directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of bufexamac to that of the internal standard, respectively.

$$\text{Amount (mg) of bufexamac } (C_{12}H_{17}NO_3) = \text{amount (mg) of bufexamac for assay} \times \frac{Q_T}{Q_S}$$

Internal standard solution—A solution of diphenylimidazole in methanol (1 in 5000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 275 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°C.

Mobile phase: Dissolve 2.5 g of sodium 1-octane sulfonate and 0.6 g of disodium dihydrogen ethylenediamine tetraacetate dihydrate in 850 mL of water, and add 400 mL of methanol, 400 mL of acetonitrile and 8 mL of acetic acid (100).

Flow rate: Adjust the flow rate so that the retention time of bufexamac is about 6 minutes.

System suitability—

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, bufexamac 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 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of bufexamac to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Bufexamac Ointment

ブフェキサマク軟膏

Bufexamac Ointment contains not less than 90% and not more than 110% of the labeled amount of bufexamac ($C_{12}H_{17}NO_3$: 223.27).

Method of preparation Prepare as directed under Ointments, with Bufexamac.

Identification To a quantity of Bufexamac Ointment, equivalent to 0.05 g of Bufexamac according to the labeled amount, add 5 mL of tetrahydrofuran, shake well, add 5 mL of ethanol (99.5), shake, centrifuge, and use the supernatant liquid as the sample solution. Separately, dissolve 0.05 g of bufexamac for assay in 10 mL of methanol, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Use a plate of silica gel for thin-layer chromatography, moisten the surface of the plate evenly by spraying with 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS, and dry the plate at 110°C for about 30 minutes. Spot 5 μL each of the sample solution and the standard solution on the plate. Develop the plate with a mixture of pentane, ethyl acetate and acetic acid (100) (7:4:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly iron (III) chloride TS on the plate: the spot from the sample solution and that from the standard solution show a red-brown color and the same *Rf* value.

Assay Weigh accurately a quantity of Bufexamac Ointment, equivalent to about 0.05 g of bufexamac ($C_{12}H_{17}NO_3$), add 40 mL of tetrahydrofuran, warm to 40°C, dissolve by shaking, cool, and add tetrahydrofuran to make exactly 50 mL. Pipet 10 mL of this solution, add exactly 5 mL of the internal standard solution and the mobile phase to make 100 mL, and filter, if necessary, through a membrane filter of 0.45-μm porosity. Discard the first 20 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.05 g of bufexamac for assay, previously dried at 105°C for 4 hours, and dissolve in tetrahydrofuran to make exactly 50 mL. Pipet 10 mL of this solution, add exactly 5 mL of the internal standard solution and the mobile phase to make 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of bufexamac to that of the internal standard, respectively.

$$\text{Amount (mg) of bufexamac } (C_{12}H_{17}NO_3) = \text{amount (mg) of bufexamac for assay} \times \frac{Q_T}{Q_S}$$

Internal standard solution—A solution of diphenylimidazole in methanol (1 in 5000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 275 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°C.

Mobile phase: Dissolve 2.5 g of sodium 1-octane sulfonate and 0.6 g of disodium dihydrogen ethylenediamine tetraacetate dihydrate in 850 mL of water, and add 400 mL of methanol, 400 mL of acetonitrile and 8 mL of acetic acid (100).

Flow rate: Adjust the flow rate so that the retention time of bufexamac is about 6 minutes.

System suitability—

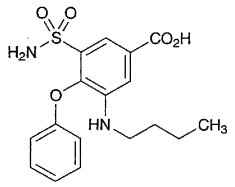
System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, bufexamac and the internal standard are eluted in this order with the resolution between these peaks being not less than 8.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of bufexamac to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Bumetanide

ブメタニド



$C_{17}H_{20}N_2O_5S$: 364.42
3-Butylamino-4-phenoxy-5-sulfamoylbenzoic acid
[*28395-03-1*]

Bumetanide, when dried, contains not less than 98.5% of $C_{17}H_{20}N_2O_5S$.

Description Bumetanide occurs as white crystals or crystalline powder.

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

It dissolves in potassium hydroxide TS.

It is gradually colored by light.

Identification **(1)** Dissolve 0.01 g of Bumetanide in 1 mL of pyridine, add 2 drops of copper (II) sulfate TS, shake, add 3 mL of water and 5 mL of chloroform, shake, and allow to stand: a light blue color develops in the chloroform layer.

(2) Dissolve 0.04 g of Bumetanide in 100 mL of phosphate buffer solution, pH 7.0, and dilute 10 mL of the solution with water to make 100 mL. Determine the absorption spectrum of the solution 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 Bumetanide, 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.

Melting point 232 - 237°C

Purity **(1)** Clarity and color of solution—Dissolve 0.050 g of Bumetanide in 2 mL of a solution of potassium hydroxide (1 in 30) and 8 mL of water: the solution is clear, and has no more color than the following control solution.

Control solution: Pipet 0.5 mL each of Cobaltous Chloride Stock CS, Ferric Chloride Stock CS and Cupric Sulfate Stock CS, mix them, and add diluted hydrochloric acid (1 in 40) to make exactly 100 mL.

(2) Chloride—Mix well 0.5 g of Bumetanide with 0.7 g of potassium nitrate and 1.2 g of anhydrous sodium carbonate, transfer, in small portions, to a red-hot platinum crucible, and red-heat until the reaction is complete. After cooling, to the residue add 14 mL of dilute sulfuric acid and 6 mL of water, boil for 5 minutes, filter, wash the residue with 10 mL of water, combine the filtrate and the washing, 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 with 0.30 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.021%).

(3) Heavy metals—Proceed with 2.0 g of Bumetanide 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).

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

(5) Related substances—Conduct this procedure without exposure to daylight, using light-resistant vessels. Dissolve 0.10 g of Bumetanide in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add methanol to make exactly 100 mL. Pipet 2 mL of this solution, add methanol to make exactly 10 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 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 chloroform, acetic acid (100), cyclohexane and methanol (32:4:4:1) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): 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, 2 hours).

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

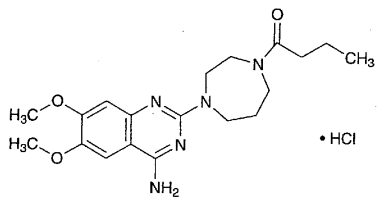
Assay Weigh accurately about 0.5 g of Bumetanide, previously dried, dissolve in 50 mL of ethanol (95), and titrate with 0.1 mol/L sodium hydroxide VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L sodium hydroxide VS
= 36.442 mg of $C_{17}H_{20}N_2O_5S$

Containers and storage Containers—Tight containers.
Storage—Light-resistant.

Bunazosin Hydrochloride

塩酸ブナゾシン



$C_{19}H_{27}N_5O_3.HCl$: 409.91
4-Amino-2-(4-butanoyl-1,4-diazepan-1-yl)-6,7-dimethoxyquinazoline monohydrochloride [*72712-76-2*]