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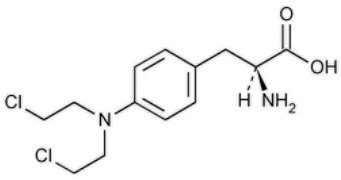
Melphalan



$C_{13}H_{18}Cl_2N_2O_2$ 305.20

L-Phenylalanine, 4-bis(2-chloroethyl)amino]-.

L-3-[*p*-[Bis(2-chloroethyl)amino]phenyl]alanine CAS RN®: 148-82-3; UNII: Q41OR9510P.

» Melphalan contains not less than 93.0 percent and not more than 100.5 percent of $C_{13}H_{18}Cl_2N_2O_2$, calculated on the dried and ionizable chlorine-free basis.

[**Caution—**Handle Melphalan with exceptional care because it is a highly potent agent.]

Packaging and storage—Preserve in tight, light-resistant, glass containers.

USP Reference standards ⟨11⟩—

USP Melphalan Hydrochloride RS

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests* ⟨197⟩*, Ultraviolet-Visible Spectroscopy: 197U*▲ (CN 1-May-2020) —

Solution: 5 µg per mL.

Medium: methanol.

B: To 1 mL of 1 in 10,000 solution in alcohol in a glass-stoppered test tube add 1 mL of pH 4.0 acid phthalate buffer (see under *Solutions* in the section *Reagents, Indicators, and Solutions*), 1 mL of a 1 in 20 solution of 4-(*p*-nitrobenzyl)pyridine in acetone, and 1 mL of saline TS. Heat on a water bath at 80° for 20 minutes, and cool quickly. Add 10 mL of alcohol and 1 mL of 1 N potassium hydroxide: a violet to red-violet color is produced.

C: Heat 100 mg with 10 mL of 0.1 N sodium hydroxide on a water bath for 10 minutes: the resulting solution, after acidification with 2 N nitric acid, responds to the tests for *Chloride* ⟨191⟩.

Specific rotation ⟨781S⟩**:** between −30° and −36°.

Test solution: 7 mg per mL, in methanol, prepared with the aid of gentle heating.

Loss on drying ⟨731⟩**:** Dry it in vacuum at 105° to constant weight: it loses not more than 7.0% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.3%.

Ionizable chlorine—Dissolve about 500 mg of Melphalan, accurately weighed, in a mixture of 75 mL of water and 2 mL of nitric acid, allow to stand for 2 minutes, and titrate with 0.1 N silver nitrate VS, determining the endpoint potentiometrically: not more than 1.0 mL of 0.1 N silver nitrate is required for each 500 mg of test specimen.

Nitrogen Determination ⟨461⟩—Determine the nitrogen content as directed under *Method II*, using about 325 mg of Melphalan, accurately weighed, and 0.1 N sulfuric acid VS for the titration: not less than 8.90% and not more than 9.45% of N is found, calculated on the dried basis.

Assay—Transfer to a beaker about 200 mg of Melphalan, accurately weighed, and dissolve in 20 mL of 0.5 N sodium hydroxide. Cover the beaker with a watch glass, and boil the solution for 30 minutes, adding water as necessary to maintain the volume. Cool, neutralize to phenolphthalein TS with acetic acid, and add 1 mL of acetic acid in excess. Titrate with 0.1 N silver nitrate VS, determining the endpoint potentiometrically, using silver and calomel electrodes, the latter modified to contain saturated potassium sulfate solution. From the results obtained in the test for *Ionizable chlorine*, calculate the volume, in mL, of 0.1 N silver nitrate that is equivalent to the ionizable chlorine in the quantity of Melphalan taken for the *Assay*, and subtract it from the *Assay* titration volume. Each mL of 0.1 N silver nitrate is equivalent to 15.26 mg of $C_{13}H_{18}Cl_2N_2O_2$.

Topic/Question	Contact	Expert Committee
MELPHALAN	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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