

Baclofen Reference Standard in 2 mL of a mixture of methanol and acetic acid (100) (4:1), and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 20  $\mu\text{L}$  each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of 1-butanol, water and acetic acid (100) (4:1:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spot from the sample solution and that from the standard solution show the same  $R_f$  value.

**Dissolution test** Perform the test with 1 tablet of Baclofen Tablets at 50 revolutions per minute according to Method 2 under the Dissolution Test, using 500 mL of water as the test solution. Take 20 mL or more of the dissolved solution 45 minutes after starting the test, and filter through a membrane filter with pore size of not more than 0.8  $\mu\text{m}$ . Discard the first 10 mL of the filtrate, pipet  $V$  mL of the subsequent, add water to make exactly  $V'$  mL so that each mL contains about 10  $\mu\text{g}$  of baclofen ( $\text{C}_{10}\text{H}_{12}\text{ClNO}_2$ ) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 0.01 g of Baclofen Reference Standard (separately determined the water content), dissolve in water to make exactly 100 mL, then pipet 10 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances,  $A_T$  and  $A_S$ , of the sample solution and the standard solution at 220 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate (%) of Baclofen Tablets in 45 minutes is not less than 70%.

Dissolution rate (%) with respect to the labeled amount of baclofen ( $\text{C}_{10}\text{H}_{12}\text{ClNO}_2$ )

$$= W_S \times \frac{A_T}{A_S} \times \frac{V'}{V} \times \frac{1}{C} \times 50$$

$W_S$ : Amount (mg) of Baclofen Reference Standard.

$C$ : Labeled amount (mg) of baclofen ( $\text{C}_{10}\text{H}_{12}\text{ClNO}_2$ ) in 1 tablet.

**Assay** Weigh accurately and powder not less than 20 Baclofen Tablets. Weigh accurately a portion of the powder, equivalent to about 0.05 g of baclofen ( $\text{C}_{10}\text{H}_{12}\text{ClNO}_2$ ), add 130 mL of 0.1 mol/L hydrochloric acid TS, shake for 10 minutes, add 0.1 mol/L hydrochloric acid TS to make exactly 200 mL, and centrifuge. Pipet 10 mL of the supernatant liquid, add 2 drops of phenolphthalein TS, neutralize with dilute sodium hydroxide TS, add water to make exactly 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.25 g of Baclofen Reference Standard (separately determined the water content), and dissolve in 0.1 mol/L hydrochloric acid TS to make exactly 100 mL. Pipet 10 mL of this solution, and add 0.1 mol/L hydrochloric acid TS to make exactly 100 mL. Pipet 10 mL of this solution, add 2 drops of phenolphthalein TS, neutralize with dilute sodium hydroxide TS, add water to make exactly 50 mL, and use this solution as the standard solution. Pipet 2 mL each of the sample solution and the standard solution, to each add 4 mL of ninhydrin-stannous chloride TS, shake, heat on a water bath for 20 minutes, and shake at once vigorously for 2 minutes. After cooling, to each solution add a mixture of water and 1-propanol (1:1)

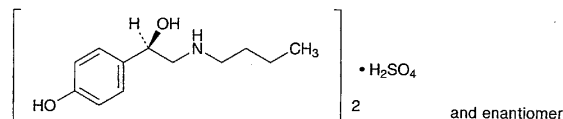
to make exactly 25 mL. Determine the absorbances,  $A_T$  and  $A_S$ , of these solutions at 570 nm as directed under the Ultraviolet-visible Spectrophotometry, using a blank prepared with 2 mL of water in the same manner.

$$\begin{aligned} & \text{Amount (mg) of baclofen (C}_{10}\text{H}_{12}\text{ClNO}_2\text{)} \\ &= \text{amount (mg) of Baclofen Reference Standard,} \\ & \quad \text{calculated on the anhydrous basis} \\ & \quad \times \frac{A_T}{A_S} \end{aligned}$$

**Containers and storage** Containers—Well-closed containers.

## Bamethan Sulfate

硫酸バメタン



$(\text{C}_{12}\text{H}_{19}\text{NO}_2)_2 \cdot \text{H}_2\text{SO}_4$ : 516.65

(*RS*)-2-Butylamino-1-(4-hydroxyphenyl)ethanol hemisulfate [5716-20-1]

Bamethan Sulfate, when dried, contains not less than 99.0% of  $(\text{C}_{12}\text{H}_{19}\text{NO}_2)_2 \cdot \text{H}_2\text{SO}_4$ .

**Description** Bamethan Sulfate occurs as white crystals or crystalline powder. It is odorless, and has a bitter taste.

It is freely soluble in water and in acetic acid (100), soluble in methanol, slightly soluble in ethanol (95), and practically insoluble in diethyl ether.

Melting point: about 169°C (with decomposition).

**Identification (1)** To 1 mL of a solution of Bamethan Sulfate (1 in 1000) add 5 mL of a solution of 4-nitrobenzenediazonium fluoroborate (1 in 2000) and 10 mL of boric acid-potassium chloride-sodium hydroxide buffer solution, pH 9.2: an orange-red color develops.

(2) Determine the absorption spectrum of a solution of Bamethan Sulfate in 0.01 mol/L hydrochloric acid TS (1 in 10,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Determine the infrared absorption spectrum of Bamethan Sulfate, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(4) A solution of Bamethan Sulfate (1 in 100) responds to the Qualitative Tests for sulfate.

**pH** Dissolve 1.0 g of Bamethan Sulfate in 10 mL of water: the pH of this solution is between 4.0 and 5.5.

**Purity (1)** Clarity and color of solution—Dissolve 1.0 g of Bamethan Sulfate in 20 mL of water: the solution is clear, and has no more color than the following control solution.

Control solution: To 1.5 mL of Matching Fluid O add diluted hydrochloric acid (1 in 40) to make 200 mL.

(2) Chloride—Perform the test with 3.5 g of Bamethan Sulfate. Prepare the control solution with 0.25 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.002%).

(3) Heavy metals—Proceed with 2.0 g of Bamethan Sulfate according to Method 1, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(4) Arsenic—Prepare the test solution with 1.0 g of Bamethan Sulfate according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(5) Related substances—Dissolve 0.10 g of Bamethan Sulfate in 2 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 2  $\mu$ L each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of chloroform and methanol (7:2) in a developing vessel saturated with ammonia vapor to a distance of about 12 cm, and air-dry the plate. Spray evenly Dragendorff's TS for spraying on the plate, air-dry for 15 minutes, spray Dragendorff's TS for spraying again, then, after 1 minute, spray evenly a solution of sodium nitrite (1 in 20), and immediately put a glass plate on the plate. Examine the plate after 30 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 4 hours).

**Residue on ignition** Not more than 0.10% (1 g).

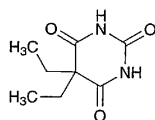
**Assay** Weigh accurately about 0.75 g of Bamethan Sulfate, previously dried, dissolve in 80 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 51.67 mg of  $(C_{12}H_{19}NO_2)_2 \cdot H_2SO_4$

**Containers and storage** Containers—Tight containers.

## Barbitol

バルピタール



$C_8H_{12}N_2O_3$ : 184.19  
5,5-Diethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione [57-44-3]

Barbitol, when dried, contains not less than 99.0% of  $C_8H_{12}N_2O_3$ .

**Description** Barbitol occurs as colorless or white crystals or a white, crystalline powder. It is odorless, and has a slightly bitter taste.

It is freely soluble in acetone and in pyridine, soluble in ethanol (95), sparingly soluble in diethyl ether, and slightly soluble in water and in chloroform.

It dissolves in sodium hydroxide TS and in ammonia TS. The pH of its saturated solution is between 5.0 and 6.0.

**Identification (1)** Boil 0.2 g of Barbitol with 10 mL of sodium hydroxide TS: the gas evolved changes moistened red litmus paper to blue.

(2) Dissolve 0.05 g of Barbitol in 5 mL of diluted pyridine (1 in 10), add 0.3 mL of copper (II) sulfate TS, shake, and allow to stand for 5 minutes: a red-purple precipitate is formed. Shake the mixture with 5 mL of chloroform: a red-purple color develops in the chloroform layer. Separately, dissolve 0.05 g of Barbitol in 2 to 3 drops of ammonia-ammonium chloride buffer solution, pH 10.7, and 5 mL of diluted pyridine (1 in 10). Add 5 mL of chloroform and 0.3 mL of copper (II) sulfate TS to the solution: a red-purple precipitate is produced in the aqueous layer. The red-purple precipitate is not dissolved in the chloroform by shaking.

(3) To 0.4 g of Barbitol add 0.1 g of anhydrous sodium carbonate and 4 mL of water, shake, and add a solution of 0.3 g of 4-nitrobenzyl chloride in 7 mL of ethanol (95). Heat the mixture on a water bath under a reflux condenser for 30 minutes, and allow to stand for 1 hour. Collect the separated crystals, wash with 7 mL of sodium hydroxide TS and a small amount of water, recrystallize from a mixture of ethanol (95) and chloroform (1:1), and dry at 105°C for 30 minutes: the crystals melt between 192°C and 196°C.

**Melting point** 189 – 192°C

**Purity (1)** Clarity and color of solution—Dissolve 0.5 g of Barbitol in 5 mL of sodium hydroxide TS: the solution is clear and colorless.

(2) Chloride—Dissolve 0.30 g of Barbitol in 20 mL of acetone, and add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: take 0.30 mL of 0.01 mol/L hydrochloric acid VS, 20 mL of acetone and 6 mL of dilute nitric acid, and add water to make 50 mL (not more than 0.035%).

(3) Sulfate—Dissolve 0.40 g of Barbitol in 20 mL of acetone, and add 1 mL of dilute hydrochloric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: take 0.40 mL of 0.005 mol/L sulfuric acid VS, 20 mL of acetone, and 1 mL of dilute hydrochloric acid, and add water to make 50 mL (not more than 0.048%).

(4) Heavy metals—Proceed with 1.0 g of Barbitol according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead solution (not more than 20 ppm).

(5) Readily carbonizable substances—Perform the test with 0.5 g of Barbitol. The solution has not more color than Matching Fluid A.

**Loss on drying** Not more than 1.0% (1 g, 105°C, 2 hours).

**Residue on ignition** Not more than 0.10% (1 g).

**Assay** Weigh accurately about 0.4 g of Barbitol, previously dried, and dissolve in 5 mL of ethanol (95) and 50 mL of chloroform. Titrate with 0.1 mol/L potassium hydroxide-ethanol VS until the color of the solution changes from yellow through light blue to purple (indicator: 1 mL of alizarin