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Naratriptan Tablets

DEFINITION

Naratriptan Tablets contain an amount of Naratriptan Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of naratriptan ($C_{17}H_{25}N_3O_2S$).

IDENTIFICATION

Delete the following:

▲• **A. Thin-Layer Chromatographic Identification Test ⟨201⟩**

Diluent: Methylene chloride and methanol (1:1)

Standard solution: 1.0 mg/mL of USP Naratriptan Hydrochloride RS prepared as follows. Transfer 5.5 mg of USP Naratriptan Hydrochloride RS to a 25-mL flask, add 1 mL of water and gently shake. Add 4.5 mL of *Diluent,* and shake for 5 min. Centrifuge at 3000 rpm for 10 min, and pass through a suitable filter of a 0.45-µm pore size.

Sample solution: Transfer a number of Tablets equivalent to 5 mg of naratriptan to a 25-mL flask, add 1.0 mL of water to wet the tablets, and gently shake to remove the Tablet film coating. Add 4.5 mL of *Diluent,* and shake for 5 min or until the Tablets have dispersed. Centrifuge at 3000 rpm for 10 min, and pass through a suitable filter of a 0.45-µm pore size.

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*)

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Developing solvent system: Methylene chloride, alcohol, and triethylamine (10:2:1)

Analysis

Sample: *Standard solution* and *Sample solution*

Acceptance criteria: The R_F value of the principal spot of the Sample solution corresponds to that of the Standard solution. ▲2S *(USP41)*

Change to read:

• ▲**A.**▲2S *(USP41)* The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay.*

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲2S *(USP41)*

ASSAY

Change to read:

• **Procedure**

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

Mobile phase: Isopropyl alcohol and *Solution A* (10:90)

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

Standard stock solution: 0.2 mg/mL of USP Naratriptan Hydrochloride RS in 0.1 N sodium hydroxide

Standard solution: 0.02 mg/mL of USP Naratriptan Hydrochloride RS in *Solution A* from *Standard stock solution*

Sample solution: Nominally (*L*/50) mg/mL of naratriptan, where *L* is the label claim in mg/Tablet, prepared as follows. Transfer 5 Tablets into an amber 250-mL volumetric flask, add 30 mL of 0.1 N sodium hydroxide, and shake on a wrist-action shaker for at least 30 min. Sonicate for 10 min with regular vigorous swirling of the flask. Add about 170 mL of *Solution A*. Allow to cool to room temperature and dilute with *Solution A* to volume. Centrifuge a portion of this solution at 3500 rpm for about 10 min, and pass through a suitable filter of 0.45-µm pore size, discarding the first 3 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 224 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲2S *(USP41)*

Column: 4.6-mm × 15-cm; 5-µm packing L11

Flow rate: 1.3 mL/min

Injection volumes

System suitability solution: 10 µL

Standard solution: 50 µL

Tablets labeled to contain 1 mg of naratriptan: 50 µL

Tablets labeled to contain 2.5 mg of naratriptan: 20 µL

▲**Run time:** NLT 1.5 times of the retention time of naratriptan▲2S *(USP41)*

System suitability

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

[NOTE—The relative retention times for 3-(1-methylpiperidin-4-yl)-1*H*-indole (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 naratriptan related compound A and naratriptan and between naratriptan related compound B and naratriptan, *System suitability solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of naratriptan ($C_{17}H_{25}N_3O_2S$) 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 Naratriptan Hydrochloride RS in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of naratriptan, 335.47

M_{r2} = molecular weight of naratriptan hydrochloride, 371.93

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 500 mL, deaerated

Apparatus 1: 100 rpm

Time: 15 min

Standard solution: USP Naratriptan Hydrochloride RS in *Medium*

[NOTE—Do not sonicate the *Standard solution* to dissolve. Dissolve USP Naratriptan Hydrochloride RS with *Medium* at about 37°.]

Sample solution: Filter portions of the solution under test and dilute with *Medium*, if necessary.

Instrumental conditions

▲(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)▲2S *(USP41)*

Mode: UV

Analytical wavelength: 226–236 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the labeled amount of naratriptan ($C_{17}H_{25}N_3O_2S$) dissolved from the difference between the first derivative absorbance values at the wavelengths of maximum and minimum in the range from 226 to 236 nm on the *Sample solution*, suitably diluted with *Medium*, if necessary, in comparison with the *Standard solution*.

Tolerances: NLT 80% (*Q*) of the labeled amount of naratriptan ($C_{17}H_{25}N_3O_2S$) is dissolved.

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

IMPURITIES

Change to read:

• **ORGANIC IMPURITIES**

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

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	97	3
35	80	20
40	80	20
41	97	3
51	97	3

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

Sample solution: Nominally (*L*/10) mg/mL of naratriptan, where *L* is the label claim in mg/Tablet, prepared as follows. Transfer 5 Tablets into a suitable amber flask. Add 20.0 mL of 0.1 N sodium hydroxide, and allow to stand for 10 min. Sonicate for 10 min with regular vigorous swirling of the flask. Add 30.0 mL of *Solution A,* and mix well. Centrifuge a portion of this solution at 3500 rpm for about 10 min and pass through a suitable filter of 0.45-µm pore size, discarding the first 3 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 15-cm; ▲4-µm▲2S *(USP41)* packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volumes

System suitability solution: 50 µL

Tablets labeled to contain 1 mg of naratriptan: 50 µL

Tablets labeled to contain 2.5 mg of naratriptan: 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 each impurity in the portion of Tablets 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 for each impurity (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	1.0	—	—
Naratriptan related compound B[a]	1.07	0.6	0.2
Bisaryl naratriptan[b]	1.26	0.6	0.2
Naratriptan pyridinium salt[c]	1.33	0.4	0.3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
N-Sulfamoylethyl naratriptan[d]	1.44	0.6	0.2
N-Sulfamoylethyl naratriptan pyridinium salt[e]	1.62	0.5	0.2
Any other individual impurity	—	1.0	0.2
Total impurities	—	—	1.5

[a] 2-[3-(1-Methyl-1,2,3,6-tetrahydropyridin-4-yl)-1*H*-indol-5-yl]ethanesulfonic acid methylamide oxalate.

[b] 2,2-Bis-[3-(1-methylpiperidin-4-yl)-1*H*-indol-5-yl]ethanesulfonic acid methylamide.

[c] 1-Methyl-4-[5-(2-methylsulfamoyl-ethyl)-1*H*-indol-3-yl]-pyridinium chloride.

[d] 2-[3-(1-Methylpiperidin-4-yl)-5-(2-methylsulfamoyl-ethyl)-indol-1-yl]ethanesulfonic acid methylamide.

[e] 4-[1,5-Bis-(2-methylsulfamoyl-ethyl)-1*H*-indol-3-yl]-1-methylpyridinium chloride.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Naratriptan Hydrochloride RS

USP Naratriptan Resolution Mixture RS

A mixture of naratriptan hydrochloride with approximately 0.1% each of naratriptan related compound A [3-(1-methylpiperidin-4-yl)-1*H*-indole hydrochloride] and naratriptan related compound B [2-[3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1*H*-indole-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 TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

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