Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: USP Monographs
DocId: GUID-371AE807-28D6-431D-B6D5-069807A765DE_4_en-US
DOI: https://doi.org/10.31003/USPNF_M35864_04_01
DOI Ref: 14ylj

Granisetron Hydrochloride Injection

DEFINITION

Granisetron Hydrochloride Injection is a sterile solution of Granisetron Hydrochloride in Water for Injection. It contains the equivalent of NLT 93.0% and NMT 107.0% of the labeled amount of granisetron ($C_{18}H_{24}N_4O$). It may contain suitable preservatives.

IDENTIFICATION

Delete the following:

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

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Developing solvent: Methylene chloride, alcohol, ammonium hydroxide, and water (60:40:2:5)

Standard solution: Dissolve USP Granisetron Hydrochloride RS in water or alcohol to obtain a solution having a concentration of granisetron that matches the concentration of granisetron in the *Sample solution.* To calculate the concentration of granisetron in the *Standard solution,* use the molecular weights of granisetron (312.41) and granisetron hydrochloride (348.87).

Sample solution: Use the undiluted Injection.

Application volume: Equal volumes of *Standard solution* and *Sample solution*, equivalent to 4–5 µg of granisetron

Analysis

Samples: *Standard solution* and *Sample solution*

Dry the spots under a current of warm air for about 5 min, and develop the plate in a paper-lined chromatographic chamber equilibrated with *Developing solvent* before use. Allow the chromatogram to develop until the solvent front has moved about 15 cm. Remove the plate, dry the plate under a current of warm air, and examine the plate under short-wavelength UV light.

Acceptance criteria: The principal spot from the *Sample solution* corresponds in appearance and R_F value to that of the *Standard solution*.▲ (USP 1-May-2021)

Add the following:

▲• **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

• **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

Change to read:

• **Procedure**

▲[Note—Protect all solutions from light.]▲ (USP 1-May-2021)

Solution A: 15.6 g/L of sodium phosphate monobasic dihydrate in water. Adjust with phosphoric acid to a pH of 2.0, prior to final dilution.

Mobile phase: Methanol, tetrahydrofuran, and *Solution A* (24: 1.1: 75)

Diluent: Methanol and water (25:75)

System suitability solution: 0.1 mg/mL of each USP Granisetron Hydrochloride RS, USP Granisetron Related Compound B RS, USP Granisetron Related Compound C RS, and USP Granisetron Related Compound D RS, in *Diluent*. Dilute with water to obtain a solution containing about *L* µg/mL of each component, where *L* is the labeled amount, in milligrams, of granisetron per milliliter of Injection.

Standard solution: (0.11 × *L*) mg/mL of USP Granisetron Hydrochloride RS in water, where *L* is the labeled amount, in milligrams, of granisetron per milliliter of Injection

Sample solution: Use the Injection diluted with water (1:10).

Chromatographic system

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

Mode: LC

Detector: UV 300 nm. ▲For *Identification A*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2021)

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

Flow rate: 1.2 mL/min

Injection volume: 15/*L* µL, where *L* is the labeled amount, in milligrams, of granisetron per milliliter of Injection

Run time: NLT 3 times the retention time of the granisetron peak

System suitability

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

[NOTE—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 2 between the granisetron and granisetron related compound C peaks, *System suitability solution*

Tailing factor: NMT 3 for the granisetron peak, *Standard solution*

Relative standard deviation: NMT 2.0% for 6 replicate injections, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of granisetron ($C_{18}H_{24}N_4O$) in each milliliter of Injection taken:

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

r_U = peak response of granisetron from the *Sample solution*

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

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

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

M_{r1} = molecular weight of granisetron, 312.41

M_{r2} = molecular weight of granisetron hydrochloride, 348.87

Acceptance criteria: 93.0%–107.0%

IMPURITIES

Change to read:

• **ORGANIC IMPURITIES**

▲[NOTE—Protect all solutions containing granisetron from light.]▲ (USP 1-MAY-2021)

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

Sample solution: Use the undiluted Injection.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

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

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

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

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

M_{r1} = molecular weight of granisetron, 312.41

M_{r2} = molecular weight of granisetron hydrochloride, 348.87

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

Acceptance criteria: See *Table 1*. Reporting threshold is 0.1%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Granisetron related compound A[a,b]	0.5–0.6	—	—
Granisetron related compound B[c]	0.7	0.8	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Granisetron	1.0	—	—
Granisetron related compound C ▲ (USP 1-May-2021)	1.2	1.0	0.7
Granisetron related compound D ▲[c] ▲ (USP 1-May-2021)	2.1–2.3	1.5	—
Any individual, unspecified impurity	—	—	0.5
Total specified impurities	—	—	1.3

[a] This is a process impurity and should not be included in the total specified impurities.

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

▲[c] To be included in total specified impurities.▲ (USP 1-May-2021)

SPECIFIC TESTS

Change to read:

• **Bacterial Endotoxins Test ⟨85⟩:** ▲Meets the requirements▲ (USP 1-May-2021)

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections

• **pH ⟨791⟩:** 4.0–6.0

• **Other Requirements:** Meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*

ADDITIONAL REQUIREMENTS

• **Labeling:** It meets the requirements for *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*. Label it to indicate the name and the quantity of any added preservative.

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, protected from light, and store at controlled room temperature.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Granisetron Hydrochloride RS

USP Granisetron Related Compound B RS

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

▲$C_{17}H_{22}N_4O$ 298.39▲ (USP 1-May-2021)

USP Granisetron Related Compound C RS

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

▲$C_{17}H_{22}N_4O \cdot HCl$ 334.85▲ (USP 1-May-2021)

USP Granisetron Related Compound D RS

1-Methyl-1*H*-indazole-3-carboxylic acid.

▲$C_9H_8N_2O_2$ 176.18▲ (USP 1-May-2021)

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

Topic/Question	Contact	Expert Committee
GRANISETRON HYDROCHLORIDE INJECTION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(2)

Current DocID: GUID-371AE807-28D6-431D-B6D5-069807A765DE_4_en-US

DOI: https://doi.org/10.31003/USPNF_M35864_04_01
DOI ref: 14ylj