

Loss on drying Not more than 1.0% (1 g, in vacuum, silica gel, 18 hours).

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

Assay Weigh accurately about 0.3 g of Norepinephrine, previously dried, dissolve in 50 mL of acetic acid for nonaqueous titration by warming, if necessary, and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from blue-purple through blue to blue-green (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

$$\begin{aligned} \text{Each mL of 0.1 mol/L perchloric acid VS} \\ = 16.918 \text{ mg of } C_8H_{11}NO_3 \end{aligned}$$

Containers and storage Containers—Tight containers.

Storage—Light-resistant, under nitrogen atmosphere, and in a cold place.

Norepinephrine Injection

Noradrenaline Hydrochloride Injection

Noreprenamine Hydrochloride Injection

ノルエピネフリン注射液

Norepinephrine Injection is an aqueous solution for injection. It contains not less than 90% and not more than 110% of the labeled amount of *dl*-norepinephrine ($C_8H_{11}NO_3$; 169.18).

Method of preparation Dissolve Norepinephrine in 0.01 mol/L hydrochloric acid TS, and prepare as directed under Injections.

Description Norepinephrine Injection is a clear, colorless liquid.

It gradually becomes a pale red color by light and by air.
pH: 2.3 – 5.0

Identification (1) Measure a volume of Norepinephrine Injection, equivalent to 1 mg of Norepinephrine according to the labeled amount, and proceed as directed in the Identification (1) under Norepinephrine.

(2) Transfer a volume of Norepinephrine Injection, equivalent to 1 mg of Norepinephrine according to the labeled amount, to each of two test tubes A and B, and proceed as directed in the Identification (2) under Norepinephrine.

Purity (1) Arterenone—Measure a volume of Norepinephrine Injection, equivalent to 0.010 g of Norepinephrine according to the labeled amount, add water to make exactly 20 mL, and determine the absorbance of this solution at 310 nm: the absorbance is not more than 0.10.

(2) Epinephrine—Measure a volume of Norepinephrine Injection, equivalent to 5 mg of Norepinephrine according to the labeled amount, add 1 mL of diluted acetic acid (100) (1 in 2) and water to make exactly 10 mL, and proceed as directed in the Purity (3) under Norepinephrine.

Assay Pipet a volume of Norepinephrine Injection, equivalent to about 5 mg of *dl*-norepinephrine ($C_8H_{11}NO_3$), add

water to make exactly 25 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.01 g of Norepinephrine Bitartrate Reference Standard, previously dried in a desiccator (in vacuum, silica gel) for 24 hours, dissolve in water to make exactly 25 mL, and use this solution as the standard solution. Pipet 5 mL each of the sample solution and the standard solution, add 0.2 mL each of starch TS, then add iodine TS dropwise with swirling until a persistent blue color is produced. Add 2 mL of iodine TS, and shake. Adjust the pH of the solution to 6.5 with 0.05 mol/L disodium hydrogenphosphate TS, add 10 mL of phosphate buffer solution, pH 6.5, and shake. Immediately after allowing to stand for 3 minutes, add sodium thiosulfate TS dropwise until a red-purple color develops, then add water to make exactly 50 mL. Determine the absorbances, A_T and A_S , of the subsequent solutions of the sample solution and the standard solution at 515 nm within 5 minutes as directed under the Ultraviolet-visible Spectrophotometry.

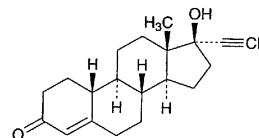
$$\begin{aligned} \text{Amount (mg) of } dl\text{-norepinephrine (} C_8H_{11}NO_3\text{)} \\ = \text{amount (mg) of Norepinephrine Bitartrate} \\ \text{Reference Standard} \\ \times \frac{A_T}{A_S} \times 0.5016 \end{aligned}$$

Containers and storage Containers—Hermetic containers, and colored containers may be used.

Storage—Light-resistant.

Norethisterone

ノルエチステロン



$C_{20}H_{26}O_2$: 298.42

17-Hydroxy-19-nor-17 α -pregn-4-en-20-yn-3-one [68-22-4]

Norethisterone, when dried, contains not less than 97.0% and not more than 103.0% of $C_{20}H_{26}O_2$.

Description Norethisterone occurs as a white to pale yellowish white, crystalline powder. It is odorless.

It is soluble in chloroform, sparingly soluble in ethanol (95) and in tetrahydrofuran, slightly soluble in diethyl ether, and very slightly soluble in water.

It is affected by light.

Identification (1) To 2 mg of Norethisterone add 2 mL of sulfuric acid: the solution shows a red-brown color and a yellow-green fluorescence. Add 10 mL of water to this solution cautiously: a yellow color develops and a yellow-brown precipitate is formed.

(2) To 0.025 g of Norethisterone add 3.5 mL of a solution of 0.05 g of hydroxylammonium chloride and 0.05 g of anhydrous sodium acetate trihydrate in 25 mL of methanol. Heat under a reflux condenser on a water bath for 5 hours, cool, and add 15 mL of water. Collect the precipitate formed, wash with 1 to 2 mL of water, recrystallize from

methanol, and dry in a desiccator (in vacuum, silica gel) for 5 hours: the crystals melt between 112°C and 118°C.

Optical rotation $[\alpha]_D^{20}$: $-23 - -27^\circ$ (after drying, 0.25 g, chloroform, 25 mL, 200 mm).

Melting point 203 – 209°C

Loss on drying Not more than 0.5% (0.5 g, in vacuum, silica gel, 4 hours).

Residue on ignition Not more than 0.1% (0.5 g).

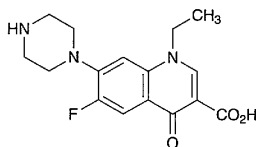
Assay Weigh accurately about 0.2 g of Norethisterone, previously dried, dissolve in 40 mL of tetrahydrofuran, add 10 mL of a solution of silver nitrate (1 in 20), and titrate with 0.1 mol/L sodium hydroxide VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L sodium hydroxide VS
= 29.843 mg of $C_{20}H_{26}O_2$

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

Norfloxacin

ノルフロキサシン



$C_{16}H_{18}FN_3O_3$: 319.33

1-Ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(piperazin-1-yl)quinoline-3-carboxylic acid [70458-96-7]

Norfloxacin, when dried, contains not less than 99.0% of $C_{16}H_{18}FN_3O_3$.

Description Norfloxacin occurs as a white to pale yellow crystalline powder.

It is freely soluble in acetic acid (100), slightly soluble in ethanol (99.5) and in acetone, very slightly soluble in methanol, and practically insoluble in water.

It dissolves in dilute hydrochloric acid TS and in sodium hydroxide TS.

It is hygroscopic.

It is gradually colored by light.

Identification (1) Dissolve 0.01 g of Norfloxacin in a solution of sodium hydroxide (1 in 250) to make 100 mL. To 5 mL of this solution add a solution of sodium hydroxide (1 in 250) to make 100 mL. Determine the absorption spectrum of this 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 wavelength.

(2) Dissolve a suitable amount of Norfloxacin in a suitable amount of acetone, evaporate the acetone under reduced pressure, and dry the residue. Determine the infrared absorption spectrum of the residue so obtained 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.

Purity (1) Sulfate—Dissolve 1.0 g of Norfloxacin in 7 mL of 0.5 mol/L sodium hydroxide TS and 23 mL of water, and add 1 drop of phenolphthalein TS. Add gradually diluted hydrochloric acid (1 in 3) to this solution until the red color disappears, then add 0.5 mL of dilute hydrochloric acid, and cool in ice for 30 minutes. Filter through a glass filter (G4), and wash the residue with 10 mL of water. Combine the filtrate and the washing, 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. To 0.50 mL of 0.005 mol/L sulfuric acid VS add 7 mL of 0.5 mol/L sodium hydroxide TS and 1 drop of phenolphthalein TS, add diluted hydrochloric acid (1 in 3) until the red color disappears, then add 1.5 mL of dilute hydrochloric acid, 1 or 2 drops of bromophenol blue TS and water to make 50 mL (not more than 0.024%).

(2) Heavy metals—Proceed with 2.0 g of Norfloxacin according to Method 2, and perform the test. Prepare the control solution with 3.0 mL of Standard Lead Solution (not more than 15 ppm).

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

(4) Related substances—Conduct this procedure without exposure to light, using light-resistant vessels. Dissolve 0.10 g of Norfloxacin in 50 mL of a mixture of methanol and acetone (1:1), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of methanol and acetone (1:1) to make exactly 100 mL. Pipet 2 mL of this solution, add a mixture of methanol and acetone (1:1) 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 20 μ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography (5 – 7 μ m in particle diameter). Develop with a mixture of methanol, chloroform, toluene, diethylamine and water (20:20:10:7:4) to a distance of about 9 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm and 366 nm): the number of the spot other than the principal spot from the sample solution is not more than 2 and they are not more intense than the spot from the standard solution.

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 0.5 g of Norfloxacin, previously dried, dissolve in 50 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
= 31.933 mg of $C_{16}H_{18}FN_3O_3$

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