdot C_2H_7NO$ 268.35

2(1*H*)-Pyridinone, 6-cyclohexyl-1-hydroxy-4-methyl-, compound with 2-aminoethanol (1:1).

6-Cyclohexyl-1-hydroxy-4-methyl-2(1*H*)-pyridone compound with 2-aminoethanol (1:1) CAS RN®: 41621-49-2; UNII: 50MD4SB4AP.

» Ciclopirox Olamine contains not less than 97.5 percent and not more than 101.5 percent of ciclopirox olamine ($C_{12}H_{17}NO_2 \cdot C_2H_7NO$).

Packaging and storage—Preserve in tight containers, protected from light. Store between 5° and 25°.

USP Reference standards ⟨11⟩—

USP Ciclopirox Olamine RS

USP Ciclopirox Related Compound A RS

3-Cyclohexyl-4,5-dihydro-5-methyl-5-isoxazolyl acetic acid.

USP Ciclopirox Related Compound B RS

6-Cyclohexyl-4-methyl-2-pyrone.

Change to read:

Identification, ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

pH ⟨791⟩**:** between 8.0 and 9.0, in a mixture with water (1:100).

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

Monoethanolamine content—Dissolve about 300 mg, accurately weighed, in 25 mL of glacial acetic acid. Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 6.108 mg of C_2H_7NO. The content of monoethanolamine (C_2H_7NO) is not less than 223 mg and not more than 230 mg per g of ciclopirox olamine ($C_{12}H_{17}NO_2 \cdot C_2H_7NO$) found in the *Assay*.

Related compounds—[Note—Carry out the operations avoiding exposure to actinic light. All materials that are in direct contact with Ciclopirox Olamine (e.g., column materials, reagents, solvents, etc.) should contain only very low amounts of extractable metal cations.]

Mobile phase—Prepare a filtered and degassed mixture of an edetate disodium solution (0.96 in 1000), acetonitrile, and glacial acetic acid (770:230:0.1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Rinsing solution—Prepare a mixture of water, acetonitrile, glacial acetic acid, and acetylacetone (500:500:1:1).

Standard stock solution—Dissolve USP Ciclopirox Related Compound A RS and USP Ciclopirox Related Compound B RS, accurately weighed, in an appropriate volume of acetonitrile and *Mobile phase* solution (approximate ratio, 1:7). Further dilute with *Mobile phase* to obtain a solution having a known final concentration of about 1.5 mg of each per mL.

Standard solution A—Dilute 1.0 mL of *Standard stock solution* to 200.0 mL with a mixture of *Mobile phase* and acetonitrile (9:1).

Standard solution B—Dilute 2.0 mL of *Standard solution A* to 10.0 mL with a mixture of *Mobile phase* and acetonitrile (9:1).

Test solution—Dissolve 40 mg of Ciclopirox Olamine, accurately weighed, in a mixture of 2 mL of acetonitrile, 20 µL of glacial acetic acid, and 15 mL of *Mobile phase*. If necessary, use an ultrasonic bath to dissolve. Dilute with *Mobile phase* to 20.0 mL, and mix.

Resolution solution—Mix 5 mL of *Standard stock solution* with 5 mL of the *Test solution*.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a detector capable of recording at both 220 nm and 298 nm and a 4.0-mm × 8-cm column that contains packing L10. [Note—Ciclopirox related compound A has an intense absorbance at 220 nm, and 6-cyclohexyl-4-methyl-2(1*H*)-pyridone, ciclopirox related compound B, and ciclopirox have intense absorbances at 298 nm.] The flow rate is about 0.7 mL per minute. Chromatograph the *Resolution solution* at 298 nm, and record the peak responses as directed for *Procedure:* the resolution, *R,* between the ciclopirox related compound B peak and the ciclopirox peak is not less than 2.0. Chromatograph *Standard solution B* at 298 nm, and record the peak responses as directed for *Procedure:* the chromatogram obtained shows at 298 nm a peak

corresponding to ciclopirox related compound B with a signal-to-noise ratio of not less than 3. Chromatograph the *Test solution* at 298 nm, and record the peak responses as directed for *Procedure:* the tailing factor for the ciclopirox peak is less than 2.0.

Procedure—Separately inject equal volumes (about 10 µL) of *Standard solution A, Standard solution B,* and the *Test solution* into the chromatograph, and record the chromatograms. [NOTE—In order to ensure desorption of disruptive metal ions, every new column must be rinsed with the *Rinsing solution* over a period of not less than 15 hours and then with *Mobile phase* for not less than 5 hours with a flow rate of 0.2 mL per minute. The chromatographic run time is not less than 2.5 times the retention time of the ciclopirox peak.] The relative retention times are about 0.5 for ciclopirox related compound A, 0.9 for 6-cyclohexyl-4-methyl-2(1*H*)-pyridone, 1.0 for ciclopirox, and 1.3 for ciclopirox related compound B. The peak response at 220 nm of the ciclopirox related compound A peak in the chromatogram obtained from the *Test solution* is not more than the peak response at 220 nm of the corresponding peak in the chromatogram obtained from *Standard solution A* (0.5% with reference to ciclopirox). The sum of responses at 298 nm of the impurity peaks in the chromatogram obtained from the *Test solution* is not more than the peak response at 298 nm of the ciclopirox related compound B peak in the chromatogram obtained from *Standard solution A* (0.5% with reference to ciclopirox). At 298 nm disregard any peak due to the solvent and any peak with a response less than the response of the ciclopirox related compound B peak in the chromatogram obtained from *Standard solution B* at 298 nm (0.1% with reference to ciclopirox).

Assay—Dissolve 200 mg of Ciclopirox Olamine, accurately weighed, in 2 mL of methanol. Add 38 mL of water, mix, and titrate with 0.1 N sodium hydroxide VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary corrections. Determine the factor of the 0.1 N sodium hydroxide VS using 100 mg of benzoic acid, accurately weighed, and titrate under the conditions prescribed above. Each mL of 0.1 N sodium hydroxide is equivalent to 26.84 mg of ciclopirox olamine ($C_{12}H_{17}NO_2 \cdot C_2H_7NO$).

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

Topic/Question	Contact	Expert Committee
CICLOPIROX OLAMINE	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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