Azosemide Tablets

アゾセミド錠

Azosemide Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of azosemide ($C_{12}H_{11}ClN_6O_2S_2$: 370.84).

Method of preparation Prepare as directed under Tablets, with Azosemide.

Identification To a quantity of powdered Azosemide Tablets, equivalent to 60 mg of Azosemide, add dilute sodium hydroxide TS to make 100 mL, shake, and filter. To 1 mL of the filtrate add dilute sodium hydroxide TS to make 100 mL. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits maxima between 234 nm and 238 nm, between 272 nm and 276 nm and between 324 nm and 330 nm.

Purity Primary aromatic amines —To a quantity of powdered Azosemide Tablets, equivalent to 20 mg of Azosemide, add 5 mL of *N*,*N*-dimethylformamide, and allow to stand with occasional shaking. Add 12 mL of water, 1.0 mL of a solution of sodium nitrite (1 in 200) and 2.0 mL of diluted hydrochloric acid (1 in 10) under ice-cooling, shake, and allow to stand for 3 minutes. Add 1.0 mL of ammonium amidosulfate TS, shake thoroughly, allow to stand for 3 minutes. Add 1.0 mL of a solution of *N*-1-naphthylethylenediamine dihydrochloride (1 in 200), shake. Add *N*,*N*-dimethylformamide to make exactly 50 mL, centrifuge, and use the supernatant as the sample solution. Determine the absorbance of the sample solution at 540 nm as directed under Ultraviolet-visible Spectrophotometry *<2.24>*, using a solution prepared in the same manner with 5 mL of *N*,*N*-dimethylformamide under ice-cooling, as the blank: the absorbance is not more than 0.15.

Uniformity of dosage unit *<6.02>* Perform the Mass variation test, or the Content uniformity test according to the following method: it meets the requirement.

To 1 tablet of Azosemide Tablets add dilute sodium hydroxide TS to make exactly *V* mL so that each mL contains about 0.6 mg of azosemide ($C_{12}H_{11}ClN_6O_2S_2$), shake thoroughly, and centrifuge. Pipet 10 mL of the supernatant liquid, add dilute sodium hydroxide TS to make exactly 100 mL. Pipet 10 mL of this solution, add dilute sodium hydroxide TS to make exactly 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 60 mg of azosemide for assay, previously dried at 105℃ for 3 hours, and dissolve in dilute sodium hydroxide TS to make exactly 100 mL. Pipet 10 mL of this solution, and add dilute sodium hydroxide TS to make exactly 100 mL. Pipet 10 mL of this solution, add dilute sodium hydroxide TS to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, at 274 nm of the sample solution and standard solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*.

Amount (mg) of azosemide ($C_{12}H_{11}ClN_6O_2S_2$)
$= M_S \times A_T / A_S \times V / 100$

M_S: Amount (mg) of azosemide for assay taken

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of 2nd fluid for dissolution test as the dissolution medium, the dissolution rate in 60 minutes of 30-mg tablet and in 90 minutes of 60-mg tablet are not less than 70%, respectively.

Start the test with 1 tablet of Azosemide Tablets, withdraw not less than 20 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.5 μm. Discard the first 10 mL of the filtrate, pipet *V* mL of the subsequent filtrate, and add the dissolution medium to make exactly *V'* mL so that each mL contains about 33 μg of azosemide ($C_{12}H_{11}ClN_6O_2S_2$). Pipet 8 mL of this solution, add 0.2 mol/L sodium hydroxide TS to make exactly 20 mL, and use this solution as the sample solution. Separately, weigh accurately about 22 mg of azosemide for assay, previously dried at 105℃ for 3 hours, and dissolve in 0.2 mol/L sodium hydroxide TS to make exactly 100 mL. Pipet 5 mL of this solution, add 0.2 mol/L sodium hydroxide TS to make exactly 50 mL. Pipet 15 mL of this solution, add the dissolution medium to make exactly 25 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, at 274 nm of the sample solution and standard solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*.

Dissolution rate (%) with respect to the labeled amount of azosemide ($C_{12}H_{11}ClN_6O_2S_2$)
$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 135$

M_S: Amount (mg) of azosemide for assay taken
C: Labeled amount (mg) of azosemide ($C_{12}H_{11}ClN_6O_2S_2$) in 1 tablet

Assay Weigh accurately the mass of not less than 20 tablets of Azosemide Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 60 mg of azosemide ($C_{12}H_{11}ClN_6O_2S_2$), add dilute sodium hydroxide TS to make exactly 100 mL, shake thoroughly, and filter. Discard the first 5 mL of the filtrate, pipet 5 mL of the subsequent filtrate, add exactly 10 mL of the internal standard solution, add the mobile phase to make 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 60 mg of azosemide for assay, previously dried at 105℃ for 3 hours, dissolve in dilute sodium hydroxide TS to make exactly 100 mL. Pipet 5 mL of this solution, add exactly 10 mL of the internal standard solution, add the mobile phase to make 100 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and calculate the ratios, Q_T and Q_S of the peak area of azosemide to that of the internal standard.

Amount (mg) of azosemide ($C_{12}H_{11}ClN_6O_2S_2$)
$= M_S \times Q_T / Q_S$

M_S: Amount (mg) of azosemide for assay taken

Internal standard solution — A solution of propyl parahydroxybenzoate in the mobile phase (3 in 5000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25℃.

Mobile phase: A mixture of 0.03 mol/L potassium dihydrogen phosphate, acetonitrile and methanol (55:27:18)

Flow rate: Adjust so that the retention time of azosemide is about 5 minutes.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, azosemide and the internal standard are eluted in this order with the resolution between these peaks being not less than 8.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratio of the peak area of azosemide to that of the internal standard is not more than 1.0%.

Containers and storage Containers —Tight containers.

Add the following to 9.41 Reagents, Test Solutions:

Azosemide for assay $C_{12}H_{11}ClN_6O_2S_2$ [Same as the monograph Azosemide]