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Pantoprazole Sodium Delayed-Release Tablets

DEFINITION

Pantoprazole Sodium Delayed-Release Tablets contain an amount of Pantoprazole Sodium equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$).

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.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Dilute ammonium hydroxide: Ammonium hydroxide and water (50:50)

Buffer: 3.85 g/L of ammonium acetate and 1.1 g/L of tetrabutylammonium hydrogen sulfate in water. Adjust with *Dilute ammonium hydroxide* to a pH of 7.9.

Mobile phase: Acetonitrile and *Buffer* (35:65)

Diluent: Acetonitrile and 0.02 N sodium hydroxide (50:50)

System suitability solution: 0.2 mg/mL of USP Pantoprazole Sodium RS and 0.0004 mg/mL each of USP Pantoprazole Related Compound A RS and USP Pantoprazole Related Compound B RS in 0.02 N sodium hydroxide. Sonicate to dissolve, if necessary.

Standard solution: 0.2 mg/mL of USP Pantoprazole Sodium RS prepared as follows. Transfer a suitable amount of USP Pantoprazole Sodium RS to a suitable volumetric flask, add 0.02 N sodium hydroxide to about 60% of the final volume and sonicate for about 5 min to dissolve. To this solution add about 2% of the final volume of acetonitrile, and dilute with 0.02 N sodium hydroxide to volume.

Sample solution: Nominally 0.2 mg/mL of pantoprazole from Tablets prepared as follows. Transfer 5 Tablets to a suitable volumetric flask. [Note—Use 50- or 100-mL volumetric flasks for Tablets containing 20 or 40 mg of pantoprazole per Tablet, respectively.] Add *Diluent* to about 60% of the final volume, shake mechanically for about 60 min, and dilute with *Diluent* to volume. Pass through a suitable filter, and dilute the filtrate with 0.02 N sodium hydroxide to obtain a solution having a known concentration of about 0.2 mg/mL, based on the label claim.

Chromatographic system

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

Mode: LC

Detector: UV 290 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 3 times the retention time of pantoprazole

System suitability

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

Suitability requirements

Resolution: NLT 3 between pantoprazole and pantoprazole related compound A, *System suitability solution*

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

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) in the portion of Tablets taken:

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

r_U = peak response of pantoprazole from the *Sample solution*

r_S = peak response of pantoprazole from the *Standard solution*

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

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

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution ⟨711⟩**

Test 1: Proceed as directed for *Dissolution ⟨711⟩, Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure*.

Acid stage

Acid stage medium: 0.1 N hydrochloric acid; 1000 mL

Apparatus 2: 75 rpm

Time: 120 min

Mobile phase: Acetonitrile, triethylamine, and water (40:1:60). Adjust with phosphoric acid to a pH of 7.0 ± 0.05.

Diluent: pH 6.8 phosphate buffer and 0.5 N sodium hydroxide (50:50)

Standard stock solution: 0.4 mg/mL of USP Pantoprazole Sodium RS prepared as follows. Transfer about 20 mg of USP Pantoprazole Sodium RS to a 50-mL volumetric flask. Add about 30 mL of 0.02 N sodium hydroxide, and sonicate until dissolved. Add 2 mL of acetonitrile, and dilute with 0.02 N sodium hydroxide to volume.

Standard solution: 0.02 mg/mL of USP Pantoprazole Sodium RS from the *Standard stock solution* in *Diluent*

Sample solution: After 120 min pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, and immediately dilute a portion of the filtrate by a factor of 2 with 0.5 N sodium hydroxide. Transfer the Tablets to the vessels containing the *Buffer stage medium*.

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

Column: 4.6-mm × 7.5-cm; 3-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of pantoprazole

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved in the *Acid stage*:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times D \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_U = peak response of pantoprazole from the *Sample solution*

r_S = peak response of pantoprazole from the *Standard solution*

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

V = volume of *Acid stage medium*, 1000 mL

D = dilution factor for the *Sample solution*, 2

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

L = label claim (mg/Tablet)

Tolerances: NMT 10% of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 phosphate buffer; 1000 mL

Apparatus 2: 75 rpm

Time: 30 min

Standard solution: Prepared as directed in the *Acid stage*.

Sample solution: After 30 min, pass a portion of the sample solution under test through a suitable filter of 0.45-µm pore size and immediately dilute a portion of the filtrate by a factor of 2 with 0.5 N sodium hydroxide.

Chromatographic system: Proceed as directed in the *Acid stage*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times D \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_U = peak response of pantoprazole from the *Sample solution*

r_S = peak response of pantoprazole from the *Standard solution*

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

V = volume of *Buffer stage medium*, 1000 mL

D = dilution factor for the *Sample solution*, 2

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*. Proceed as directed for *Dissolution ⟨711⟩, Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure*.

Acid stage

Acid stage medium: 0.1 N hydrochloric acid; 1000 mL

Apparatus 2: 100 rpm

Time: 2 h

Standard stock solution: 0.46 mg/mL of USP Pantoprazole Sodium RS prepared as follows. Transfer a quantity of USP Pantoprazole Sodium RS to a suitable volumetric flask. Dissolve first in 0.1 N sodium hydroxide, using 10% of the final volume, then dilute with pH 6.8 phosphate buffer to volume. Mix well until a clear solution is obtained.

Acid stage standard solution: ▲(L/10000)▲ (ERR 1-Dec-2023) mg/mL of USP Pantoprazole Sodium RS from the *Standard stock solution* in *Acid stage medium*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 10-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: UV 305 nm

Path length: 4 cm

Blank: *Acid stage medium*

Analysis

Samples: *Acid stage standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved in the *Acid stage*:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Acid stage standard solution*

C_S = concentration of USP Pantoprazole Sodium RS in the *Acid stage standard solution* (mg/mL)

V = volume of *Acid stage medium*, 1000 mL

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

L = label claim (mg/Tablet)

Tolerances: NMT 10% of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 phosphate buffer; 1000 mL

Apparatus 2: 100 rpm

Time: 45 min

Standard stock solution: Prepare as directed in the *Acid stage*.

Buffer stage standard solution: (L/1000) ▲mg/mL▲ (ERR 1-Dec-2023) of USP Pantoprazole Sodium RS▲ from the *Standard stock solution* in *Buffer stage medium*,▲ (ERR 1-Dec-2023) where L is the label claim in mg/Tablet

Sample solution: After 2 h in *Acid stage medium*, continue with *Buffer stage medium* as follows. Completely drain the vessel of *Acid stage medium* carefully and add *Buffer stage medium*. After 45 min, pass a portion of the solution under test through a suitable filter of 10-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: UV 288 nm

Path length: 0.5 cm

Blank: *Buffer stage medium*

Analysis

Samples: *Buffer stage standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Buffer stage standard solution*

C_S = concentration of USP Pantoprazole Sodium RS in the *Buffer stage standard solution* (mg/mL)

V = volume of the *Buffer stage medium*, 1000 mL

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that the product meets *USP Dissolution Test 3*. Proceed as directed for *Dissolution ⟨711⟩, Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure*.

Acid stage

Acid stage medium: 0.1 N hydrochloric acid; 1000 mL

Apparatus 2: 100 rpm

Time: 2 h

Dilute ammonia solution: Transfer 40 mL of strong ammonia solution to a 100-mL volumetric flask, and dilute with water to volume.

Buffer: 1.5 g/L of ammonium acetate in water. Adjust with *Dilute ammonia solution* to a pH of 7.0.

Mobile phase: Methanol and *Buffer* (40:60)

Acid stage standard solution: 0.4 mg/mL of USP Pantoprazole Sodium RS prepared as follows. Transfer a suitable quantity of USP Pantoprazole Sodium RS to a suitable volumetric flask, add 10% of the final volume of methanol, sonicate, and dilute with *Mobile phase* to volume.

Sample solution: 0.4 mg/mL of pantoprazole prepared as follows. After 2 h in the *Acid stage medium*, completely drain the vessel of *Acid stage medium* carefully, remove the Tablet from the vessel, and dry it with tissue paper. Transfer the Tablet to a suitable volumetric flask, add 20% of the final volume of methanol, and sonicate for about 20 min. Dilute with *Mobile phase* to volume. Mix well, centrifuge, and use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Autosampler temperature: 4°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Acid stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Acid stage standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved in the *Acid stage*:

$$\text{Result} = A - [(r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times (1/L) \times 100]$$

A = percentage of pantoprazole as determined in the *Assay*

r_U = peak response of pantoprazole from the *Sample solution*

r_S = peak response of pantoprazole from the *Acid stage standard solution*

C_S = concentration of USP Pantoprazole Sodium RS in the *Acid stage standard solution* (mg/mL)

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

L = label claim (mg/Tablet)

Tolerances: NMT 10% of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 phosphate buffer; 1000 mL

Apparatus 2: 100 rpm

Time: 45 min

Buffer stage standard solution: (L/1000) mg/mL of USP Pantoprazole Sodium RS from the *Acid stage standard solution* in *Buffer stage medium*, where L is the label claim in mg/Tablet

Sample solution: Proceed as directed in the *Acid stage* with a new set of Tablets. After 2 h, proceed with *Buffer stage medium* as follows. Completely drain the vessel of *Acid stage medium* carefully and add the *Buffer stage medium*. After 45 min, withdraw 10 mL of the solution under test, and pass it through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Autosampler temperature: 4°

Flow rate: 1 mL/min

Injection volume: 50 µL

Analysis

Samples: *Buffer stage standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_U = peak response of pantoprazole from the *Sample solution*

r_S = peak response of pantoprazole from the *Buffer stage standard solution*

C_S = concentration of USP Pantoprazole Sodium RS in the *Buffer stage standard solution* (mg/mL)

V = volume of *Buffer stage medium*, 1000 mL

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

Test 4: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 4*. Proceed as directed for *Dissolution ⟨711⟩, Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure*.

Acid stage

Acid stage medium: 0.1 N hydrochloric acid; 1000 mL, degassed

Apparatus 2: 100 rpm, with sinkers

Time: 2 h

Buffer

0.77 g/L of ammonium acetate in water. Adjust with acetic acid or ammonium hydroxide to a pH of 8.5 ± 0.1.

Solution A: Acetonitrile and *Buffer* (30:70)

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
6	100	0
17	27	73
18	100	0
22	100	0

Diluent: Acetonitrile and water and (30:70)

System suitability solution: 0.23 mg/mL of USP Pantoprazole Sodium RS and 6.8 µg/mL of USP Pantoprazole Related Compound A RS in *Diluent*

Acid stage standard solution: 0.23 mg/mL of USP Pantoprazole Sodium RS in *Diluent*

Sample solution: Nominally 0.2 mg/mL of pantoprazole prepared as follows. After 2 h in the *Acid stage medium*, carefully remove the Tablet from the vessel and transfer to a suitable volumetric flask. Add 50% of the final volume of *Diluent*, and sonicate for about 20 min, but NMT about 60 min, swirling the flask every few minutes. Dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

Column: 3.9-mm × 15-cm; 5-µm packing L1

Temperatures

Autosampler: 4°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Acid stage standard solution*

Suitability requirements

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

Relative standard deviation: NMT 2.0%, *Acid stage standard solution*

Analysis

Samples: *Acid stage standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved in the *Acid stage*:

$$\text{Result} = A - [(r_U/r_S) \times C_S \times (1/L) \times (M_{r1}/M_{r2}) \times 100]$$

A = percentage of pantoprazole as determined in the *Assay*

r_U = peak response of pantoprazole from the *Sample solution*

r_S = peak response of pantoprazole from the *Acid stage standard solution*

C_S = concentration of USP Pantoprazole Sodium RS in the *Acid stage standard solution* (mg/mL)

L = label claim (mg/Tablet)

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

Tolerances: NMT 10% (Q) of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

Buffer stage

Buffer stage medium: 76.0 g/L of tribasic sodium phosphate dodecahydrate in water. Add 250 mL of this solution to 750 mL of *Acid stage medium*, adjust with hydrochloric acid or sodium hydroxide to a pH of 6.80 ± 0.05; 1000 mL, degassed.

Apparatus 2: 100 rpm, with sinkers

Time: 45 min

Buffer stage standard stock solution: 1.6 mg/mL of USP Pantoprazole Sodium RS in methanol

Buffer stage standard solution: L/1000 mg/mL of USP Pantoprazole Sodium RS RS from the *Buffer stage standard stock solution* in *Buffer stage medium*, where L is the label claim in mg/Tablet

Sample solution: Transfer a Tablet with the sinker to the vessel containing *Acid stage medium*, and proceed as directed for the *Acid stage*. After 2 h, continue with *Buffer stage medium* as follows. Completely drain the *Acid stage medium* carefully and add the *Buffer stage medium*. After 45 min, withdraw 10 mL of the solution under test, and pass it through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: UV 289 nm

Blank: *Buffer stage medium*

Analysis

Samples: *Buffer stage standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Buffer stage standard solution*

C_S = concentration of USP Pantoprazole Sodium RS in the *Buffer stage standard solution* (mg/mL)

V = volume of *Buffer stage medium*, 1000 mL

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

Test 5: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 5*. Proceed as directed for *Dissolution ⟨711⟩, Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure*.

Acid stage

Acid stage medium: 0.1 N hydrochloric acid; 900 mL, degassed

Apparatus 1: 100 rpm

Time: 2 h

Buffer: 8.77 g/L of dibasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 8.0.

Diluent: Acetonitrile and 0.01 N sodium hydroxide (50:50)

Mobile phase: Acetonitrile and *Buffer* (35:65)

Acid stage standard solution: 0.22 mg/mL of USP Pantoprazole Sodium RS in *Diluent*

Acid stage sample solution: Nominally 0.2 mg/mL of pantoprazole prepared as follows. After 2 h in the *Acid stage medium*, drain and remove the Tablet from the basket and transfer to a suitable volumetric flask. Add 80% of the final volume of *Diluent* and swirl until the Tablet disintegrates completely. Sonicate for about 25 min, shaking the flask every few minutes. Dilute with *Diluent* to volume. Centrifuge an aliquot, then pass a portion of the supernatant through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

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

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of pantoprazole

System suitability

Sample: *Acid stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Acid stage standard solution* and *Acid stage sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved in the *Acid stage*:

$$\text{Result} = A - (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

A = percentage of pantoprazole as determined in the *Assay*

r_U = peak response of pantoprazole from the *Acid stage sample solution*

r_S = peak response of pantoprazole from the *Acid stage standard solution*

C_S = concentration of USP Pantoprazole Sodium RS in the *Acid stage standard solution* (mg/mL)

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

L = label claim (mg/Tablet)

Tolerances: NMT 10% of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 phosphate buffer; 900 mL, degassed

Apparatus 1: 100 rpm

Time: 45 min

Buffer and **Mobile phase:** Prepare as directed in the *Acid Stage*.

Buffer stage standard solution: (L/900) mg/mL of USP Pantoprazole Sodium RS from the *Acid stage standard solution* in *Buffer stage medium*, where L is the label claim in mg/Tablet. Immediately mix 5 mL of the solution with 1 mL of 0.1 N sodium hydroxide.

Buffer stage sample solution: After 2 h in the *Acid stage medium* continue with *Buffer stage medium* as follows. Completely drain the *Acid stage medium* carefully leaving the Tablet in the basket and add the *Buffer stage medium*. After 45 min, withdraw 10 mL of the solution under test, and pass it through a suitable filter of 0.45-µm pore size. Mix 5 mL of the test solution with 1 mL of 0.1 N sodium hydroxide.

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

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

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of pantoprazole

System suitability

Sample: *Buffer stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Buffer stage standard solution* and *Buffer stage sample solution*

Calculate the percentage of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_U = peak response of pantoprazole from the *Buffer stage sample solution*

r_S = peak response of pantoprazole from the *Buffer stage standard solution*

C_S = concentration of USP Pantoprazole Sodium RS in the *Buffer stage standard solution* (mg/mL)

V = volume of *Buffer stage medium*, 900 mL

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of pantoprazole ($C_{16}H_{15}F_2N_3O_4S$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Mobile phase, System suitability solution, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Diluted standard solution: 0.0004 mg/mL of USP Pantoprazole Sodium RS from *Standard solution* in 0.02 N sodium hydroxide

Sensitivity solution: 0.2 µg/mL of USP Pantoprazole Sodium RS from *Diluted standard solution* in 0.02 N sodium hydroxide

System suitability

Samples: *System suitability solution*, *Diluted standard solution*, and *Sensitivity solution*

[NOTE—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 3 between pantoprazole and pantoprazole related compound A, *System suitability solution*

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

Relative standard deviation: NMT 10.0%, *Diluted standard solution*

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

Analysis

Samples: *Diluted standard solution* and *Sample solution*

Calculate the percentage of any impurity in the portion of Tablets taken:

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

r_U = peak response of any impurity from the *Sample solution*

r_S = peak response of pantoprazole from the *Diluted standard solution*

C_S = concentration of USP Pantoprazole Sodium RS in the *Diluted standard solution* (mg/mL)

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

M_{r1} = molecular weight of pantoprazole, 383.37

M_{r2} = molecular weight of pantoprazole sodium, 405.35

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Pantoprazole	1.0	—
Pantoprazole related compounds D[a] and F[b]	1.2	0.5[c]
Pantoprazole related compound A	1.3	0.5
Pantoprazole related compound B	2.7	0.3
Any other individual impurity	—	0.2
Total impurities	—	1.0

[a] 5-Difluoromethoxy-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1-methyl-1*H*-benzimidazole.

[b] 6-Difluoromethoxy-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1-methyl-1*H*-benzimidazole.

[c] Impurities D and F are not fully resolved and should be integrated together.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.

• **LABELING:** Label Tablets to indicate that they must not be split, chewed, or crushed before administration. When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Pantoprazole Sodium RS

USP Pantoprazole Related Compound A RS

5-(Difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfonyl]-1*H*-benzimidazole.

$C_{16}H_{15}F_2N_3O_5S$ 399.37

USP Pantoprazole Related Compound B RS

5-(Difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylthio]-1*H*-benzimidazole.

$C_{16}H_{15}F_2N_3O_3S$ 367.37

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
PANTOPRAZOLE SODIUM DELAYED-RELEASE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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