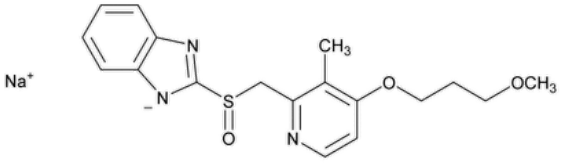
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Nov-2020
Document Type: USP Monographs
DocId: GUID-365B86E9-E171-41A2-BBFA-4F1740A06350_3_en-US
DOI: https://doi.org/10.31003/USPNF_M1421_03_01
DOI Ref: g3n7v

Rabeprazole Sodium



$C_{18}H_{20}N_3NaO_3S$ (anhydrous) 381.42
$C_{18}H_{20}N_3NaO_3S \cdot xH_2O$ (hydrated form)
1*H*-Benzimidazole, 2-({[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]methyl}sulfinyl)-, sodium salt;
2-({[4-(3-Methoxypropoxy)-3-methylpyridin-2-yl]methyl}sulfinyl)benzimidazole sodium salt CAS RN®: 117976-90-6; UNII: 3L36P16U4R.

DEFINITION

Rabeprazole Sodium contains NLT 98.0% and NMT 102.0% of rabeprazole sodium ($C_{18}H_{20}N_3NaO_3S$), calculated on the dried basis. The hydrated form contains NLT 98.0% and NMT 102.0% of rabeprazole sodium ($C_{18}H_{20}N_3NaO_3S$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

▲[Note—If the spectra obtained in the solid state shows differences, dissolve the substance to be examined and the reference substance separately in methanol, evaporate to dryness, and record new spectra using the residues.]▲ (USP 1-Aug-2020)

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

• **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sodium*:** Meets the requirements

ASSAY

Change to read:

• **Procedure**

[Note—Protect solutions containing rabeprazole from light.]

Buffer 1: 4.35 g/L of dibasic potassium phosphate▲ in water.▲ (USP 1-Aug-2020) Adjust with phosphoric acid to a pH of 7.0.

Buffer 2: Dissolve 17.4 g of dibasic potassium phosphate in 950 mL of water, adjust ▲with 2 N▲ (USP 1-Aug-2020) potassium hydroxide to a pH of 11.3, and dilute with water to 1000 mL. Pass through a suitable filter of 0.45-µm pore size.

Solution A: Acetonitrile and *Buffer 1* (5:95)

Solution B: Methanol

Solution C: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
0	100	0	0
2	100	0	0
7	85	0	15

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
27	30	40	30
32	15	55	30

Return to original conditions and re-equilibrate the system for 10 min.

Diluent: Methanol and *Buffer 2* (20:80)

Standard solution: 0.1 mg/mL of USP Rabeprazole Sodium RS in *Diluent*

Sample solution: 0.1 mg/mL of Rabeprazole Sodium in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

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

Temperatures

Autosampler: 6°

Column: 45°

Flow rate: 1 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of rabeprazole sodium ($C_{18}H_{20}N_3NaO_3S$) in the portion of Rabeprazole Sodium 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 Rabeprazole Sodium RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the dried basis for the anhydrous form or on the anhydrous basis for the hydrated form

IMPURITIES

Change to read:

• **Organic Impurities**

[Note—Protect solutions containing rabeprazole from light.]

Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 1.0 mg/mL of USP Rabeprazole Sodium RS and 0.002 mg/mL each of USP Rabeprazole Related Compound A RS, USP Rabeprazole Related Compound B RS, USP Rabeprazole Related Compound C RS, USP Rabeprazole Related Compound D RS, USP Rabeprazole Related Compound E RS, and USP Rabeprazole Related Compound F RS in *Diluent*

Sensitivity solution: 0.5 µg/mL of USP Rabeprazole Sodium RS in *Diluent*

Standard solution: 0.001 mg/mL of USP Rabeprazole Sodium RS in *Diluent*

Sample solution: 1.0 mg/mL of Rabeprazole Sodium in *Diluent*

System suitability

Samples: *System suitability solution*, *Sensitivity solution*, and *Standard solution* ▲▲ (USP 1-Aug-2020)

Suitability requirements

Peak-to-valley ratio: NLT 1.5 for rabeprazole related compound F and rabeprazole, *System suitability solution*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Rabeprazole Sodium taken:

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

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

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

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

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

Acceptance criteria: See *Table 2*. ▲The reporting threshold is▲ (USP 1-Aug-2020) 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
▲Rabeprazole related compound A▲ (USP 1-Aug-2020)	0.32	0.15
Benzimidazolol[a]	0.47	0.10
▲Rabeprazole related compound C▲ (USP 1-Aug-2020)	0.50	0.10
Rabeprazole sulfone *N*-oxide[b]	0.74	0.10
▲Rabeprazole related compound B▲ (USP 1-Aug-2020)	0.76	0.15
Methoxy analog[c]	0.82	0.15
▲Rabeprazole related compound D▲ (USP 1-Aug-2020)	0.90	0.8
▲Rabeprazole related compound F▲ (USP 1-Aug-2020)	0.98	0.10
Rabeprazole	1.0	—
Methoxy sulfide analog[d]	1.04	0.10
▲Rabeprazole related compound E▲ (USP 1-Aug-2020)	1.24	0.15
Any ▲unspecified▲ (USP 1-Aug-2020) impurity	—	0.10

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Total impurities	—	1.0

[a] 1*H*-Benzimidazol-2-ol.

[b] 2-{[(1*H*-Benzimidazol-2-yl)sulfonyl]methyl}-4-(3-methoxypropoxy)-3-methylpyridine 1-oxide.

[c] 2-{[(4-Methoxy-3-methylpyridin-2-yl)methyl]sulfinyl}benzimidazole.

[d] 2-{[(4-Methoxy-3-methylpyridin-2-yl)methyl]thio}benzimidazole.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

[Note—Perform this test for the anhydrous form.]

Analysis: Dry under vacuum over phosphorus pentoxide for 24 h.

Acceptance criteria: NMT 1.0%

• **Water Determination** ⟨921⟩, *Method I*

[Note—Perform this test where it is labeled as a hydrated form.]

[Note—Hydranal Composite 5 is a suitable titrant.]

Sample: 0.2 g

Acceptance criteria: NMT 7.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at room temperature.

• **Labeling:** Where it is the hydrated form, the label so indicates.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Rabeprazole Sodium RS

USP Rabeprazole Related Compound A RS

▲[Note—May be available as monosodium or disodium salt.]▲ (USP 1-Aug-2020)

Sodium 1-(1*H*-benzimidazol-2-yl)-3-methyl-4-oxo-1,4-dihydropyridine-2-carboxylate.
$C_{14}H_{10}N_3NaO_3$ 291.24

▲Disodium 1-(1*H*-benzimidazol-2-yl)-3-methyl-4-oxo-1,4-dihydropyridine-2-carboxylate. $C_{14}H_9N_3Na_2O_3$ 313.22▲ (USP 1-Aug-2020)

USP Rabeprazole Related Compound B RS

2-{[(1*H*-Benzimidazol-2-yl)sulfinyl]methyl}-4-(3-methoxypropoxy)-3-methylpyridine 1-oxide.
$C_{18}H_{21}N_3O_4S$ 375.44

USP Rabeprazole Related Compound C RS

1*H*-Benzimidazole-2-thiol.
$C_7H_6N_2S$ 150.20

USP Rabeprazole Related Compound D RS

2-({[4-(3-Methoxypropoxy)-3-methyl-2-pyridyl]methyl}sulfonyl)benzimidazole.
$C_{18}H_{21}N_3O_4S$ 375.44

USP Rabeprazole Related Compound E RS

2-{[4-(3-Methoxypropoxy)-3-methyl-2-pyridyl]methylthio}benzimidazole.
$C_{18}H_{21}N_3O_2S$ 343.44

USP Rabeprazole Related Compound F RS

2-{[(4-Chloro-3-methyl-2-pyridyl)methyl]sulfinyl}benzimidazole.
$C_{14}H_{12}ClN_3OS$ 305.78

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(3)

Current DocID: GUID-365B86E9-E171-41A2-BBFA-4F1740A06350_3_en-US

DOI: https://doi.org/10.31003/USPNF_M1421_03_01

DOI ref: g3n7v