Pyridostigmine Bromide Tablets

DEFINITION
Pyridostigmine Bromide Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of pyridostigmine bromide ($C_9H_{13}BrN_2O_2$).

IDENTIFICATION
- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B. IDENTIFICATION TESTS—GENERAL ⟨191⟩,** *Chemical Identification Tests, Bromide*
  Sample solution: Shake a quantity of finely powdered Tablets, equivalent to 100 mg of pyridostigmine bromide, with 20 mL of water for 5 min, and filter the mixture. Use the filtrate.
  Acceptance criteria: Meet the requirements

ASSAY
- **PROCEDURE**
  Mobile phase: Dissolve 1 g of sodium 1-heptanesulfonate in 500 mL of water in a 1000-mL volumetric flask, and add 5.0 mL of triethylamine and 100 mL of acetonitrile. Dilute with water to volume, and mix. Adjust with phosphoric acid to a pH of 3.0.
  Diluent: Mix 11.2 g of phosphoric acid with 500 mL of water, and adjust with a 50% sodium hydroxide solution to a pH of 7.0. Dilute with water to 1000 mL.
  Standard solution: 0.25 mg/mL of USP Pyridostigmine Bromide RS in *Diluent*
  Sample solution: Nominally 0.25 mg/mL of pyridostigmine bromide prepared as follows. Finely powder NLT 20 Tablets and transfer a portion of the powder, equivalent to about 50 mg of pyridostigmine bromide, to a suitable volumetric flask. Add about 50% of the flask volume of *Diluent,* and shake for 30 min. Dilute with *Diluent* to volume, mix, and centrifuge. Use the supernatant.
  Chromatographic system
  (See *Chromatography ⟨621⟩, System Suitability*.)
  Mode: LC
  Detector: UV 270 nm
  Column: 4-mm × 30-cm; packing L1
  Flow rate: 2 mL/min
  Injection volume: 20 µL
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Tailing factor: NMT 1.5
  Relative standard deviation: NMT 1.0%
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of pyridostigmine bromide ($C_9H_{13}BrN_2O_2$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Pyridostigmine Bromide RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of pyridostigmine bromide in the *Sample solution* (mg/mL)

  Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS
- **DISSOLUTION ⟨711⟩**
  Medium: Water; 900 mL
  Apparatus 2: 50 rpm
  Time: 60 min
  Standard solution: USP Pyridostigmine Bromide RS in *Medium* at a known concentration approximately the same as that of the *Sample solution*
  Sample solution: Dilute with *Medium* and filter to obtain a concentration that is similar to that of the *Standard solution*.
  Instrumental conditions
  Mode: UV
  Analytical wavelength: 270 nm
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of pyridostigmine bromide ($C_9H_{13}BrN_2O_2$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Pyridostigmine Bromide RS in the *Standard solution* (mg/mL)
V = volume of *Medium*, 900 mL
L = label claim of pyridostigmine bromide (mg/Tablet)

  Tolerances: NLT 80% (Q) of the labeled amount of pyridostigmine bromide ($C_9H_{13}BrN_2O_2$) is dissolved.
- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**
  Solution A: 4.3 g/L of sodium dodecyl sulfate in water. Adjust with phosphoric acid to a pH of 2.0.
  Mobile phase: Acetonitrile and *Solution A* (30:70)
  System suitability solution: 5 µg/mL each of USP Pyridostigmine Bromide RS and USP Pyridostigmine Related Compound A RS in *Mobile phase*
  Sensitivity solution: 0.4 µg/mL of USP Pyridostigmine Bromide RS in *Mobile phase*
  Standard solution 1: 0.005 mg/mL of USP Pyridostigmine Bromide RS in *Mobile phase*
  Standard solution 2: 0.06 mg/mL of USP Pyridostigmine Bromide RS in *Mobile phase*
  Sample solution: Nominally 1 mg/mL of pyridostigmine bromide prepared as follows. Transfer a portion of powdered Tablets equivalent to 100 mg of pyridostigmine bromide to a suitable volumetric flask with 100 mL of *Mobile phase*. Shake for 30 min, and pass a portion of the solution through a glass fiber filter.
  Chromatographic system
  (See *Chromatography ⟨621⟩, System Suitability*.)
  Mode: LC
  Detector: UV 220 nm
  Column: 4.6-mm × 25-cm; 5-µm packing L1
  Flow rate: 1.1 mL/min
  Injection volume: 20 µL
  Run time: •NLT• (IRA 1-Nov-2017) 2 times the retention time of pyridostigmine
  System suitability
  Samples: *System suitability solution*, *Sensitivity solution*, and *Standard solution 1*

[NOTE—See *Table 1* for the relative retention times.]

System suitability requirements

Resolution: NLT 1.5 between pyridostigmine and pyridostigmine related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution 1*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution 1*, *Standard solution 2*, and *Sample solution*

Calculate the percentage of pyridostigmine related compound A and any individual unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of ● pyridostigmine related compound A or any individual unspecified degradation product ● (IRA 1-Nov-2017) from the *Sample solution*

r_S = peak response of pyridostigmine from *Standard solution 1*

C_S = concentration of USP Pyridostigmine Bromide RS in *Standard solution 1* (mg/mL)

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

Calculate the percentage of pyridostigmine related compound B in the portion of Tablets taken:

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

r_U = peak response of pyridostigmine related compound B from the *Sample solution*

r_S = peak response of pyridostigmine from *Standard solution 2*

C_S = concentration of USP Pyridostigmine Bromide RS in *Standard solution 2* (mg/mL)

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

Acceptance criteria: See *Table 1*. Disregard any peak below 0.04%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Pyridostigmine related compound B[a]	0.75	●0.2● (IRA 1-Nov-2017)
Pyridostigmine related compound A	0.92	●0.2● (IRA 1-Nov-2017)
Pyridostigmine	1.0	—
Any individual unspecified degradation product	—	0.2
Total ●● (IRA 1-Nov-2017) degradation products	—	●0.5● (IRA 1-Nov-2017)

[a] 3-Hydroxy-1-methylpyridin-1-ium bromide.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Pyridostigmine Bromide RS
  USP Pyridostigmine Related Compound A RS
  Pyridin-3-yl dimethylcarbamate.
  $C_8H_{10}N_2O_2$ 166.18