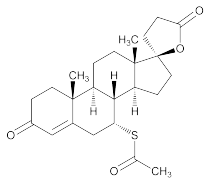
Spironolactone



$C_{24}H_{32}O_4S$ 416.57

Pregn-4-ene-21-carboxylic acid, 7-(acetylthio)-17-hydroxy-3-oxo-, γ-lactone, (7α,17α)-;
17-Hydroxy-7α-mercapto-3-oxo-17α-pregn-4-ene-21-carboxylic acid γ-lactone acetate [52-01-7].

DEFINITION
Spironolactone contains NLT 97.0% and NMT 103.0% of $C_{24}H_{32}O_4S$, calculated on the dried basis.

IDENTIFICATION
- **A. Infrared Absorption** ⟨**197K**⟩
- **B. Ultraviolet Absorption** ⟨**197U**⟩
  Sample solution: 10 µg/mL in methanol
  Analytical wavelength: 238 nm
  Acceptance criteria: Absorptivities, calculated on the dried basis, do not differ by more than 3.0%.
- **C.**
  Sample solution: Add 100 mg to a mixture of 10 mL of water and 2 mL of 1 N sodium hydroxide.
  Analysis: Boil the mixture for 3 min, cool, and add 1 mL of glacial acetic acid and 1 mL of lead acetate TS.
  Acceptance criteria: A brown-to-black precipitate of lead sulfide is formed.

ASSAY
- **Procedure**
  Mobile phase: Methanol and water (60:40)
  Standard solution: 0.5 mg/mL of USP Spironolactone RS in a mixture of acetonitrile and water (1:1)
  Sample solution: 0.5 mg/mL of Spironolactone in a mixture of acetonitrile and water (1:1)
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 230 nm
  Column: 4.6-mm × 15-cm; packing L1
  Flow rate: 1 mL/min
  Injection size: 20 µL
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Tailing factor: NMT 2.0
  Relative standard deviation: NMT 1.5%
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of spironolactone ($C_{24}H_{32}O_4S$) in the portion of sample taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Spironolactone RS in the *Standard solution* (mg/mL)
C_U = concentration of Spironolactone in the *Sample solution* (mg/mL)

  Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES
- **Limit of Mercapto Compounds**
  Sample solution: Shake 2.0 g with 30 mL of water, and filter.
  Analysis: To 15 mL of the filtrate add 3 mL of starch TS, and titrate with 0.010 N iodine. Perform a blank determination, and make any necessary correction.
  Acceptance criteria: NMT 0.10 mL of 0.010 N iodine is consumed.
- **Ordinary Impurities** ⟨**466**⟩
  Standard solution: Chloroform
  Test solution: Chloroform
  Eluant: Butyl acetate
  Visualization: 5

SPECIFIC TESTS
- **Optical Rotation,** *Specific Rotation* ⟨**781S**⟩**:** –41° to –45°
  Sample solution: 10 mg/mL in alcohol
- **Loss on Drying** ⟨**731**⟩**:** Dry a sample at 105° for 2 h: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS
- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨**11**⟩
  USP Spironolactone RS

Spironolactone Compounded Oral Suspension

DEFINITION
Spironolactone Compounded Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of spironolactone ($C_{24}H_{32}O_4S$). Prepare Spironolactone Compounded Oral Suspension 5 mg/mL as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Spironolactone tablet(s)[a] equivalent to	500 mg
Ora-Blend[b], a sufficient quantity to make	100 mL

[a] Spironolactone 25-mg tablet, Qualitest Pharmaceuticals, Huntsville, AL.
[b] Perrigo Pharmaceuticals, Allegan, MI.

Crush the *Spironolactone tablet(s)* to a fine powder, and pass through a 40-mesh sieve. Wet the powder with a small amount of *Ora-Blend*, and triturate to make a smooth paste. Add the *Ora-Blend* to make the mortar contents pourable. Transfer the contents stepwise and quantitatively to a calibrated container using the remainder of the *Ora-Blend*. Add sufficient *Ora-Blend* to bring to final volume. Shake to mix well.

ASSAY
- **Procedure**
  Mobile phase: Mix 435 mL of water with 2.7 mL of phosphoric acid and 50 mL of methanol. Combine the solution with 515 mL of acetonitrile and mix well. Filter and degas.
  Standard solution: 0.2 mg/mL of USP Spironolactone RS in *Mobile phase*
  Sample solution: Shake each bottle of Oral Suspension thoroughly. Transfer 1.0 mL of Oral Suspension into a 25-mL volumetric flask, dilute with *Mobile phase* to volume, and mix well to dissolve.