Pantoprazole Sodium Delayed-Release Tablets

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Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 3 Expert Committee has revised the Pantoprazole Sodium Delayed-Release Tablets monograph. The purpose for the revision is to add *Dissolution Test 5* to accommodate FDA-approved drug products with different tolerances than the existing dissolution tests.

- *Dissolution Test 5* was validated using a Waters XTerra RP 18 brand of L1 packing column. The typical retention time for pantoprazole is about 2.5 min.

Existing references to reagents have been updated for consistency with the reagent entry names. For additional information about reagent cross-references, please see the related Compendial Notice.

The Pantoprazole Sodium Delayed-Release Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Andrea F. Carney, Scientific Liaison (301-816-8155 or afc@usp.org).

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

- The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **PROCEDURE**

Solution A: Dissolve 3.85 g of ammonium acetate and 1.1 g of tetrabutylammonium hydrogen sulfate in 1 L of water, and adjust with ammonium hydroxide solution diluted 1:1 with water to a pH of 7.9.

Diluent: Mixture of acetonitrile and 0.02 N sodium hydroxide (1:1)

Mobile phase: Prepare a mixture of acetonitrile and *Solution A* (35:65).

Standard solution: Transfer a weighed quantity of USP Pantoprazole Sodium RS to a suitable volumetric flask, add 0.02 N sodium hydroxide to about 60% of the final volume, sonicate for 5 min to dissolve, add about 2% of acetonitrile, and dilute with 0.02 N sodium hydroxide to volume to obtain a solution having a known concentration of about 0.2 mg/mL of pantoprazole sodium.

System suitability solution: Prepare a solution in 0.02 N sodium hydroxide, using sonication if necessary, containing about 0.2 mg/mL of pantoprazole sodium and about 0.0004 mg/mL each of USP Pantoprazole Related Compound A RS and USP Pantoprazole Related Compound B RS.

Sample solution: Transfer 5 Tablets into 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 of pantoprazole, based on the label claim.

Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 290 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection size: 20 µL

System suitability
Samples: *Standard solution* and *System suitability solution*
Suitability requirements
Resolution: NLT 3 between pantoprazole and pantoprazole related compound A, *System suitability solution*
Tailing factor: NMT 2.0, *System suitability solution*
Relative standard deviation: NMT 2.0% for replicate injections, *Standard solution*

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{16}H_{15}F_2N_3O_4S$ 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 from the *Sample solution*
r_S = peak response 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
Determine the amount of pantoprazole dissolved in the *Acid stage* using the following procedure.
Sample solution: After 120 min, withdraw an aliquot, pass 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*.
Diluent: Prepare a mixture of pH 6.8 phosphate buffer and 0.5 N sodium hydroxide (1:1).
Mobile phase: Acetonitrile, triethylamine, and water (40:1:60). Adjust with phosphoric acid to a pH of 7.0 ± 0.05.
Standard stock solution: 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: Transfer 1.0 mL of the *Standard stock solution* to a 20-mL volumetric flask, and dilute with *Diluent* to volume.
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 size: 10 µL
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 amount of pantoprazole released, as a percentage, in the *Acid stage*:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of pantoprazole sodium in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of pantoprazole, 383.37
M_{r2} = molecular weight of pantoprazole sodium, 405.35
V = volume of *Medium*, 1000 mL
L = Tablet label claim (mg)
D = dilution factor for the *Sample solution*, 2

Tolerances: NMT 10% of the labeled amount of pantoprazole is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 phosphate buffer; 1000 mL

Apparatus 2: 75 rpm

Time: 30 min

Analysis: After 30 min, withdraw an aliquot, pass 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. Determine the amount of pantoprazole dissolved in the *Buffer stage* using the same procedure as for the *Acid stage.*

Tolerances: NLT 75% (*Q*) of the labeled amount of pantoprazole 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: 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, to obtain a solution having a known concentration of about 0.46 mg of pantoprazole sodium per mL. Mix well until a clear solution is obtained. Calculate the concentration in mg of pantoprazole per mL, the molecular weights of pantoprazole and pantoprazole sodium being 383.37 and 405.35, respectively.

Acid stage standard solution: Dilute an appropriate volume of the *Standard stock solution* to 1 L with *Acid stage medium* in such a way as to obtain a final concentration of about 10% of the Tablet label claim per L.

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

Analysis:

Determine the amount of pantoprazole dissolved by using UV absorption at the wavelength of about 305 nm on portions of the *Sample solution* in comparison to the *Acid stage working standard solution* using a 4-cm path length cell and *Acid stage medium* as blank. Drain the *Acid stage medium* from each vessel and replace with *Buffer stage medium*.

Calculate the amount of pantoprazole dissolved:

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

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of pantoprazole in the *Acid stage standard solution* (mg/mL)
V = volume of *Medium*, 1000 mL
L = Tablet label claim of pantoprazole (mg)

Tolerances: NMT 10% of the labeled amount of pantoprazole 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: Dilute an appropriate volume of the *Standard stock solution* as described under *Acid stage* to 250 mL with *Buffer stage medium* in such a way as to obtain a final concentration of about 100% of the Tablet label claim per L.

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

Analysis: Determine the amount of pantoprazole dissolved by using UV absorption at the wavelength of maximum absorbance at about 288 nm on portions of the *Sample solution* in comparison to *Buffer stage standard solution* using a 0.5-cm path length cell and *Buffer stage medium* as blank.

Calculate the amount of pantoprazole dissolved:

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

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Buffer stage standard solution*
C_S = concentration of pantoprazole in the *Buffer stage standard solution* (mg/mL)
V = volume of the *Buffer stage medium*, 1000 mL
L = Tablet label claim (mg)

Tolerances: NLT 75% (*Q*) of the labeled amount of pantoprazole 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 solution: Transfer 1.5 g of ammonium acetate to a 1000-mL volumetric flask. Dissolve in and dilute with water to volume. Adjust the pH with *Dilute ammonia solution* to 7.0 ± 0.1.

Mobile phase: Methanol and *Buffer solution* (2:3)

Standard solution: 0.4 mg/mL. Transfer a 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: After 2 h in the *Acid stage medium,* decant the medium from the vessel, 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 to obtain a final concentration of about 0.4 mg/mL of pantoprazole. 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
Temperature
Column: Ambient
Autosampler: 4°
Flow rate: 1.5 mL/min
Injection size: 10 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 7500 theoretical plates
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the amount of pantoprazole released, as a percentage, in the *Acid stage*:

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

A = percentage of pantoprazole as determined in the *Assay*
r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of pantoprazole sodium in the *Standard solution* (mg/mL)
D_U = dilution factor of the *Sample solution*
M_{r1} = molecular weight of pantoprazole, 383.37
M_{r2} = molecular weight of pantoprazole sodium, 405.35
L = Tablet label claim (mg)

Tolerances: NMT 10% of the labeled amount of pantoprazole is dissolved.

Buffer stage
Buffer stage medium: pH 6.8 phosphate buffer; 1000 mL
Apparatus 2: 100 rpm
Time: 45 min
Standard solution: Further dilute an appropriate volume of the *Standard solution* prepared in the *Acid stage* with *Buffer stage medium* to obtain a solution having a known concentration of about 0.04 mg/mL.
Sample solution: Transfer a separate Tablet to the vessel containing *Acid stage medium*, and proceed as directed for the *Acid stage*. After 2 h, decant the *Acid stage medium*, add the *Buffer stage medium*, and operate the apparatus at the specified conditions. After 45 min, withdraw 10 mL of the solution under test, and pass it through a suitable filter of 0.45-µm pore size.
Analysis: Determine the amount of pantoprazole released to the *Buffer stage medium* using the same chromatographic procedure as directed for the *Acid stage*, with the exception of injecting about 50 µL of the *Standard solution* and *Sample solution*.
Calculate the amount of pantoprazole dissolved:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of pantoprazole sodium in the *Standard solution* (mg/mL)
M_{r1} = molecular weight of pantoprazole, 383.37
M_{r2} = molecular weight of pantoprazole sodium, 405.35
V = volume of *Medium*, 1000 mL
L = Tablet label claim (mg)

Tolerances: NLT 75% (Q) of the labeled amount of pantoprazole 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
Determine the amount of pantoprazole remaining in the Tablet, using the following procedure.
Diluent: Water and acetonitrile (7:3)
Buffer solution: 771 mg/L of ammonium acetate in water. Adjust with acetic acid or ammonium hydroxide to a pH of 8.5 ± 0.1.
Solution A: *Buffer solution* and acetonitrile (7:3)
Solution B: Acetonitrile
Mobile phase: See the gradient table below.

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

System suitability solution: Prepare a solution containing 0.0068 mg/mL of USP Pantoprazole Related Compound A in *Diluent*. Transfer 10 mL of this solution to a 100-mL volumetric flask, add 23 mg of USP Pantoprazole Sodium RS, and dilute with *Diluent* to volume.
Acid stage standard solution: 0.23 mg/mL of USP Pantoprazole Sodium RS in *Diluent*
Sample solution: 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 20 min (but not more than 60 min), swirling the flask every few min. Dilute with *Diluent* to volume to obtain a final concentration of about 0.2 mg/mL of pantoprazole.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 290 nm
Column: 3.9-mm × 15-cm; 5-µm packing L1
Temperature
Column: 30°
Autosampler: 4°
Flow rate: 1 mL/min
Injection size: 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*
Calculate the percentage of pantoprazole released:

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

A = percentage of pantoprazole as determined in the *Assay*
r_U = peak area from the *Sample solution*
r_S = peak area from the *Acid stage standard solution*
C_S = concentration of the *Acid stage standard solution* (mg/mL)
L = Tablet label claim (mg)
D_U = dilution factor of the *Sample solution*
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 is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 phosphate buffer (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 solution: 1.6 mg/mL of USP Pantoprazole Sodium RS in methanol. This solution is stable for 5 days at room temperature and 7 days when refrigerated. Dilute this solution with *Buffer stage medium* to obtain a concentration of L/1000 mg/mL, where L is the Tablet label claim in mg.
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, remove the *Acid stage medium*, add the *Buffer stage medium*, and operate the apparatus under the specified conditions. After 45 min, withdraw 10 mL of the solution under test, and pass it through a suitable filter of 0.45-µm pore size.
Analytical wavelength: UV 289 nm
Path length cell: 1 cm
Blank: *Buffer stage medium*
Calculate the percentage of pantoprazole released:

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

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Buffer stage standard solution*
C_S = concentration of the *Buffer stage standard solution* (mg/mL)
L = Tablet label claim (mg)
M_{r1} = molecular weight of pantoprazole, 383.37
M_{r2} = molecular weight of pantoprazole sodium, 405.35
V = volume of *Buffer stage medium*, 1000 mL

Tolerances: NLT 75% (Q) of the labeled amount of pantoprazole 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

Determine the amount of pantoprazole dissolved in the *Acid stage* using the following procedure.
Diluent: Acetonitrile and 0.01 N sodium hydroxide (50:50)
Buffer solution: 8.77g/L of dibasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 8.0.
Mobile phase: Acetonitrile and *Buffer solution* (35:65)
Acid stage standard solution: 0.22 mg/mL of USP Pantoprazole Sodium RS in *Diluent*
Acid stage sample solution: After 2 h in the *Acid stage medium*, drain and remove the Tablet from the basket. Transfer to a suitable volumetric flask. Add 80% of the final volume of *Diluent* and swirl until the Tablet disintegrates completely. Sonicate for 25 min, shaking the flask every few minutes. Dilute with *Diluent* to volume to obtain a final concentration of about 0.2 mg/mL of pantoprazole. 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 x 15-cm; 5-µm packing L1
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 *Acid stage sample solution*
Calculate the labeled amount of pantoprazole released, as percentage, in the *Acid stage*:

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

A = percentage of pantoprazole as determined in the *Assay*
r_U = peak area from the *Acid stage sample solution*
r_S = peak area from the *Acid stage standard solution*
C_S = concentration of USP Pantoprazole Sodium RS in the *Acid stage standard solution* (mg/mL)
D = dilution factor of the *Acid stage sample solution* (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 is dissolved.

Buffer stage

Buffer stage medium: pH 6.8 phosphate buffer (see *Buffer Solutions*); 900 mL, degassed
Apparatus 1: 100 rpm
Time: 45 min
Buffer stage standard solution: Dilute the *Acid stage standard solution* with *Buffer stage medium* to obtain a concentration equivalent to (L/900) mg/mL, where L is the label claim in milligrams. Immediately mix 5 mL of

the resultant solution with 1 mL of 0.1 N sodium hydroxide.

Buffer stage sample solution: After 2 h in the *Acid stage medium*, carefully drain the Tablet in the basket. Remove the *Acid stage medium*, add the *Buffer stage medium* and operate the apparatus under the specified conditions. 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.

Buffer, Mobile phase,and **Chromatographic system:** Proceed as directed in *Acid stage*, except for *Injection volume*.

Injection volume: 20 µL

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 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 the *Buffer stage sample solution*
r_S = peak response 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*, 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 is dissolved.▲ (RB 1-May-2019)

• **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩**:** Meet the requirements

IMPURITIES

ORGANIC IMPURITIES

• **PROCEDURE**

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

Standard solution: 0.0004 mg/mL. Dilute the *Standard solution*, prepared as directed in the *Assay*, with 0.02 N sodium hydroxide.

System suitability

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

Suitability requirements

[NOTE—Identify the components on the basis of the relative retention times shown in *Impurity Table 1*.]

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%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Record the chromatograms for at least three times the retention time of the pantoprazole peak.

Calculate the percentage of each 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 for each impurity from the *Sample solution*
r_S = peak response 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: The limits are given in *Impurity Table 1*. The reporting level for impurities is 0.1%.

Impurity Table 1

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

[a] 5-(Difluoromethoxy)-2-[(*RS*)-[(3,4-dimethoxypyridin-2-yl)methyl]sulfinyl]-1-methyl-1*H*-benzimidazole.
[b] 6-(Difluoromethoxy)-2-[(*RS*)-[(3,4-dimethoxypyridin-2-yl)methyl]sulfinyl]-1-methyl-1*H*-benzimidazole.
[c] Impurities D and F are not fully resolved and should be integrated together.
[d] 5-(Difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridyl)methyl]sulfonyl]-1*H*-benzimidazole.
[e] 5-(Difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridyl)methyl]thio]-1*H*-benzimidazole.

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 Related Compound A RS
5-(Difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl)methyl]sulfonyl]-1*H*-benzimidazole.
$C_{16}H_{15}F_2N_3O_5S$ 399.37

USP Pantoprazole Related Compound B RS
5-(Difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl)methyl]thio]-1*H*-benzimidazole.
$C_{16}H_{15}F_2N_3O_3S$ 367.37

USP Pantoprazole Sodium RS