Description Baclofen occurs as a white to pale yellowish white, crystalline powder.

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

It dissolves in dilute hydrochloric acid.

Identification (1) To 5 mL of a solution of Baclofen (1 in 1000) add 1 mL of ninhydrin TS, and heat on a water bath for 3 minutes: a blue-purple color develops.

(2) Determine the absorption spectrum of a solution of Baclofen in 0.1 mol/L hydrochloric acid TS (1 in 2000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Baclofen Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Perform the test with Baclofen as directed under the Flame Coloration Test (2): a green color appears.

Purity (1) Chloride—Dissolve 0.5 g of Baclofen in 50 mL of acetic acid (100), and add water to make 100 mL. To 10 mL of this solution 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: to 0.30 mL of 0.01 mol/L hydrochloric acid VS add 5 mL of acetic acid (100), 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.21%).

(2) Heavy metals—Proceed with 2.0 g of Baclofen according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

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

(4) Related substances—Dissolve 0.050 g of Baclofen in 50 mL of the mobile phase, and use this solution as the sample solution. Pipet 1.0 mL and 1.5 mL of the sample solution, to each add the mobile phase to make exactly 100 mL, and use these solutions as the standard solution (1) and the standard solution (2), respectively. Perform the test with 25 μL each of the sample solution and the standard solutions (1) and (2) as directed under the Liquid Chromatography according to the following conditions. Determine each peak height of these solutions: each height of the peaks other than the peak of baclofen from the sample solution is not larger than the peak height of baclofen from the standard solution (1), and the total height of these peaks is not larger than the peak height of baclofen from the standard solution (2).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 268 nm).

Column: A stainless steel column 4 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: A mixture of methanol and diluted acetic acid (100) (1 in 900) (3:2).

Flow rate: Adjust the flow rate so that the retention time of baclofen is about 4 minutes.

Time span of measurement: About 3 times as long as the retention time of baclofen after the solvent peak.

System suitability—

Test for required detection: Adjust the sensitivity so that the peak height of baclofen obtained from 25 μL of the standard solution (1) is between 5 and 10 mm.

System performance: Dissolve 0.40 g of Baclofen and 5 mg of methyl parahydroxybenzoate in 200 mL of the mobile phase. To 10 mL of this solution add the mobile phase to make 100 mL. When the procedure is run with 25 μL of this solution under the above operating conditions, baclofen and methyl parahydroxybenzoate are eluted in this order with the resolution between these peaks being not less than 5.

System repeatability: When the test is repeated 6 times with 25 μL of the standard solution (1) under the above operating conditions, the relative standard deviation of the peak heights of baclofen is not more than 3.0%.

Water Not more than 1.0% (1 g, direct titration).

Residue on ignition Not more than 0.30% (1 g).

Assay Weigh accurately about 0.5 g of Baclofen, dissolve in 80 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue to greenish blue (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 21.366 mg of $C_{10}H_{12}ClNO_2$

Containers and storage Containers—Well-closed containers.

Baclofen Tablets

バクロフェン錠

Baclofen Tablets contain not less than 93% and not more than 107% of the labeled amount of baclofen ($C_{10}H_{12}ClNO_2$: 213.66).

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

Identification (1) To a portion of powdered Baclofen Tablets, equivalent to 0.01 g of Baclofen according to the labeled amount, add 10 mL of water, shake well, and filter. To 5 mL of the filtrate add 1 mL of ninhydrin TS, and proceed as directed in the Identification (1) under Baclofen.

(2) To a portion of powdered Baclofen Tablets, equivalent to 0.025 g of Baclofen according to the labeled amount, add 50 mL of 0.1 mol/L hydrochloric acid TS, shake for 15 minutes, and filter. Determine the absorption spectrum of the filtrate as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 257 nm and 261 nm, between 264 nm and 268 nm, and between 272 nm and 276 nm.

(3) To a portion of powdered Baclofen Tablets, equivalent to 0.01 g of Baclofen according to the labeled amount, add 2 mL of a mixture of methanol and acetic acid (100) (4:1), shake well, centrifuge, and use the supernatant liquid as the sample solution. Separately, dissolve 0.01 g of

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 μL 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 *Rf* 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 μm. 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 μg of baclofen ($C_{10}H_{12}ClNO_2$) 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 ($C_{10}H_{12}ClNO_2$)

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

W_S: Amount (mg) of Baclofen Reference Standard.
C: Labeled amount (mg) of baclofen ($C_{10}H_{12}ClNO_2$) 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 ($C_{10}H_{12}ClNO_2$), 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.

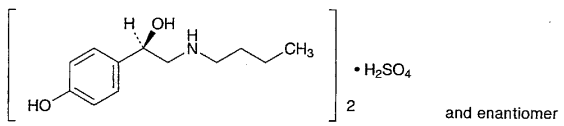
Amount (mg) of baclofen ($C_{10}H_{12}ClNO_2$)
= amount (mg) of Baclofen Reference Standard, calculated on the anhydrous basis

$$\times \frac{A_T}{A_S}$$

Containers and storage Containers—Well-closed containers.

Bamethan Sulfate

硫酸バメタン



$(C_{12}H_{19}NO_2)_2.H_2SO_4$: 516.65
(*RS*)-2-Butylamino-1-(4-hydroxyphenyl)ethanol hemisulfate [*5716-20-1*]

Bamethan Sulfate, when dried, contains not less than 99.0% of $(C_{12}H_{19}NO_2)_2.H_2SO_4$.

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.