Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-B5D82D8B-14A3-412E-BA9E-B01612349838_7_en-US
DOI: https://doi.org/10.31003/USPNF_M80107_07_01
DOI Ref: y67q6

Sumatriptan Nasal Spray

DEFINITION

Sumatriptan Nasal Spray is an aqueous, buffered solution of Sumatriptan. It is supplied in a form suitable for nasal administration. It contains NLT 90.0% and NMT 110.0% of the labeled amount of sumatriptan ($C_{14}H_{21}N_3O_2S$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (CN 1-May-2020)

Sample: To the contents of one vial of Nasal Spray add 1 mL of a saturated sodium chloride solution. Add 1 mL of a saturated solution of sodium carbonate, and shake vigorously for about 30 s. To the solution so obtained add 2 mL of isopropyl alcohol, shake vigorously for about 30 s, and allow to stand until the phases separate. Transfer the organic phase to a suitable glass vial. Repeat the extraction with a second 2-mL portion of isopropyl alcohol, and transfer the organic phase to the same vial. Evaporate the solution under a stream of nitrogen. Dry the residue in an oven at 100° for 30 min, allow to cool to room temperature in a desiccator, and prepare a mull by the addition of 1–2 drops of mineral oil.

Acceptance criteria: Meets the requirements

Add the following:

▲• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲1S *(USP41)*

ASSAY

Change to read:

• **Procedure**

Buffer: Dissolve 1.7 mL of dibutylamine, 0.6 mL of phosphoric acid, and 3.9 g of monobasic sodium phosphate dihydrate in water. Adjust with a solution of 50% (w/v) sodium hydroxide to a pH of 6.5, and dilute with water to 1 L.

Mobile phase: Acetonitrile and *Buffer* (25:75)

Diluent: Dissolve 3.9 g of monobasic sodium phosphate dihydrate in water. Adjust with a solution of 50% (w/v) sodium hydroxide to a pH of 6.5, and dilute with water to 1 L. Mix 750 mL of the resulting solution with 250 mL of acetonitrile.

System suitability solution: 0.14 mg/mL of USP Sumatriptan Succinate RS and 0.07 mg/mL of USP Sumatriptan Succinate Related Compound C RS in *Diluent*

Standard solution: 0.14 mg/mL of USP Sumatriptan Succinate RS in *Diluent*

Sample solution: Nominally equivalent to 0.1 mg/mL of sumatriptan in *Diluent* from an appropriate volume of Nasal Spray

Chromatographic system

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

Mode: LC

Detector: UV 282 nm

Column: 4.6-mm × 20-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 4 times the retention of sumatriptan ▲1S *(USP41)*

System suitability

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

[Note—The relative retention times for sumatriptan succinate related compound C and sumatriptan are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between sumatriptan succinate related compound C and sumatriptan, *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 sumatriptan ($C_{14}H_{21}N_3O_2S$) in the portion of Nasal Spray 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 Sumatriptan Succinate RS▲ (ERR 1-Oct-2018) in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of sumatriptan, ▲295.40▲1S *(USP41)*

M_{r2} = molecular weight of sumatriptan succinate, ▲413.49▲1S *(USP41)*

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Deliverable Volume**

Analysis: Test 10 vials separately. Weigh each vial before and after actuation, and calculate the individual volume delivered, in µL, then calculate the mean volume delivered:

$$\text{Result} = (W_1 - W_2)/D$$

W_1 = weight of the individual vial before actuation (mg)

W_2 = weight of the individual vial after actuation (mg)

D = density of the nasal solution

Acceptance criteria: The volume of each spray delivered is between 80 and 120 µL, and the mean volume is between 90 and 110 µL.

IMPURITIES

Change to read:

• **Limit of Sumatriptan Related Compound A**

Buffer: Dissolve 77.1 g of ammonium acetate in 100 mL of water.

Mobile phase: Methanol and *Buffer* (90:10)

Diluent: Prepare as directed in the *Assay*.

Standard solution: ▲0.007 mg/mL▲1S *(USP41)* of USP Sumatriptan Succinate Related Compound A RS in *Diluent*

Sample solution: Nominally equivalent to 1.0 mg/mL of sumatriptan in *Diluent* from an appropriate volume of Nasal Spray

Chromatographic system

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

Mode: LC

Detector: UV 282 nm

Column: 4.6-mm × 20-cm; packing L3

Flow rate: 2 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 2 times the retention of sumatriptan related compound A▲1S *(USP41)*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of sumatriptan succinate related compound A in the portion of Nasal Spray taken:

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

r_U = peak response of sumatriptan related compound A from the *Sample solution*

r_S = peak response of sumatriptan related compound A from the *Standard solution*

C_S = concentration of ▲USP Sumatriptan Succinate Related Compound A RS▲1S *(USP41)* in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of sumatriptan related compound A, ▲495.68▲1S *(USP41)*

M_{r2} = molecular weight of sumatriptan succinate related compound A, ▲613.77▲1S *(USP41)*

Acceptance criteria: NMT 1.5%

Change to read:

• **Organic Impurities**

Buffer: Dissolve 1.7 mL of dibutylamine, 0.6 mL of phosphoric acid, and 3.9 g of monobasic sodium phosphate dihydrate in water. Adjust with a solution of 50% (w/v) sodium hydroxide to a pH of 7.5, and dilute with water to 1 L.

Mobile phase: Acetonitrile and *Buffer* (25:75)

Diluent: Prepare as directed in the *Assay*.

System suitability solution: 1.4 mg/mL of USP Sumatriptan Succinate RS and 1 µg/mL of USP Sumatriptan Succinate Related Compound C RS in *Diluent*

Identification solution: 3 mg/mL of USP Sumatriptan Succinate Related Impurities RS in *Diluent*

Sample solution: Nominally equivalent to 1 mg/mL of sumatriptan in *Diluent* from an appropriate volume of Nasal Spray

Chromatographic system: Proceed as directed in the *Assay*. ▲▲1S *(USP41)*

System suitability

Sample: *System suitability solution*

▲[Note—See *Table 1* for the relative retention times.]▲1S *(USP41)*

Suitability requirements

Resolution: NLT 1.5 between sumatriptan succinate related compound C and sumatriptan

Analysis

Samples: ▲*Identification solution* and▲1S *(USP41)* *Sample solution*

Calculate the percentage of each ▲degradation product▲1S *(USP41)* in the portion of Nasal Spray taken:

$$\text{▲Result} = (r_U/r_T) \times (1/F) \times 100\text{▲1S } (USP41)$$

r_U = peak response of each ▲degradation product▲1S *(USP41)* from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

▲Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Sumatriptan *N*-oxide[a]	0.3	1.0	1.5
Sumatriptan amino[b]	0.4	1.0	1.5
3-Hydroxy-2-oxo sumatriptan[c]	0.46	0.35	1.5

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Sumatriptan monomethyl[d]	0.6	1.0	1.5
Sumatriptan pyrroloindolium analog[e]	0.64	0.22	1.5
Sumatriptan succinate related compound C	0.9	1.0	1.5
Sumatriptan	1.0	1.0	—
Total degradation products[f]	—	—	4.0▲1S *(USP41)*

[a] *N*-Methyl-1-{3-[2-(dimethylamino *N*-oxide)ethyl]-1*H*-indol-5-yl}methanesulfonamide.

[b] [3-(2-Aminoethyl)-1*H*-indol-5-yl]-*N*-methylmethanesulfonamide.

[c] 1-{3-[2-(Dimethylamino)ethyl]-3-hydroxy-2-oxoindolin-5-yl}-*N*-methylmethanesulfonamide.

[d] *N*-Methyl-1-{3-[2-(methylamino)ethyl]-1*H*-indol-5-yl}methanesulfonamide.

[e] 3a-Hydroxy-1,1-dimethyl-5-(*N*-methylsulfamoylmethyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indol-1-ium sulfate.

[f] Includes the amount of sumatriptan related compound A determined in the test for *Limit of Sumatriptan Related Compound A*.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^2 cfu/mL, and it meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa* in 1 mL.

• **pH ⟨791⟩:** 5.0–6.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, and store between 2° and 30°.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Sumatriptan Succinate RS

USP Sumatriptan Succinate Related Compound A RS

[3-[2-(Dimethylamino)ethyl]-2-({3-[2-(dimethylamino)ethyl]-1*H*-indol-5-yl}methyl)-1*H*-indol-5-yl]-*N*-methylmethanesulfonamide succinate salt.

$C_{27}H_{37}N_5O_2S \cdot C_4H_6O_4$ 613.77

USP Sumatriptan Succinate Related Compound C RS

{3-[2-(Dimethylamino)ethyl]-1-(hydroxymethyl)-1*H*-indol-5-yl}-*N*-methylmethanesulfonamide succinate salt.

$C_{15}H_{23}N_3O_3S \cdot ½C_4H_6O_4$ 384.47

USP Sumatriptan Succinate Related Impurities RS

▲Mixture of sumatriptan succinate, sumatriptan monomethyl, sumatriptan succinate related compound C, sumatriptan *N*-oxide, and sumatriptan amino.▲1S *(USP41)*

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

Topic/Question	Contact	Expert Committee
SUMATRIPTAN NASAL SPRAY	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(3)
Current DocID: GUID-B5D82D8B-14A3-412E-BA9E-B01612349838_7_en-US
DOI: https://doi.org/10.31003/USPNF_M80107_07_01
DOI ref: y67q6