

## Acetylcysteine

Acetylcysteine contains not less than 98.0 percent and not more than 102.0 percent of C<sub>5</sub>H<sub>9</sub>NO<sub>3</sub>S, calculated on the dried basis.

Packaging and storage— Preserve in tight containers, and store at controlled room temperature.

[USP Acetylcysteine RS](#). USP *L*-Phenylalanine RS.

[Identification, Infrared Absorption](#) [197K](#) .

[Specific rotation](#) [781S](#) : between +21°C and +27°C .

Test solution— In a 25-mL volumetric flask mix 1.25 g with 1 mL of edetate disodium solution (1 in 100), add 7.5 mL of sodium hydroxide solution (1 in 25), and mix to dissolve. Dilute to volume with pH 7.0 buffer (prepared by mixing 29.5 mL of 1 N sodium hydroxide, 50 mL of 1 M monobasic potassium phosphate, and sufficient water to make 100 mL and, using a pH meter, adjusting to a pH of 7.0 ±0.1 by adding, as necessary, more of either solution).

[pH](#) [791](#) : between 2.0 and 2.8, in a solution (1 in 100).

[Loss on drying](#) [731](#) — Dry it at a pressure of about 50 mm of mercury at 70 for 4 hours: it loses not more than 1.0% of its weight.

[Residue on ignition](#) [281](#) — Transfer to a tared fused silica dish about 2 g, weigh accurately, heat on a hot plate until thoroughly charred, cool, add 1 mL of sulfuric acid, and heat gently until fuming ceases. Ignite at 600 until the carbon is consumed. Not more than 0.5% is found.

[Heavy metals, Method II](#) [231](#) — [Caution—Exercise care since explosion may occur. ] In a dropwise manner, wet the test specimen with 2 mL of nitric acid, and proceed as directed for the Test Preparation: the limit is 0.001%.

**Assay—**

**Mobile phase**— Dissolve 6.8 g of monobasic potassium phosphate in 1000 mL of water, pass through a membrane filter having a 0.45- $\mu\text{m}$  porosity, and degas. Adjust with phosphoric acid to a pH of 3.0.

Internal standard solution— Dissolve about 1 g of USP l-Phenylalanine RS in 200 mL of freshly prepared sodium metabisulfite solution (1 in 2000).

**Standard preparation**— Dissolve an accurately weighed quantity of [USP Acetylcysteine RS](#) in sodium metabisulfite solution (1 in 2000) to obtain a solution having a known concentration of about 10 mg per mL. Pipet 10.0 mL of this solution and 10.0 mL of Internal standard solution into a 200-mL volumetric flask, dilute with sodium metabisulfite solution (1 in 2000) to volume, and mix to obtain a Standard preparation having a known concentration of about 0.5 mg per mL of [USP Acetylcysteine RS](#).

**Assay preparation**— Transfer about 1000 mg of Acetylcysteine, accurately weighed, to a 100-mL volumetric flask. Dissolve in and dilute with sodium metabisulfite solution (1 in 2000) to volume, and mix. Pipet 10.0 mL of this solution and 10.0 mL of Internal standard solution into a 200-mL volumetric flask, dilute with sodium metabisulfite solution (1 in 2000) to volume, and mix.

**Chromatographic system**— The liquid chromatograph is equipped with a 214-nm detector and a 3.9-mm  $\times$  30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the relative standard deviation for replicate injections is not more than 2.0%; and the resolution, R, between acetylcysteine and dl-phenylalanine is not less than 6.

**Procedure**— Separately inject equal volumes (about 5  $\mu\text{L}$ ) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.5 for acetylcysteine and 1.0 for l-phenylalanine. Calculate the quantity, in mg, of  $\text{C}_5\text{H}_9\text{NO}_3\text{S}$  in the portion of Acetylcysteine taken by the formula:

$$2000C(\text{RU} / \text{RS})$$

in which C is the concentration, in mg per mL, of [USP Acetylcysteine RS](#) in the Standard preparation; and RU and RS are the ratios of the peak response of acetylcysteine to that of l-phenylalanine obtained from the Assay preparation and the Standard preparation, respectively.