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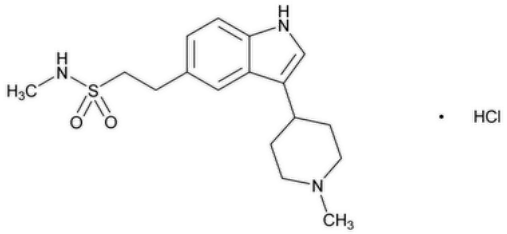
Naratriptan Hydrochloride



$C_{17}H_{25}N_3O_2S \cdot HCl$ 371.93

1*H*-Indole-5-ethanesulfonamide, *N*-methyl-3-(1-methyl-4-piperidinyl)-, monohydrochloride;

N-Methyl-3-(1-methyl-4-piperidyl)indole-5-ethanesulfonamide monohydrochloride CAS RN®: 143388-64-1; UNII: 10X8X4P12Z.

Change to read:

DEFINITION

Naratriptan Hydrochloride contains NLT 98.0% and NMT 101.0% of naratriptan hydrochloride ($C_{17}H_{25}N_3O_2S \cdot HCl$), calculated on the anhydrous and solvent-free basis.

▲▲ (USP 1-May-2021)

IDENTIFICATION

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

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

Delete the following:

▲• **C. Identification Tests—General ⟨191⟩, *Chloride*:** It meets the requirements of test C.▲ (USP 1-May-2021)

Add the following:

▲• **C. Chloride**

[**Caution—**This test evolves chlorine gas.]

Sample: Mix the solid under test with an equal weight of manganese dioxide and moisten with sulfuric acid.

Analysis: Gently heat the *Sample*, while exposing moistened starch iodide paper to the evolving gas.

Acceptance criteria: A gas evolves producing a blue color on the paper.▲ (USP 1-May-2021)

ASSAY

Change to read:

• **Procedure**

▲[Note—Store the *System suitability solution*, *Standard solution*, and *Sample solution* in a cool place, protected from light.]▲ (USP 1-May-2021)

Solution A: Dilute 0.6 mL of phosphoric acid with water to 900 mL. Adjust with triethylamine to a pH of 2.5.

Mobile phase: Isopropyl alcohol and *Solution A* (1:9)

System suitability solution: 0.7 mg/mL of USP Naratriptan Resolution Mixture RS in *Mobile phase*

Standard solution: 0.11 mg/mL of USP Naratriptan Hydrochloride RS in *Mobile phase*

Sample solution: 0.11 mg/mL of Naratriptan Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 282 nm

Column: 4.6-mm × 15-cm; 3-µm packing L11

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 2 times the retention time of naratriptan▲ (USP 1-May-2021)

System suitability

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

[NOTE—The relative retention times for naratriptan related compound A, naratriptan, and naratriptan related compound B are 0.9, 1.0, and 1.1, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the naratriptan related compound A and naratriptan peaks; NLT 1.5 between the naratriptan and naratriptan related compound B peaks, *System suitability solution*

Relative standard deviation: ▲NMT 0.73%▲ (USP 1-May-2021) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of naratriptan hydrochloride ($C_{17}H_{25}N_3O_2S \cdot HCl$) in the portion of Naratriptan Hydrochloride 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 Naratriptan Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Naratriptan Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–101.0% on the anhydrous and solvent-free basis

IMPURITIES

Change to read:

• **ORGANIC IMPURITIES**

▲[NOTE—Store the *System suitability solution* and *Sample solution* in a cool place, protected from light.]▲ (USP 1-MAY-2021)

Buffer: 5.75 g/L of monobasic ammonium phosphate in water. Adjust with phosphoric acid to a pH of 3.00 ± 0.05.

Solution A: Acetonitrile and *Buffer* (3:97)

Solution B: Acetonitrile and *Buffer* (20:80)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
35	0	100
40	0	100
41	100	0
51	100	0

System suitability solution: 0.11 mg/mL of USP Naratriptan Resolution Mixture RS in water

Sample solution: 0.11 mg/mL of Naratriptan Hydrochloride in water

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 15-cm; 4-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

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

Suitability requirements

Resolution: NLT 1.5 between naratriptan and naratriptan related compound B

Analysis

Sample: *Sample solution*

Calculate the percentage of any individual impurity in the portion of Naratriptan Hydrochloride taken:

$$\text{Result} = \{(r_U/F)/[r_N + \Sigma(r_U/F)]\} \times 100$$

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

F = relative response factor (see Table 2)

r_N = peak response of naratriptan from the *Sample solution*

Acceptance criteria: See Table 2.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
▲Naratriptan related compound A▲ (USP 1-May-2021)	0.93	1.0	0.2
Naratriptan	1.00	—	—
▲Naratriptan related compound B▲ (USP 1-May-2021)	1.04	0.6	0.1
▲Bisaryl naratriptan[a]▲ (USP 1-May-2021)	1.18	0.6	0.2
▲Naratriptan pyridinium[b]▲ (USP 1-May-2021)	1.25	0.4	0.2
▲*N*-Sulfamoylethyl naratriptan[c]▲ (USP 1-May-2021)	1.36	0.6	0.3
▲*N*-Sulfamoylethyl naratriptan pyridinium[d]▲ (USP 1-May-2021)	1.44	0.5	0.1
▲*N*-Sulfamoylethyl naratriptan amide[e]▲ (USP 1-May-2021)	1.48	1.0	0.2
▲Naratriptan ethyl analog[f]▲ (USP 1-May-2021)	1.90	1.0	0.2
Any other individual impurity	—	1.0	0.1
Total impurities	—	—	1.5

[a] *N*-Methyl-2,2-bis[3-(1-methylpiperidin-4yl)-1*H*-indol-5-yl]ethanesulfonamide; Also known as 2,2-Bis-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]ethanesulfonic acid methylamide.

[b] 1-Methyl-4-{5-[2-(*N*-methylsulfamoyl)ethyl]-1*H*-indol-3-yl}pyridin-1-ium; Also known as 1-Methyl-4-[5-(2-methylsulfamoyl-ethyl)-1*H*-indol-3-yl]-pyridinium.

[c] 2,2'-[3-(1-Methylpiperidin-4-yl)-1*H*-indole-1,5-diyl]bis(*N*-methylethanesulfonamide); Also known as 2-[3-(1-Methylpiperidin-4-yl)-5-(2-methylsulfamoyl-ethyl)-indol-1-yl]ethanesulfonic acid methylamide.

[d] 4-[1,5-Bis(2-(*N*-methylsulfamoyl)ethyl)-1*H*-indol-3-yl]-1-methylpyridin-1-ium; Also known as 4-[1,5-Bis-(2-methylsulfamoyl-ethyl)-1*H*-indol-3-yl]-1-methylpyridinium.

[e] *N*-Methyl-2-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]-*N*-[2-(*N*-methylsulfamoyl)ethyl]ethanesulfonamide; Also known as 2-[3-(1-Methylpiperidin-4-yl)-1*H*-indol-5-yl]ethane-sulfonic acid methyl-(2-methylsulfamoyl-ethyl)amide.

[f] 5-Ethyl-3-(1-methylpiperidin-4-yl)-1*H*-indole.

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I*: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store below 30°.

• **USP Reference Standards** ⟨11⟩

USP Naratriptan Hydrochloride RS

USP Naratriptan Resolution Mixture RS

Contains a mixture of Naratriptan Hydrochloride with approximately 0.1% each of the following compounds:

Naratriptan related compound A: [3-(1-Methylpiperidin-4-yl)-1*H*-indole hydrochloride].

Naratriptan related compound B: [2-[3-(1-Methyl-1,2,3,6-tetrahydropyridin-4-yl)-1*H*-indol-5-yl]ethanesulfonic acid methylamide oxalate].

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

Topic/Question	Contact	Expert Committee
NARATRIPTAN HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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