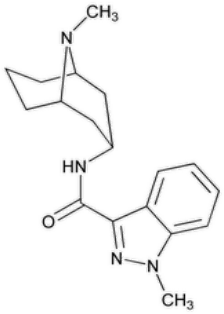
https://trungtamthuoc.com/

Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-DD638A4B-AF4E-4A96-BA0E-5EF71B0C4390_4_en-US
DOI: https://doi.org/10.31003/USPNF_M10437_04_01
DOI Ref: yr4d9

© 2025 USPC
Do not distribute

Granisetron



$C_{18}H_{24}N_4O$ 312.41

1*H*-Indazole-3-carboxamide, 1-methyl-*N*-(9-methyl-9-azabicyclo[3.3.1]-non-3-yl)-, *endo*-;

1-Methyl-*N*-(9-methyl-*endo*-9-azabicyclo[3.3.1]non-3-yl)-1*H*-indazole-3-carboxamide CAS RN®: 109889-09-0.

DEFINITION

Granisetron contains NLT 98.0% and NMT 102.0% of granisetron ($C_{18}H_{24}N_4O$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

ASSAY

• **Procedure**

Mobile phase: Dilute 1.6 mL of phosphoric acid with water to 800 mL, and then add 200 mL of acetonitrile. Add 1.0 mL of hexylamine. Adjust with triethylamine to a pH of 7.5 ± 0.05 (about 4 mL is needed).

System suitability solution: Transfer 2 mL of a solution containing about 1.0 mg/mL of granisetron in *Mobile phase* to a colorless glass vial, stopper it, and either expose the solution to sunlight for 4 h or place it under a UV lamp for 16 h (granisetron undergoes partial degradation to granisetron related compound C). A degradation of at least about 0.3% of granisetron to granisetron related compound C must be obtained, as shown by the appearance of a corresponding peak in the chromatogram. If it is not obtained, again expose the solution to sunlight or place it under a UV lamp.

Standard solution: 1.0 mg/mL of USP Granisetron RS in *Mobile phase*

Sample solution: 1.0 mg/mL of Granisetron in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 305 nm

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 3.5 between granisetron and granisetron related compound C, *System suitability solution*

OFFICIAL

www.webofpharma.com

https://trungtamthuoc.com/

Tailing factor: NMT 2.0 for the granisetron peak, *System suitability solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of granisetron ($C_{18}H_{24}N_4O$) in the portion of Granisetron 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 Granisetron RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Limit of Granisetron Related Compound E**

Diluent: Acetonitrile and water (80:20)

Standard solution: 0.075 mg/mL of USP Granisetron Related Compound E RS in *Diluent*

[Note—USP Granisetron Related Compound E RS is the acetate salt of (1*R*,3*r*,5*S*)-9-methyl-9-azabicyclo[3.3.1]nonan-3-amine. Use the correction factor stated on the label of the USP Reference Standard to calculate the concentration, as appropriate.]

Sample solution: 50 mg/mL of Granisetron in *Diluent*

Chromatographic system

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

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Ethyl acetate, isopropyl alcohol, and ammonium hydroxide (50:30:6.5)

Analysis

Samples: *Standard solution* and *Sample solution*

Proceed as directed in the chapter and develop the chromatogram until the solvent front has moved about half of the length of the plate. Dry the plate in air, and expose it to iodine vapor for 30 min.

Acceptance criteria: Any spot corresponding to granisetron related compound E from the *Sample solution* is not more intense than the corresponding spot from the *Standard solution* (NMT 0.15%).

- **Organic Impurities**

[Note—Protect all solutions containing granisetron from light.]

Mobile phase, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.001 mg/mL of USP Granisetron RS in *Mobile phase*

Sample solution: 1.0 mg/mL of Granisetron in *Mobile phase*. Inject this solution within 4 h of preparation.

System suitability

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

Suitability requirements

Resolution: NLT 3.5 between granisetron and granisetron related compound C, *System suitability solution*

Tailing factor: NMT 2.0 for the granisetron peak, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Granisetron 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 granisetron from the *Standard solution*

OFFICIAL

https://trungtamthuoc.com/

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

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

Acceptance criteria: See *Table 1*. The reporting threshold for impurities is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
1-Methylindazole acid (granisetron related compound D)[a]	0.4	0.10
1-Desmethyl granisetron (granisetron related compound B)[b]	0.5	0.15
Granisetron 2-methyl isomer (granisetron related compound A)[c]	0.7	0.15
9-Desmethyl granisetron (granisetron related compound C)[d]	0.8	0.2
Granisetron	1.0	—
Any other individual impurity	—	0.10
Total impurities	—	1.0

[a] 1-Methyl-1*H*-indazole-3-carboxylic acid.

[b] *N*-[(1*R*,3*r*,5*S*)-9-Methyl-9-azabicyclo[3.3.1]non-3-yl]-1*H*-indazole-3-carboxamide.

[c] 2-Methyl-*N*-[1*R*,3*r*,5*S*)-9-methyl-9-azabicyclo[3.3.1]non-3-yl]-2*H*-indazole-3-carboxamide.

[d] *N*-[(1*R*,3*r*,5*S*)-9-Azabicyclo[3.3.1]non-3-yl]-1-methyl-1*H*-indazole-3-carboxamide.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards** ⟨11⟩

USP Granisetron RS

USP Granisetron Related Compound E RS

Granisetron amine acetate;
(1*R*,3*r*,5*S*)-9-Methyl-9-azabicyclo[3.3.1]nonan-3-amine acetate.

$C_9H_{18}N_2 \cdot C_2H_4O_2$ 214.31

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

Topic/Question	Contact	Expert Committee
GRANISETRON	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

OFFICIAL

www.webofpharma.com

https://trungtamthuoc.com/
Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(6)
Current DocID: GUID-DD638A4B-AF4E-4A96-BA0E-5EF71B0C4390_4_en-US
DOI: https://doi.org/10.31003/USPNF_M10437_04_01
DOI ref: yr4d9
OFFICIAL