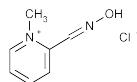


Pralidoxime Chloride



$C_7H_9ClN_2O$ 172.61

Pyridinium, 2-(hydroxymino)methyl-1-methyl-, chloride. 2-Formyl-1-methylpyridinium chloride oxime [51-15-0].

» Pralidoxime Chloride contains not less than 97.0 percent and not more than 102.0 percent of $C_7H_9ClN_2O$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Labeling—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

USP Reference standards (11)—

USP Endotoxin RS

USP Pralidoxime Chloride RS

Identification—

A: *Infrared Absorption* (197M).

B: A solution (1 in 10) responds to the tests for *Chloride* (191).

C: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Melting range (741): between 215° and 225°, with decomposition.

Loss on drying (731)—Dry it at 105° for 3 hours: it loses not more than 2.0% of its weight.

Residue on ignition (281): not more than 0.5%.

Heavy metals, Method I (231): 0.002%.

Chloride content—Dissolve about 300 mg, accurately weighed, in 150 mL of water, add 20 mL of glacial acetic acid and 10 drops of (*p*-*tert*-octylphenoxy)nonaethoxyethanol, and titrate with 0.1 N silver nitrate *VS*, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N silver nitrate is equivalent to 3.545 mg of Cl. Not less than 20.2% and not more than 20.8%, calculated on the dried basis, is found.

Other requirements—Where the label states that Pralidoxime Chloride is sterile, it meets the requirements for *Sterility Tests* (71) and for *Bacterial endotoxins* under *Pralidoxime Chloride for Injection*. Where the label states that Pralidoxime Chloride must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements for *Bacterial endotoxins* under *Pralidoxime Chloride for Injection*.

Assay—

Dilute phosphoric acid solution—Transfer 10 mL of phosphoric acid to a 100-mL volumetric flask containing 50 mL of water, and mix. Dilute with water to volume, and mix.

Tetraethylammonium chloride solution—Transfer about 170 mg of tetraethylammonium chloride to a 1-liter volumetric flask, add 3.4 mL of *Dilute phosphoric acid solution*, and add water to dissolve the mixture. Dilute with water to volume, and mix.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile and *Tetraethylammonium chloride solution* (52:48). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

Standard preparation—Dissolve a suitable quantity of USP Pralidoxime Chloride RS, accurately weighed, in water to obtain a *Standard solution* having a known concentration of about 1.25 mg per mL. (Reserve a portion of the *Standard solution* for the *System suitability preparation*.) Pipet 2.0 mL of this solution into a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Assay preparation—Transfer about 62.5 mg of Pralidoxime Chloride, accurately weighed, to a 50-mL volumetric flask, dissolve in water, dilute with water to volume, mix, and filter. Pipet 2.0 mL of this solution into a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

System suitability preparation—Prepare a solution of pyridine-2-aldoxime in water having a concentration of 0.65 mg per mL. Transfer 2.0 mL of this solution to a 100-mL volumetric flask, add 2.0 mL of the *Standard solution*, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* (621))—The liquid chromatograph is equipped with a 270-nm detector and a 3- to 5-mm \times 25-cm column containing 5- μ m packing L1. The flow rate is about 1.2 mL per minute. Chromatograph the *Standard preparation* and the *System suitability preparation* by injecting about 15 μ L of these preparations, and record the peak responses as directed for *Procedure*: the resolution, *R*, between the pyridine-2-aldoxime and pralidoxime chloride peaks is not less than 4.0; the column efficiency determined from the analyte peak is not less than 4000 theoretical plates; the tailing factor for the analyte peak is not more than 2.5; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 15 μ L) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.6 for pyridine-2-aldoxime and 1.0 for pralidoxime chloride. Calculate the quantity, in mg, of $C_7H_9ClN_2O$ in the portion of Pralidoxime Chloride taken by the formula:

$$2.5C(r_u / r_s)$$

in which *C* is the concentration, in μ g per mL, of USP Pralidoxime Chloride RS in the *Standard preparation*; and *r_u* and *r_s* are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Pralidoxime Chloride for Injection

» Pralidoxime Chloride for Injection contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of pralidoxime chloride ($C_7H_9ClN_2O$).

Packaging and storage—Preserve in *Containers for Sterile Solids* as described under *Injections* (1).

USP Reference standards (11)—

USP Endotoxin RS

USP Pralidoxime Chloride RS

Identification—

A: *Infrared Absorption* (197M).

B: A solution (1 in 10) meets the requirements of the tests for *Chloride* (191).

C: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Completeness of solution (641)—The contents of 1 container dissolve in 10 mL of water to yield a clear solution.

Constituted solution—At the time of use, it meets the requirements for *Constituted Solutions* under *Injections* (1).

Bacterial endotoxins (85)—It contains not more than 0.10 USP Endotoxin Unit per mg of pralidoxime chloride.

pH (791): between 3.5 and 4.5, in a solution (1 in 20).

Other requirements—It meets the requirements for *Loss on drying* and *Heavy metals* under *Pralidoxime Chloride*. It also meets the requirements for *Sterility Tests* (71), *Uniformity of Dosage Units* (905), and *Labeling* under *Injections* (1).

Assay—

Dilute phosphoric acid solution, Tetraethylammonium chloride solution, Mobile phase, Standard preparation, System suitability preparation, and Chromatographic system—Proceed as directed in the *Assay* under *Pralidoxime Chloride*.

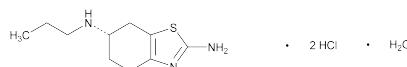
Assay preparation—Select an accurately counted number of containers of Pralidoxime Chloride for Injection, the combined contents of which are equivalent to about 10 g of pralidoxime chloride. Dissolve the contents of each container in water, and combine all of the solutions in a 1000-mL volumetric flask. Rinse each container with water, and add the rinsings to the volumetric flask. Dilute with water to volume, and mix. Transfer 25.0 mL of the resulting solution to a 200-mL volumetric flask, dilute with water to volume, and mix. Transfer 2.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Pralidoxime Chloride*. Calculate the quantity, in mg, of pralidoxime chloride ($C_7H_9ClN_2O$) in each container of Pralidoxime Chloride for Injection taken by the formula:

$$400(C/N)(r_U / r_S)$$

in which N is the number of containers selected for the *Assay preparation*, and the other terms are as defined therein.

Pramipexole Dihydrochloride



$C_{10}H_{17}N_3S \cdot 2HCl \cdot H_2O$ 302.26
Benzothiazole-2,6-diamine, 4,5,6,7-tetrahydro- N^6 -propyl-, dihydrochloride, monohydrate, (S)-; (S)-2-Amino-4,5,6,7-tetrahydro-6-(propylamino)benzothiazole dihydrochloride monohydrate [191217-81-9].

DEFINITION

Pramipexole Dihydrochloride contains NLT 98.0% and NMT 102.0% of $C_{10}H_{19}Cl_2N_3S$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** (197A) or (197M)
Wavelength range: (197A), 3800 cm^{-1} to 650 cm^{-1} ; (197M), 4000 cm^{-1} to 600 cm^{-1}
- **B.** The retention time of the major peak in the *Sample solution* corresponds to that of pramipexole (*S*-enantiomer) in the *System suitability solution* in the test for *Enantiomeric Purity*.
- **C. IDENTIFICATION TESTS—GENERAL, Chloride** (191)
Sample: 1 mg/mL of Pramipexole Dihydrochloride in water
Acceptance criteria: Meets the requirements of the silver nitrate precipitate test

ASSAY

• PROCEDURE

Solution A: Dissolve 9.1 g of potassium dihydrogen phosphate and 5.0 g of sodium 1-octanesulfonate monohydrate in 1 L of water. Adjust with phosphoric acid to a pH of 3.0.

Solution B: Acetonitrile and *Solution A* (1:1)

Diluent: Acetonitrile and *Solution A* (1:4)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
15	20	80
15.1	60	40
20	60	40

System suitability solution: 1.5 mg/mL of USP Pramipexole Dihydrochloride RS and 0.8 mg/mL of USP Pramipexole Related Compound A RS in *Diluent*

Standard solution: 1.5 mg/mL of USP Pramipexole Dihydrochloride RS in *Diluent*

Sample solution: 1.5 mg/mL of Pramipexole Dihydrochloride in *Diluent*

Chromatographic system

(See *Chromatography* (621), *System Suitability*.)

Mode: LC

Detector: UV 264 nm

Column: 4.6-mm \times 15-cm; 5- μm packing L1

Column temperature: $40 \pm 5^\circ$

Flow rate: 1.5 mL/min

Injection volume: 5 μL

System suitability

Samples: *System suitability solution* and *Standard solution*

[**NOTE**—The relative retention times for pramipexole related compound A and pramipexole are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6.0 between pramipexole related compound A and pramipexole, *System suitability solution*

Tailing factor: NMT 2.0 for pramipexole, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{10}H_{19}Cl_2N_3S$ in the portion of Pramipexole Dihydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Pramipexole Dihydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of the *Sample solution* (mg/mL)

M_{r1} = molecular weight of pramipexole dihydrochloride, 284.26

M_{r2} = molecular weight of pramipexole dihydrochloride monohydrate, 302.26

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **RESIDUE ON IGNITION** (281): NMT 0.10%

- **HEAVY METALS, Method I** (231)

Standard solution: Standard Lead Solution, 10 ppm

Sample solution: Ash 2 g of Pramipexole Dihydrochloride until an almost dry, carbonized mass is obtained. Cool the residue, add 2.0 mL of concentrated nitric acid