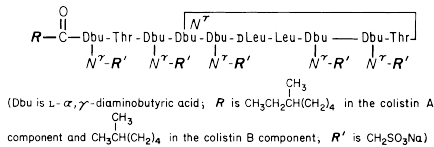


number of Tablets taken to prepare the *Test preparation*; and *L* is the labeled amount of colistipol hydrochloride, in g per Tablet.

## Colistimethate Sodium



$\text{C}_{58}\text{H}_{105}\text{N}_{16}\text{Na}_5\text{O}_{28}\text{S}_5$  (colistin A component) 1749.82  
 $\text{C}_{57}\text{H}_{103}\text{N}_{16}\text{Na}_5\text{O}_{28}\text{S}_5$  (colistin B component) 1735.80  
 Colistimethate sodium.  
 Pentasodium colistimethanesulfonate [8068-28-8;  
 21362-08-3].

» Colistimethate Sodium has a potency equivalent to not less than 390  $\mu\text{g}$  of colistin per mg.

**Packaging and storage**—Preserve in *Containers for Sterile Solids* as described under *Injections* (1).

**Labeling**—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

### USP Reference standards (11)—

USP Colistimethate Sodium RS  
 USP Endotoxin RS

**Constituted solution**—At the time of use, it meets the requirements for *Constituted Solutions* under *Injections* (1).

**Identification, Infrared Absorption** (197K).

**pH** (791): between 6.5 and 8.5, in a solution containing 10 mg per mL.

**Loss on drying** (731)—Dry about 100 mg, accurately weighed, in a capillary-stoppered bottle in vacuum at a pressure not exceeding 5 mm of mercurial at 60° for 3 hours: it loses not more than 7.0% of its weight.

**Heavy metals, Method II** (231): not more than 0.003%.

**Free colistin**—Dissolve 80 mg in 3 mL of water, and add 0.05 mL of silicotungstic acid solution (1 in 10): no immediate precipitate is formed.

**Other requirements**—Where the label states that Colistimethate Sodium is sterile, it meets the requirements for *Sterility* and *Bacterial endotoxins* under *Colistimethate for Injection*. Where the label states that Colistimethate Sodium must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements for *Bacterial endotoxins* under *Colistimethate for Injection*.

### Assay—

**Assay preparation**—Dissolve a suitable quantity of Colistimethate Sodium, accurately weighed, in 2.0 mL of water, add a sufficient accurately measured volume of *Buffer No. 6* to obtain a solution having a convenient concentration.

**Procedure**—Proceed as directed for Colistimethate Sodium under *Antibiotics—Microbial Assays* (81), using an accurately measured volume of *Assay preparation* diluted quantitatively with *Buffer No. 6* to yield a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.

## Colistimethate for Injection

» Colistimethate for Injection contains an amount of Colistimethate Sodium equivalent to not less than 90.0 percent and not more than 120.0 percent of the labeled amount of colistin.

**Packaging and storage**—Preserve in *Containers for Sterile Solids* as described under *Injections* (1).

### USP Reference standards (11)—

USP Colistimethate Sodium RS  
 USP Endotoxin RS

**Constituted solution**—At the time of use, it meets the requirements for *Constituted Solutions* under *Injections* (1).

**Bacterial endotoxins** (85)—It contains not more than 2.0 USP Endotoxin Units per mg of colistin.

**Sterility** (71)—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*.

**Other requirements**—It responds to the *Identification* test and meets the requirements for *pH*, *Loss on drying*, *Heavy metals*, and *Free colistin* under *Colistimethate Sodium*. It meets also the requirements for *Uniformity of Dosage Units* (905) and for *Constituted Solutions* and *Labeling* under *Injections* (1).

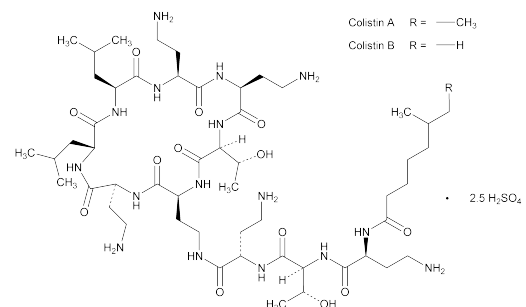
### Assay—

**Assay preparation 1** (where it is represented as being in a single-dose container)—Constitute Colistimethate for Injection in a volume of water, accurately measured, corresponding to the volume of diluent specified in the labeling. Withdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe, and quantitatively dilute with *Buffer No. 6* to obtain a solution having a convenient concentration.

**Assay preparation 2** (where the label states the quantity of colistin equivalent in a given volume of constituted solution)—Constitute Colistimethate for Injection in a volume of water, accurately measured, corresponding to the volume of diluent specified in the labeling. Quantitatively dilute an accurately measured volume of the constituted solution with *Buffer No. 6* to obtain a solution having a convenient concentration.

**Procedure**—Proceed as directed for Colistimethate Sodium under *Antibiotics—Microbial Assays* (81), using an accurately measured volume of *Assay preparation* diluted quantitatively with *Buffer No. 6* to yield a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.

## Colistin Sulfate



Colistin, sulfate.  
 Colistins sulfate [1264-72-8].

» Colistin Sulfate is the sulfate salt of an antibacterial substance produced by the growth of *Bacillus polymyxa* var. *colistinus*. It has a potency

equivalent to not less than 500 µg of colistin per mg.

**Packaging and storage**—Preserve in tight containers.

**USP Reference standards** (11)—

USP Colistin Sulfate RS

**Identification**—

**A:** Dissolve about 20 mg in 2 mL of buffer solution, prepared by adjusting 50 mL of 1 M monobasic potassium phosphate with 1 N sodium hydroxide to a pH of 7.0, diluting with water to 100 mL, and mixing. Add 0.2 mL of ninhydrin solution (1 in 200) and boil: a purple color is produced.

**B:** It meets the requirements of the tests for *Sulfate* (191).

**C:** *Liquid Chromatographic Identification Test*—

*Mobile phase*—Prepare a mixture of 0.1 M tribasic sodium phosphate and acetonitrile (77:23), and adjust with phosphoric acid to a pH of 3.0. Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

*Standard solution*—Prepare a solution of USP Colistin Sulfate RS in *Mobile phase* having a concentration of about 6 mg per mL. Protect this solution from light.

*Test solution*—Prepare a solution of Colistin Sulfate in *Mobile phase* having a concentration of about 6 mg per mL. Protect this solution from light.

*Chromatographic system* (see *Chromatography* (621))—The liquid chromatograph is equipped with a 212-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1 mL per minute.

*Procedure*—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, and record the chromatograms. The chromatogram obtained from the *Test solution* corresponds qualitatively with that obtained from the *Standard solution*, exhibiting a major peak corresponding to colistin A and minor peaks at relative retention times of about 0.55 (colistin B) and 0.8.

**pH** (791): between 4.0 and 7.0, in a solution containing 10 mg per mL.

**Loss on drying** (731)—Dry about 100 mg, accurately weighed, in a capillary-stoppered bottle in vacuum at a pressure not exceeding 5 mm of mer cury at 60° for 3 hours: it loses not more than 7.0% of its weight.

**Assay**—Proceed as directed for Colistin under *Antibiotics—Microbial Assays* (81).

## Colistin Sulfate for Oral Suspension

» Colistin Sulfate for Oral Suspension is a dry mixture of Colistin Sulfate with or without one or more suitable buffers, colors, diluents, dispersants, and flavors. It contains the equivalent of not less than 90.0 per cent and not more than 120.0 percent of the labeled amount of colistin.

**Packaging and storage**—Preserve in tight containers, protected from light.

**USP Reference standards** (11)—

USP Colistin Sulfate RS

**Uniformity of dosage units** (905)—

FOR SOLID PACKAGED IN SINGLE-UNIT CONTAINERS: meets the requirements.

**Deliverable volume** (698): meets the requirements.

**pH** (791): between 5.0 and 6.0, in the suspension constituted as directed in the labeling.

**Loss on drying** (731)—Dry about 100 mg, accurately weighed, in a capillary-stoppered bottle in vacuum at a pressure

not exceeding 5 mm of mer cury at 60° for 3 hours: it loses not more than 3.0% of its weight.

**Assay**—Constitute Colistin Sulfate for Oral Suspension as directed in the labeling. Proceed as directed under *Antibiotics—Microbial Assays* (81) using an accurately measured volume of this suspension, freshly mixed and free from air bubbles, diluted quantitatively with *Buffer No. 6* to yield a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.

## Colistin and Neomycin Sulfates and Hydrocortisone Acetate Otic Suspension

» Colistin and Neomycin Sulfates and Hydrocortisone Acetate Otic Suspension is a sterile suspension containing the equivalent of not less than 90.0 percent and not more than 135.0 percent of the labeled amount of colistin, not less than 90.0 percent and not more than 125.0 percent of the labeled amount of neomycin, and not less than 90.0 percent and not more than 110.0 percent of the labeled amount of hydrocortisone acetate (C<sub>23</sub>H<sub>32</sub>O<sub>6</sub>). It contains one or more suitable buffers, detergents, dispersants, and preservatives.

NOTE—Where Colistin and Neomycin Sulfates and Hydrocortisone Acetate Otic Suspension is prescribed, without reference to the quantity of colistin, neomycin, or hydrocortisone acetate contained therein, a product containing 3.0 mg of colistin, 3.3 mg of neomycin, and 10 mg of hydrocortisone acetate per mL shall be dispensed.

**Packaging and storage**—Preserve in tight containers.

**USP Reference standards** (11)—

USP Colistin Sulfate RS

USP Neomycin Sulfate RS

USP Hydrocortisone Acetate RS

**Sterility** (71): meets the requirements, 0.25 mL from each container being transferred directly to 90 mL of each medium.

**pH** (791): between 4.8 and 5.2.

**Assay for colistin**—Proceed as directed under *Antibiotics—Microbial Assays* (81), using a freshly mixed, accurately measured volume of Otic Suspension diluted quantitatively and stepwise with *Buffer No. 6* to yield a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.

**Assay for neomycin**—Proceed as directed under *Antibiotics—Microbial Assays* (81), using a freshly mixed, accurately measured volume of Otic Suspension diluted quantitatively and stepwise with *Buffer No. 3* to yield a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.

**Assay for hydrocortisone acetate**—

*Reagent blank*—Dilute 200 mL of 22 N sulfuric acid with 100 mL of dehydrated alcohol.

*Phenylhydrazine reagent*—Dissolve 43.33 mg of phenylhydrazine hydrochloride in 100 mL of *Reagent blank*.

*Standard preparation*—Dissolve a suitable quantity of USP Hydrocortisone Acetate RS, accurately weighed, in chloroform, and dilute quantitatively and stepwise with chloroform to obtain a solution having a known concentration of about 10 µg per mL.