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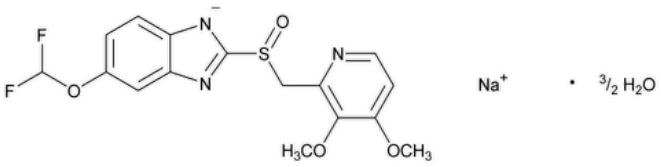
Pantoprazole Sodium

Change to read:



$C_{16}H_{14}F_2N_3NaO_4S \cdot$ ▲3/2▲ (USP 1-Dec-2023) H_2O 432.37

▲1*H*-Benzimidazole, 5-(difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl)methyl]sulfinyl]-,▲ (USP 1-Dec-2023) sodium salt, hydrate (2:3);

5-(Difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridyl)methyl]sulfinyl]benzimidazole, sodium salt, sesquihydrate CAS RN®: 164579-32-2; UNII: 6871619Q5X.

▲Anhydrous

$C_{16}H_{14}F_2N_3NaO_4S$ 405.35 CAS RN®: 138786-67-1; UNII: S9363155XL.

Pantoprazole (free acid)

$C_{16}H_{15}F_2N_3O_4S$ 383.37 CAS RN®: 102625-70-7; UNII: D8TST4O562.▲ (USP 1-Dec-2023)

DEFINITION

Pantoprazole Sodium contains NLT 98.0% and NMT 102.0% of pantoprazole sodium ($C_{16}H_{14}F_2N_3NaO_4S$), calculated on the anhydrous basis.

IDENTIFICATION

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K

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

Change to read:

• **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sodium*:** Meets the requirements ▲▲ (USP 1-Dec-2023)

ASSAY

Change to read:

• **Procedure**

[Note—Protect solutions containing pantoprazole sodium from light.]

Buffer: 1.32 g/L of dibasic ammonium phosphate in water, adjusted with phosphoric acid to a pH of 7.5

▲Solvent▲ (USP 1-Dec-2023) mixture: Acetonitrile and methanol ▲(70:30)▲ (USP 1-Dec-2023)

Solution A: ▲*Solvent*▲ (USP 1-Dec-2023) *mixture* and ▲*Buffer*▲ (USP 1-Dec-2023) (15:85)

Solution B: ▲*Solvent*▲ (USP 1-Dec-2023) *mixture*

Mobile phase: See *Table 1*. ▲▲ (USP 1-Dec-2023)

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	86	14
10	86	14

Time (min)	Solution A (%)	Solution B (%)
35	42	58
▲40	86	14
50	86	14

Diluent 1: Acetonitrile and water (50:50)▲ (USP 1-Dec-2023)

Diluent ▲2:▲ (USP 1-Dec-2023) Dilute 25 mL of ammonium hydroxide with water to 500 mL.

▲▲ (USP 1-Dec-2023)

Standard stock solution: 0.4 mg/mL of USP Pantoprazole Sodium RS ▲prepared as follows. Transfer a suitable amount of USP Pantoprazole Sodium RS to a suitable volumetric flask containing 10%–20% of the final volume of *Diluent 1*,▲ (USP 1-Dec-2023) and dilute with *Diluent* ▲*2*▲ (USP 1-Dec-2023) to volume.

Standard solution: 0.06 mg/mL of USP Pantoprazole Sodium RS from the *Standard stock solution* in *Diluent* ▲*2*▲ (USP 1-Dec-2023)

Sample stock solution: ▲0.4 mg/mL of Pantoprazole Sodium prepared as follows.▲ (USP 1-Dec-2023) Transfer about 20 mg of Pantoprazole Sodium to a 50-mL volumetric flask. Dissolve in ▲*Diluent 1* at 10%–20% of the final volume,▲ (USP 1-Dec-2023) and dilute with *Diluent* ▲*2*▲ (USP 1-Dec-2023) to volume.

Sample solution: 0.06 mg/mL of Pantoprazole Sodium from the *Sample stock solution* in *Diluent* ▲*2*▲ (USP 1-Dec-2023)

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1

Temperatures

Autosampler: 4°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: ▲▲ (USP 1-Dec-2023) *Standard solution*

▲▲ (USP 1-Dec-2023)

Suitability requirements

▲Tailing factor: NMT 2.0▲ (USP 1-Dec-2023)

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pantoprazole sodium ($C_{16}H_{14}F_2N_3NaO_4S$) in the portion of Pantoprazole Sodium taken:

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

r_U = peak response ▲of pantoprazole▲ (USP 1-Dec-2023) from the *Sample solution*

r_S = peak response ▲of pantoprazole▲ (USP 1-Dec-2023) from the *Standard solution*

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

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

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

IMPURITIES

Change to read:

• **Organic Impurities**

▲[Note—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 2* is recommended when impurities C, D, E, and F are potential related compounds.]▲ (USP 1-Dec-2023)

[Note—Protect solutions containing pantoprazole sodium from light.]

▲**Procedure**▲ (USP 1-Dec-2023) **1**

▲**Buffer,**▲ (USP 1-Dec-2023) **Mobile phase,** ▲**Diluent 1,**▲ (USP 1-Dec-2023) **Diluent** ▲**2,**▲ (USP 1-Dec-2023) **Standard stock solution, Sample stock solution,** and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.0004 mg/mL of USP Pantoprazole Sodium RS from the *Standard stock solution* in *Diluent* ▲*2*

Sensitivity solution: 0.2 µg/mL of USP Pantoprazole Sodium RS from the *Standard solution* in *Diluent 2*▲ (USP 1-Dec-2023)

Sample solution: *Sample stock solution*

System suitability

Samples: ▲▲ (USP 1-Dec-2023) *Standard solution* ▲and *Sensitivity solution*▲ (USP 1-Dec-2023)

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

Suitability requirements

▲▲ (USP 1-Dec-2023)

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

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-Dec-2023)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲any▲ (USP 1-Dec-2023) impurity in the portion of Pantoprazole Sodium taken:

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

r_U = peak response of ▲any▲ (USP 1-Dec-2023) impurity 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 = concentration of Pantoprazole Sodium in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. The reporting ▲threshold▲ (USP 1-Dec-2023) is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
▲▲ (USP 1-Dec-2023) Pantoprazole related compound A	0.52	0.20
Pantoprazole	1.0	—
▲▲ (USP 1-Dec-2023) Pantoprazole related compound B	1.7	0.15
Any ▲unspecified▲ (USP 1-Dec-2023) impurity	—	0.10
Total impurities	—	0.5

▲**Procedure**▲ (USP 1-Dec-2023) **2**

Solution A: 1.74 g/L of dibasic potassium phosphate ▲in water.▲ (USP 1-Dec-2023) Adjust with a solution of phosphoric acid (330 g/L) to a pH of ▲7.0.▲ (USP 1-Dec-2023)

Solution B: Acetonitrile

Mobile phase: See *Table 3*. ▲▲ (USP 1-Dec-2023)

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	80	20
40	20	80
▲45	80	20
55	80	20▲ (USP 1-Dec-2023)

Diluent: Acetonitrile and 0.001 N sodium hydroxide ▲(50:50)▲ (USP 1-Dec-2023)

System suitability solution: 0.46 mg/mL of USP Pantoprazole Sodium RS, and 1.3 µg/mL each of USP Pantoprazole Related Compound A RS, USP Pantoprazole Related Compound B RS, USP Pantoprazole Related Compound C RS, USP Pantoprazole Related Compounds D and F Mixture RS, and USP Pantoprazole Related Compound E RS in *Diluent*

Standard solution: 0.03 mg/mL of USP Pantoprazole Sodium RS in *Diluent*

▲**Sensitivity solution:** 0.2 µg/mL of USP Pantoprazole Sodium RS from the *Standard solution* in *Diluent*▲ (USP 1-Dec-2023)

Sample solution: 0.46 mg/mL of Pantoprazole Sodium in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 290 and 305 nm

Column: ▲4.0-mm▲ (USP 1-Dec-2023) × 12.5-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution*, *Standard solution* (at 290 nm), ▲and *Sensitivity solution* (at 290 nm)▲ (USP 1-Dec-2023)

[NOTE—See *Table 4* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between pantoprazole related compound E and pantoprazole related compounds D and F, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-Dec-2023)

Analysis

[NOTE—Pantoprazole related compound C is monitored at 305 nm, and all other compounds are monitored at 290 nm.]

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲any▲ (USP 1-Dec-2023) impurity in the portion of Pantoprazole Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of ▲any▲ (USP 1-Dec-2023) impurity from the *Sample solution*

r_S = peak response of pantoprazole ▲▲ (USP 1-Dec-2023) from the *Standard solution*

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

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

F = relative response factor (see *Table 4*)

Acceptance criteria: See *Table 4*. ▲▲ (USP 1-Dec-2023) The reporting ▲threshold▲ (USP 1-Dec-2023) is 0.05%.

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
▲▲ (USP 1-Dec-2023) Pantoprazole related compound C	0.6	3.3	0.10[a]
▲▲ (USP 1-Dec-2023) Pantoprazole related compound A	0.9	1.0	0.20
Pantoprazole	1.0	—	—
▲▲ (USP 1-Dec-2023) Pantoprazole related compound D and ▲▲ (USP 1-Dec-2023) pantoprazole related compound F	1.2	1.0	0.20[b]
▲▲ (USP 1-Dec-2023) Pantoprazole related compound E	1.3	1.0	0.10
▲▲ (USP 1-Dec-2023) Pantoprazole related compound B	1.5	1.0	0.15
Any ▲unspecified▲ (USP 1-Dec-2023) impurity	—	—	0.10
Total impurities	—	—	0.5

[a] At 305 nm.

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

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** 4.5%–8.0%

Add the following:

▲• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states that Pantoprazole Sodium must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins are such that the requirement under the relevant dosage form monograph(s) in which Pantoprazole Sodium is used can be met.▲ (USP 1-Dec-2023)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers. Store at room temperature.

Change to read:

• **Labeling:** If a test for *Organic Impurities* other than ▲*Procedure*▲ (USP 1-Dec-2023) *1* is used, then the labeling states the test with which the article complies. ▲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 1-Dec-2023)

Change to read:

• **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.▲ (USP 1-Dec-2023)

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

USP Pantoprazole Related Compound B RS

▲5-(Difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylthio]-1*H*-benzimidazole.▲ (USP 1-Dec-2023)

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

USP Pantoprazole Related Compound C RS

5-(Difluoromethoxy)-1*H*-benzimidazole-2-thiol.

$C_8H_6F_2N_2OS$ 216.21

USP Pantoprazole Related Compounds D and F Mixture RS

Contains a mixture of the following two compounds:
5-(Difluoromethoxy)-2-[(*RS*)-[(3,4-dimethoxypyridin-2-yl)methyl]sulfinyl]-1-methyl-1*H*-benzimidazole;
6-(Difluoromethoxy)-2-[(*RS*)-[(3,4-dimethoxypyridin-2-yl)methyl]sulfinyl]-1-methyl-1*H*-benzimidazole.

$C_{17}H_{17}F_2N_3O_4S$ 397.40

USP Pantoprazole Related Compound E RS

6,6'-Bis(difluoromethoxy)-2,2'-bis[[(3,4-dimethoxypyridin-2-yl)methyl]sulfinyl]-1*H*,1'*H*-5,5'-bibenzimidazole.

$C_{32}H_{28}F_4N_6O_8S_2$ 764.72

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

Topic/Question	Contact	Expert Committee
PANTOPRAZOLE SODIUM	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 48(2)

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