(2) Sulfate—Perform the test with 0.30 g of Dibucaine Hydrochloride. Prepare the control solution with 0.35 mL of 0.005 mol/L sulfuric acid VS (not more than 0.056%).

(3) Heavy metals—Proceed with 1.0 g of Dibucaine Hydrochloride according to Method 1, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(4) Related substances—Dissolve 0.20 g of Dibucaine Hydrochloride in 5 mL of ethanol (95), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add ethanol (95) to make exactly 20 mL, then pipet 2 mL of this solution, add ethanol (95) to make exactly 20 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL 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 ethyl acetate, water and acetic acid (100) (3:1:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet (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 2.0% (1 g, in vacuum, phosphorus (V) oxide, 80°C, 5 hours).

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

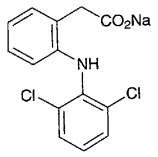
**Assay** Weigh accurately about 0.3 g of Dibucaine Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 18.997 mg of $C_{20}H_{29}N_3O_2.HCl$

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

# Diclofenac Sodium

ジクロフェナクナトリウム




$C_{14}H_{10}Cl_2NNaO_2$: 318.13
Monosodium 2-(2,6-dichlorophenylamino)phenylacetate
[*15307-79-6*]

Diclofenac Sodium, when dried, contains not less than 98.5% of $C_{14}H_{10}Cl_2NNaO_2$.

**Description** Diclofenac Sodium occurs as white to pale yellowish white crystals or crystalline powder.

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

It is hygroscopic.

**Identification** (1) To 1 mL of a solution of Diclofenac Sodium in methanol (1 in 250) add 1 mL of nitric acid: a dark red color develops.

(2) Perform the test with 5 mg of Diclofenac Sodium as directed under the Flame Coloration Test (2): a light green color appears.

(3) Determine the infrared absorption spectrum of Diclofenac Sodium, 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 Diclofenac Sodium (1 in 100) responds to the Qualitative Tests for sodium salt.

**Purity** (1) Heavy metals—Proceed with 2.0 g of Diclofenac Sodium 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).

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

(3) Related substances—Dissolve 0.05 g of Diclofenac Sodium in 50 mL of the mobile phase, and use this solution as the sample solution. Pipet 2 mL of the sample solution, and add the mobile phase to make exactly 50 mL. Pipet 5 mL of this solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of these solutions as directed under the Liquid Chromatography. Determine each peak area of these solutions by the automatic integration method: the area of each peak other than the peak of diclofenac from the sample solution is not larger than the peak area of the standard solution.

*Operating conditions—*

Detector: An ultraviolet absorption photometer (wavelength: 240 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (7 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: A mixture of methanol and diluted acetic acid (100) (3 in 2500) (4:3).

Flow rate: Adjust the flow rate so that the retention time of diclofenac is about 20 minutes.

Time span of measurement: About twice as long as the retention time of diclofenac after the solvent peak.

*System suitability—*

System performance: Dissolve 0.035 g of ethyl parahydroxybenzoate and 0.05 g of propyl parahydroxybenzoate in 100 mL of the mobile phase. To 1 mL of this solution add the mobile phase to make 50 mL. When the procedure is run with 20 μL of this solution under the above operating conditions, ethyl parahydroxybenzoate and propyl 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 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of diclofenac is not more than 2.0%.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 3 hours).

**Assay** Weigh accurately about 0.5 g of Diclofenac Sodium, previously dried, dissolve with 40 mL of water in a separator, add 2 mL of dilute hydrochloric acid, and extract the precipitate formed with 50 mL of chloroform. Extract again with two 20-mL portions of chloroform, and filter the extract each time through a pledget of absorbent cotton moistened with chloroform. Wash the tip of the separator and the absorbent cotton with 15 mL of chloroform, combine the washing with the extracts, add 10 mL of a solution of 1 mol/L hydrochloric acid TS in ethanol (99.5) (1 in 100), and titrate with 0.1 mol/L potassium hydroxide-ethanol VS from the first equivalent point to the second equivalent point (potentiometric titration).

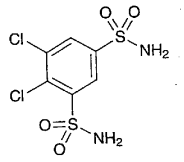
Each mL of 0.1 mol/L potassium hydroxide-ethanol VS
= 31.813 mg of $C_{14}H_{10}Cl_2NNaO_2$

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

# Diclofenamide

## Dichlorphenamide

ジクロフェナミド



$C_6H_6Cl_2N_2O_4S_2$: 305.16
4,5-Dichlorobenzene-1,3-disulfonamide [*120-97-8*]

Diclofenamide, when dried, contains not less than 98.0% of $C_6H_6Cl_2N_2O_4S_2$.

**Description** Diclofenamide occurs as a white, crystalline powder.

It is very soluble in *N,N*-dimethylformamide, soluble in ethanol (95), and very slightly soluble in water.

It dissolves in sodium hydroxide TS.

**Identification** **(1)** Dissolve 0.01 g of Diclofenamide in 100 mL of 0.01 mol/L sodium hydroxide TS. To 10 mL of the solution add 0.1 mL of hydrochloric acid. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Diclofenamide Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

**(2)** Determine the infrared absorption spectrum of Diclofenamide, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Diclofenamide Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

**Melting point** 237 - 240°C

**Purity** **(1)** Chloride—Dissolve 0.10 g of Diclofenamide in 10 mL of *N,N*-dimethylformamide, 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: to 0.45 mL of 0.01 mol/L hydrochloric acid VS add 10 mL of *N,N*-dimethylformamide, 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.160%).

**(2)** Selenium—To 0.10 g of Diclofenamide add 0.5 mL of a mixture of perchloric acid and sulfuric acid (1:1) and 2 mL of nitric acid, and heat on a water bath until no more brown gas evolves and the solution becomes to be a light yellow clear solution. After cooling, add 4 mL of nitric acid to this solution, then add water to make exactly 50 mL, and use this solution as the sample solution. Separately, pipet 3 mL of Standard Selenium Solution, add 0.5 mL of a mixture of perchloric acid and sulfuric acid (1:1) and 6 mL of nitric acid, then add water to make exactly 50 mL, and use this solution as the standard solution. Perform the test with the sample solution and the standard solution as directed under the Atomic Absorption Spectrophotometry according to the following conditions, and determine constant absorbances, $A_T$ and $A_S$, obtained on a recorder after rapid increasing of the absorption: $A_T$ is smaller than $A_S$ (not more than 30 ppm).

Perform the test by using a hydride generating system and a thermal absorption cell.

Lamp: An selenium hollow cathode lamp

Wavelength: 196.0 nm

Temperature of sample atomizer: When an electric furnace is used, about 1000°C.

Carrier gas: Nitrogen or Argon

**(3)** Heavy metals—Proceed with 2.0 g of Diclofenamide 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)** Related substances—Dissolve 0.10 g of Diclofenamide in 50 mL of the mobile phase, and use this solution as the sample solution. Pipet 2 mL of the sample solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of these solutions by the automatic integration method: the total area of the peaks other than the peak of diclofenamide from the sample solution is not larger than the peak area of diclofenamide from the standard solution.

*Operating conditions—*

Detector, column, column temperature, mobile phase, flow rate, and selection of column: Proceed as directed in the operating conditions in the Assay.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of diclofenamide obtained from 10 μL of the standard solution is between 5 mm and 10 mm.

Time span of measurement: About 5 times as long as the retention time of diclofenamide.

**Loss on drying** Not more than 1.0% (1 g, in vacuum at a pressure not exceeding 0.67 kPa, 100°C, 5 hours).

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

**Assay** Weigh accurately about 0.05 g each of Diclofenamide and Diclofenamide Reference Standard, previous-