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Penicillamine Tablets

» Penicillamine Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_5H_{11}NO_2S$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—

USP Penicillamine RS

USP Penicillamine Disulfide RS $C_{10}H_{20}N_2O_4S_2$

Identification—

A: Transfer a portion of finely powdered Tablets, equivalent to about 100 mg of penicillamine, to a 10-mL volumetric flask, dilute with methanol to volume, add 2 drops of 3 N hydrochloric acid, mix, and filter. Use the filtrate as the test solution. Prepare a Standard solution by dissolving 100 mg of USP Penicillamine RS in 10 mL of methanol, adding 2 drops of 3 N hydrochloric acid, and mixing. Separately apply 10-µL portions of the test solution and the Standard solution to a suitable thin-layer chromatographic plate (see *Chromatography ⟨621⟩*) coated with a 0.25-mm layer of chromatographic silica gel mixture, heated at 105° for 30 minutes, and allowed to cool before use. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of butyl alcohol, glacial acetic acid, and water (8:2:2) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate, mark the solvent front, allow the solvent to evaporate, and place the plate in an atmosphere of iodine vapors. After a few minutes, spray the plate with a 1 in 300 solution of ninhydrin in dehydrated alcohol, heat it at 105° for about 10 minutes, allow it to cool, and examine it: the R_F values, colors, and intensities of the principal spots obtained from the test solution correspond to those obtained from the Standard solution.

B: A portion of powdered Tablets responds to *Identification* test *C* under *Penicillamine*.

Dissolution ⟨711⟩—

Medium: 0.5% edetate disodium and 0.05% sodium lauryl sulfate solution; 900 mL.

Apparatus 1: 100 rpm.

Time: 60 minutes.

Mobile phase—Prepare a filtered and degassed solution of 0.01 M dibasic sodium phosphate and 0.01 M monobasic potassium phosphate (60:40). If necessary, adjust the solution by the addition of 0.01 M dibasic sodium phosphate or 0.01 M monobasic potassium phosphate to a pH of 7.0 ± 0.1.

Standard solution—Prepare a solution of USP Penicillamine RS in 0.5% edetate disodium and 0.05% sodium lauryl sulfate solution having an accurately known concentration of about 0.28 mg per mL.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph replicate injections of the *Standard solution*, and record the peak responses as directed for *Procedure:* the relative standard deviation is not more than 2.0%, and the resolution factor between the solvent peak and penicillamine is not less than 1.5.

Procedure—Separately inject equal volumes (about 80 µL) of the *Standard solution* and a filtered portion of the solution under test into the chromatograph, record the chromatograms, measure the responses for the major peaks, and calculate the amount of $C_5H_{11}NO_2S$ dissolved per Tablet.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_5H_{11}NO_2S$ is dissolved in 60 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Loss on drying ⟨731⟩—Dry about 100 mg of finely ground Tablets, accurately weighed, in a capillary-stoppered bottle in vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 hours: it loses not more than 3.0% of its weight.

Penicillamine disulfide—

Diluent—Prepare as directed in the *Assay.*

Mobile phase, Resolution solution, and *Chromatographic system*—Proceed as directed in the *Assay* under *Penicillamine*.

Standard preparation—Dissolve an accurately weighed quantity of USP Penicillamine Disulfide RS in *Diluent* to obtain a solution having a known concentration of about 0.025 mg per mL.

Test preparation—Use the *Assay preparation.*

Chromatographic system—Proceed as directed in the *Assay* under *Penicillamine*. Chromatograph the *Standard preparation*, and record the penicillamine disulfide peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—[NOTE—Use peak areas where peak responses are indicated.] Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Test preparation* into the chromatograph, record the chromatograms, and measure the responses for the penicillamine disulfide peaks. Calculate the percentage of penicillamine disulfide ($C_{10}H_{20}N_2O_4S_2$) in the portion of Tablets taken by the formula:

$$20{,}000(C/L)(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Penicillamine Disulfide RS in the *Standard preparation*, L is the quantity, in mg, of penicillamine in each Tablet based on the labeled amount, and r_U and r_S are the penicillamine disulfide peak responses obtained from the *Test preparation* and the *Standard preparation*, respectively: not more than 3.0% of penicillamine disulfide is found.

Assay—

Diluent—Dissolve 5.0 g of edetate disodium in water to make 1000 mL of solution.

Mobile phase, Resolution solution, and *Chromatographic system*—Proceed as directed in the *Assay* under *Penicillamine*.

Standard preparation—Dissolve an accurately weighed quantity of USP Penicillamine RS in *Diluent* to obtain a solution having a known concentration of about 1.25 mg per mL.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 250 mg of penicillamine, to a 200-mL volumetric flask, add about 150 mL of *Diluent*, shake for 5 minutes, and allow the mixture to stand for 90 minutes. Dilute with *Diluent* to volume, and mix. Filter a portion of this solution through a suitable filter of 1 µm or finer porosity, and use the clear filtrate as the *Assay preparation.*

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Penicillamine*. Calculate the quantity, in mg, of penicillamine ($C_5H_{11}NO_2S$) in the portion of Tablets taken by the formula:

$$200C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Penicillamine RS in the *Standard preparation*, and r_U and r_S are the penicillamine peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

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

Topic/Question	Contact	Expert Committee
PENICILLAMINE TABLETS	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

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