of USP Mesalamine RS, equivalent to about 1% of the labeled amount of $C_7H_7NO_3$, in the same *Medium*.

*Tolerances*—The percentage of the labeled amount of $C_7H_7NO_3$ dissolved from the units tested conforms to the *Acceptance Table* shown below. Continue testing through all levels unless the results conform at an earlier level.

**Acceptance Table**

| Level | Number Tested | Criteria |
|---|---|---|
| $L_1$ | 6 | No individual value exceeds 1% dissolved. |
| $L_2$ | 6 | Average of the 12 units ($L_1 + L_2$) is not more than 1% dissolved, and no individual unit is greater than 10% dissolved. |
| $L_3$ | 12 | Average of the 24 units ($L_1 + L_2 + L_3$) is not more than 1% dissolved, and not more than one individual unit is greater than 10% dissolved. |

BUFFER STAGE 2—Add 50 mL of *Sodium hydroxide solution* to each dissolution vessel to adjust to a pH of 7.2, and continue the run.

*Procedure*—Determine the amount of $C_7H_7NO_3$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 332 nm on filtered portions of the solution under test, suitably diluted with *Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Mesalamine RS in the same *Medium*.

*Tolerances*—Not less than 80% *(Q)* of the labeled amount of $C_7H_7NO_3$ is dissolved. The requirements are met if the quantities dissolved from the product conform to *Acceptance Table 4*. Continue testing through all levels unless the results conform at an earlier level.

**Uniformity of dosage units** ⟨905⟩**:** meet the requirements for *Weight Variation*.

**Chromatographic purity—**

*Mobile phase*—Proceed as directed in the *Assay.*

*Chromatographic system*—Proceed as directed in the *Assay*. To evaluate the system suitability requirements, use the *System suitability preparation, Standard stock preparation,* and the *Standard preparation* prepared as directed in the *Assay.*

*Test solution*—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 400 mg of mesalamine, to a 500-mL volumetric flask. Add 50 mL of 1 N hydrochloric acid, and sonicate to dissolve. Shake by mechanical means for 10 minutes, dilute with water to volume, mix, and pass through a filter having a 0.5-µm or finer porosity. [NOTE—Use an aliquot of this solution for the *Assay preparation*.]

*Procedure*—Inject a volume (about 20 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure the areas for all the peaks. Calculate the percentage of each impurity in the portion of Tablets taken by the formula:

$$100(r_i / r_s)$$

in which $r_i$ is the peak response for each impurity; and $r_s$ is the sum of the responses of all the peaks: the largest secondary peak is not more than 1.0% of the total area; not more than 0.5% of any other individual impurity is found; and not more than 2.0% of total impurities is found.

**Assay—**

*Mobile phase*—Dissolve 4.3 g of sodium 1-octanesulfonate in 1 L of water. Adjust with phosphoric acid to a pH of 2.15, pass through a filter having a 0.45-µm or finer porosity, and degas.

*System suitability preparation*—Transfer about 20 mg each of 3-aminosalicylic acid and USP Salicylic Acid RS, accurately weighed, to a 200-mL volumetric flask. Dissolve in 50 mL of 1 N hydrochloric acid, sonicating to dissolve, dilute with water to volume, and mix. Dilute the solution so obtained quantitatively and stepwise with water, and mix to obtain a solution having known concentrations of about 0.01 mg each of 3-aminosalicylic acid and salicylic acid per mL.

*Standard stock preparation*—Transfer about 25 mg of USP Mesalamine RS, accurately weighed, to a 25-mL volumetric flask. Dissolve in 5 mL of 0.25 N hydrochloric acid, sonicating to dissolve, dilute with water to volume, and mix.

*Standard preparation*—Transfer 10.0 mL of *Standard stock preparation* and 5.0 mL of *System suitability preparation* to a 50-mL volumetric flask. Dilute with water to volume, mix, and pass through a filter having a 0.5-µm or finer porosity.

*Assay preparation*—Pipet a 25.0-mL aliquot of the *Test solution*, obtained as directed for the *Chromatographic purity* test, into a 100-mL volumetric flask, dilute with water to volume, mix, and pass through a filter having a 0.5-µm or finer porosity.

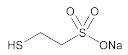
*Chromatographic system* (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 230-nm detector, a 4.6-mm × 3.3-cm analytical column that contains 3-µm base-deactivated packing L1, and two 4.6-mm × 3.0-cm precolumns, each containing 10-µm packing L1 and being located between the pump and the injector. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between mesalamine and salicylic acid or 3-aminosalicylic acid is not less than 2; the tailing factor is not more than 2; and the relative standard deviation for replicate injections is not more than 2.0%.

*Procedure*—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of mesalamine ($C_7H_7NO_3$) in the portion of Tablets taken by the formula:

$$2000C(r_U / r_S)$$

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

## Mesna




$C_2H_5NaO_3S_2$ 164.18

Ethanesulfonic acid, 2-mercapto-, monosodium salt;
Sodium 2-mercaptoethanesulfonate;
Sodium 2-sulphanylethanesulfonate [19767-45-4].

**DEFINITION**

Mesna contains NLT 96.0% and NMT 102.0% of $C_2H_5NaO_3S_2$, calculated on the dried basis.

**IDENTIFICATION**

- **A. INFRARED ABSORPTION** ⟨197K⟩
- **B. IDENTIFICATION TESTS—GENERAL,** *Sodium* ⟨191⟩**:** A solution meets the requirements of the flame test.

**ASSAY**

- **PROCEDURE**

**Sample solution:** 120 mg of Mesna in 10 mL of water

**Analysis:** To the *Sample solution* add 10 mL of 1 M sulfuric acid and 10 mL of 0.1 N iodine VS. Titrate with 0.1 N sodium thiosulfate VS, adding 1 mL of starch TS near the endpoint. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of sodium thiosulfate is equivalent to 16.42 mg of $C_2H_5NaO_3S_2$.

**Acceptance criteria:** 96.0%–102.0% on the dried basis

## IMPURITIES

### Inorganic Impurities

- **LIMIT OF CHLORIDE**

  **Chloride standard solution:** 8.24 µg/mL of sodium chloride in water

  **Sample solution:** 200 mg/mL of Mesna in carbon dioxide-free water

  **Analysis:** To 1 mL of the *Sample solution* and 15 mL of water add 1 mL of 2 M nitric acid. Add the resulting solution to 1 mL of a silver nitrate solution (17 g in 1000 mL), and allow to stand for 5 min, protected from light. To 10 mL of the *Chloride standard solution* add 5 mL of water and 1 mL of 2 M nitric acid. To this solution add 1 mL of silver nitrate solution (17 g in 1000 mL) and allow to stand for 5 min, protected from light. When viewed against a dark background, the *Sample solution* is not more turbid than the *Chloride standard solution*.

  **Acceptance criteria:** NMT 250 ppm

- **LIMIT OF SULFATE**

  **Sulfate standard solution:** 1.81 mg/mL of potassium sulfate in alcohol. Immediately before use, dilute with alcohol to 100 times its volume, and mix.

  **Sample solution:** Add 5.0 mL of the *Sample solution* prepared as directed in the test for *Limit of Chloride* to a 30-mL volumetric flask, and dilute with water to volume.

  **Analysis:** Add 3 mL of a 250-g/L solution of barium chloride to 4.5 mL of *Sulfate standard solution.* Shake and allow to stand for 1 min. To 2.5 mL of this solution add 15 mL of the *Sample solution* and 0.5 mL of acetic acid. Use 15 mL of this mixture for comparison with 15 mL of the *Sulfate standard solution,* prepared in the same manner, but using the *Sulfate standard solution* instead of the *Sample solution*. After 5 min, any opalescence in the *Sample solution* is not more intense than that in the *Sulfate standard solution*.

  **Acceptance criteria:** NMT 300 ppm

- **HEAVY METALS,** *Method I* ⟨**231**⟩**:** 10 ppm

### Organic Impurities

- **PROCEDURE**

  **Mobile phase:** In a 1000-mL volumetric flask dissolve 2.94 g of potassium dihydrogen phosphate, 2.94 g of dipotassium hydrogen phosphate, and 2.6 g of tetrabutylammonium hydrogen sulfate in about 600 mL of water. Adjust to a pH of 2.3 with phosphoric acid, add 335 mL of methanol, and dilute with water to volume.

  **System suitability solution:** 0.18 mg/mL and 0.004 mg/mL of USP Mesna RS and USP Mesna Related Compound A RS, respectively, in *Mobile phase*

  **Standard solution 1:** 8 µg/mL and 120 µg/mL of USP Mesna Related Compound A RS and USP Mesna Related Compound B RS, respectively, in *Mobile phase*

  **Standard solution 2:** 12 µg/mL of USP Mesna RS in *Mobile phase*

  **Sample solution:** 4 mg/mL of Mesna in *Mobile phase*

  **Chromatographic system**

  (See *Chromatography* ⟨621⟩*, System Suitability*.)

  **Mode:** LC

  **Detector:** UV 235 nm

  **Column:** 4.6-mm × 25-cm; 10-µm packing L1

  **Flow rate:** 1 mL/min

  **Run time:** Four times the elution time for mesna

  **Injection size:** 20 µL

  **System suitability**

  **Sample:** *System suitability solution*

  [NOTE—The relative retention times for mesna and mesna related compound A are about 1.0 and 1.4, respectively.]

  **Suitability requirements**

  **Resolution:** NLT 3.0 between mesna and mesna related compound A

  **Analysis**

  **Samples:** *Standard solution 1*, *Standard solution 2,* and *Sample solution*

  [NOTE—Identify the peaks using the relative retention times provided in *Impurity Table 1*.]

  Calculate the percentage of mesna related compound A in the portion of Mesna taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

  $r_U$ = peak response of mesna related compound A from the *Sample solution*

  $r_S$ = peak response of mesna related compound A from *Standard solution 1*

  $C_S$ = concentration of USP Mesna Related Compound A RS in *Standard solution 1* (mg/mL)

  $C_U$ = nominal concentration of Mesna in the *Sample solution* (mg/mL)

  Calculate the percentage of mesna related compound B in the portion of Mesna taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

  $r_U$ = peak response of mesna related compound B from the *Sample solution*

  $r_S$ = peak response of mesna related compound B from *Standard solution 1*

  $C_S$ = concentration of USP Mesna Related Compound B RS in *Standard solution 1* (mg/mL)

  $C_U$ = nominal concentration of Mesna in the *Sample solution* (mg/mL)

  Calculate the percentage of any specified impurities (2-(carbamimidoylsulphanyl)ethanesulfonic acid; 2-[[(guanidino)(imino)methyl]sulphanyl]ethanesulfonic acid; 2-(4,6-diamino-1,3,5-triazin-2-yl)sulphanyl-ethanesulfonic acid) and any unspecified impurities in the portion of Mesna taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times F \times 100$$

  $r_U$ = peak response of any specified or unspecified individual impurity from the *Sample solution*

  $r_S$ = peak response of mesna from *Standard solution 2*

  $C_S$ = concentration of USP Mesna RS in *Standard solution 2* (mg/mL)

  $C_U$ = nominal concentration of Mesna in the *Sample solution* (mg/mL)

  F = relative response factors (see *Impurity Table 1*)

  **Acceptance criteria**

  **Individual impurities:** See *Impurity Table 1*.

**Impurity Table 1**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| 2-(Carbamimidoylsulfanyl)ethanesulfonic acid | 0.6 | 100 | 0.3 |
| 2-[[(Guanidino)(imino)methyl]sulfanyl]ethanesulfonic acid | 0.6 | 100 | 0.3 |
| 2-(4,6-Diamino-1,3,5-triazin-2-yl)sulfanylethanesulfonic acid | 0.8 | 100 | 0.3 |
| Mesna | 1.0 | — | — |
| Mesna related compound A[a] | 1.4 | — | 0.2 |
| Mesna related compound B[b] | 2.3 | — | 3.0 |

[a] 2-(Acetysulfanyl)ethanesulfonic acid.

[b] 2,2-(Disulfanediyl)bis(ethanesulfonic acid).

**Impurity Table 1** *(Continued)*

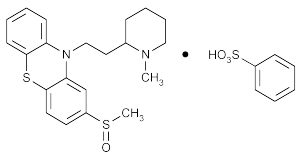
| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Individual unspecified impurities | — | — | 0.1 |
| Total unspecified impurities | — | — | 0.3 |

[a] 2-(Acetysulfanyl)ethanesulfonic acid.
[b] 2,2-(Disulfanediyl)bis(ethanesulfonic acid).

**SPECIFIC TESTS**
- **Loss on Drying:** Dry 1 g in a vacuum at a pressure not exceeding 1 mm of mercury at 60° over phosphorus pentoxide for 2 h: it loses NMT 1.0% of its weight.
- **pH** ⟨**791**⟩**:** 4.5–6.0

**ADDITIONAL REQUIREMENTS**
- **Packaging and Storage:** Preserve in a tight container, and store at room temperature.
- **USP Reference Standards** ⟨**11**⟩
  USP Mesna RS
  USP Mesna Related Compound A RS
  2-(Acetysulfanyl)ethanesulfonic acid.
  $C_4H_8O_4S_2$ 184.23
  USP Mesna Related Compound B RS
  2,2-(Disulfanediyl)bis(ethanesulfonic acid).
  $C_4H_{10}O_6S_4$ 282.38

## Mesoridazine Besylate



$C_{21}H_{26}N_2OS_2 \cdot C_6H_6O_3S$ 544.75
10*H*-Phenothiazine, 10-[2-(1-methyl-2-piperidinyl)ethyl]-2-(methylsulfinyl)-, (±)-, monobenzenesulfonate.
(±)-10-[2-(1-Methyl-2-piperidyl)ethyl]-2-(methylsulfinyl)phenothiazine monobenzenesulfonate [32672-69-8].

» Mesoridazine Besylate contains not less than 98.0 percent and not more than 102.0 percent of $C_{21}H_{26}N_2OS_2 \cdot C_6H_6O_3S$, calculated on the dried basis.

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

**USP Reference standards** ⟨11⟩**—**
USP Mesoridazine Besylate RS
NOTE—Throughout the following procedures, protect test or assay specimens, the USP Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.

**Identification—**
**A:** *Infrared Absorption* ⟨197M⟩.
**B:** *Ultraviolet Absorption* ⟨197U⟩—
*Solution:* 10 µg per mL.
*Medium:* methanol.
Absorptivities at 263 nm, calculated on the dried basis, do not differ by more than 3.0%.

**pH** ⟨791⟩**:** between 4.2 and 5.7, in a freshly prepared solution (1 in 100).

**Loss on drying** ⟨731⟩**—**Dry it at 105° for 4 hours: it loses not more than 0.5% of its weight.

**Residue on ignition** ⟨281⟩**:** not more than 0.2%.

**Heavy metals,** *Method II* ⟨231⟩**:** 0.002%.

**Selenium** ⟨291⟩**—**The absorbance of the solution from the *Test Solution,* prepared with 100 mg of Mesoridazine Besylate and 100 mg of magnesium oxide, is not greater than one-half that from the *Standard Solution* (0.003%).

**Ordinary impurities** ⟨466⟩**—**
*Test solution:* a solution in methanol having a known concentration of 14.1 mg per mL equivalent to 10 mg of mesoridazine per mL.
*Standard solution:* methanol.
*Eluant:* a mixture of chloroform, isopropyl alcohol, and ammonium hydroxide (87:12:1).
*Visualization:* 3, followed by spraying with 3% (v/v) aqueous hydrogen peroxide.
*Application volume:* 10 µL.
*Limit:* 3.0%.

**Assay—**Dissolve about 150 mg of Mesoridazine Besylate, accurately weighed, in 70 mL of acetic anhydride, and 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 27.24 mg of $C_{21}H_{26}N_2OS_2 \cdot C_6H_6O_3S$.

## Mesoridazine Besylate Injection

» Mesoridazine Besylate Injection is a sterile solution of Mesoridazine Besylate in Water for Injection. It contains mesoridazine besylate ($C_{21}H_{26}N_2OS_2 \cdot C_6H_6O_3S$) equivalent to not less than 90.0 percent and not more than 110.0 percent of the labeled amount of mesoridazine ($C_{21}H_{26}N_2OS_2$).

**Packaging and storage—**Preserve in single-dose containers, preferably of Type I glass, protected from light.

**USP Reference standards** ⟨11⟩**—**
USP Endotoxin RS
USP Mesoridazine Besylate RS
NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.

**Identification—**Dilute a volume of Injection, equivalent to about 50 mg of mesoridazine besylate, with 0.01 N hydrochloric acid to 25 mL, and proceed as directed under *Identification—Organic Nitrogenous Bases* ⟨181⟩, beginning with "Transfer the liquid to a separator": the Injection meets the requirements of the test.

**Bacterial endotoxins** ⟨85⟩**—**It contains not more than 7.0 USP Endotoxin Units per mg of mesoridazine besylate.

**pH** ⟨791⟩**:** between 4.0 and 5.0.

**Other requirements—**It meets the requirements under *Injections* ⟨1⟩.

**Assay—**[NOTE—Conduct this procedure with minimum exposure to light.] Proceed with Injection as directed under *Salts of Organic Nitrogenous Bases* ⟨501⟩, except to use 1.0 mL each of the *Standard Preparation* and the *Assay Preparation* in the *Procedure*, and determine the absorbances at the wavelength of maximum absorbance at about 262 nm. Calculate the quantity, in