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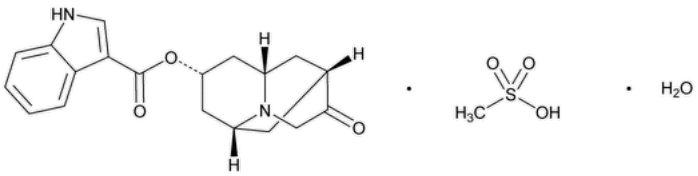
Dolasetron Mesylate



$C_{19}H_{20}N_2O_3 \cdot CH_4O_3S \cdot H_2O$ 438.49

1*H*-Indole-3-carboxylic acid, octahydro-3-oxo-2,6-methano-2*H* -quinolizin-8-yl ester, (2*α*,6*α*,8*α*,9a*β*)-, monomethanesulfonate monohydrate; Indole-3-carboxylic acid, ester with (8*r*)-hexahydro-8-hydroxy-2,6-methano-2*H*-quinolizin-3(4*H*)-one, monomethanesulfonate monohydrate CAS RN®: 878143-33-0; UNII: U3C8E5BWKR.

Anhydrous CAS RN®: 115956-13-3; UNII: 71YF100S3H.

DEFINITION

Dolasetron Mesylate contains NLT 98.0% and NMT 102.0% of $C_{19}H_{20}N_2O_3 \cdot CH_4O_3S \cdot H_2O$, calculated on the as-is basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**
- **B. Procedure**

Sample solution: 1 mg/mL

Analysis: Transfer 5–10 mg of 5,5'-methylenedisalicylic acid to a clean crucible, and heat in an oven at 150° for 5 min. Remove from the oven, and add 10 drops of the *Sample solution*. Return to the oven, and evaporate to dryness.

Acceptance criteria: A red or pink color (presence of methanesulfonic acid) develops in the white residue.

ASSAY

Change to read:

- **Procedure**

▲Solution A: Add 0.19 mL of triethylamine to each 450 mL of acetonitrile.▲ (ERR 1-Jun-2020)

Mobile phase: ▲*Solution A*,▲ (ERR 1-Jun-2020) water, and 1 M ammonium formate (450:440:110) ▲▲ (ERR 1-Jun-2020)

Standard solution: 0.04 mg/mL and 0.004 mg/mL respectively of USP Dolasetron Mesylate RS and indole-3-carboxylic acid in *Mobile phase*

Sample solution: 0.04 mg/mL of Dolasetron Mesylate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

Column: 4.6-mm × 15-cm; packing L1

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 4 between indole-3-carboxylic acid and dolasetron mesylate

Tailing factor: NMT 1.8

Relative standard deviation: NMT 1.5% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{19}H_{20}N_2O_3 \cdot CH_4O_3S \cdot H_2O$ in the Dolasetron Mesylate 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 Dolasetron Mesylate RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the as-is basis

IMPURITIES

Organic Impurities

- **Procedure**

0.01 M Dibasic ammonium phosphate solution: 1.32 g/L of dibasic ammonium phosphate. Adjust with 2.0 M phosphoric acid to a pH of 7.0.

Diluent: Acetonitrile and water (1:4)

Solution A: Acetonitrile and *0.01 M Dibasic ammonium phosphate solution* (53:1000), filtered and degassed

Solution B: Acetonitrile and *0.01 M Dibasic ammonium phosphate solution* (795:295), filtered and degassed

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	100	0
28	0	100
38	0	100
40	100	0
50	100	0

System suitability solution: 0.004 mg/mL and 0.03 mg/mL, respectively, of indole and USP Dolasetron Mesylate RS in *Diluent*

Standard solution A: 0.03 mg/mL of USP Dolasetron Mesylate RS in *Diluent*

Standard solution B: 6 mg/mL and 0.0072 mg/mL, respectively, of USP Dolasetron Mesylate RS and USP Dolasetron Mesylate Related Compound A RS in *Diluent*

Sample solution: 6 mg/mL of Dolasetron Mesylate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; packing L7

Flow rate: 1.5 mL/min

Injection size: 100 µL

System suitability

Suitability requirements

Resolution: NLT 1.5 between the first eluting peak, indole, and the second eluting peak, dolasetron mesylate from the *System suitability solution*. [Note—If the dolasetron mesylate peak is found to elute before the indole peak, condition the column as follows: fill up the column with *Solution A*, plug the column, and place the column in a convection oven at 105° for about 16 h. Retest the column.]

Relative standard deviation: NMT 5.0% for replicate injections of *Standard solution A*

Analysis

Samples: *Standard solution A*, *Standard solutionB*, and *Sample solution*

Calculate the percentage of dolasetron mesylate related compound A in the Dolasetron Mesylate taken:

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

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

r_S = peak response of dolasetron mesylate related compound A from the *Standard solution B*

C_S = concentration of USP Dolasetron Mesylate Related Compound A RS in the *Standard solution B* (mg/mL)

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

M_{r1} = molecular weight of dolasetron mesylate related compound A base, 181.2

M_{r2} = molecular weight of dolasetron mesylate related compound A hydrochloride, 217.8

Calculate the percentage of each impurity (other than dolasetron mesylate related compound A) in the portion of Dolasetron Mesylate 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 dolasetron mesylate from the *Standard solution A*

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

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

Acceptance criteria

Individual impurities: NMT 0.1%

Total impurities: NMT 0.3%

[NOTE—The reporting level for impurities is 0.05%.]

SPECIFIC TESTS

• **WATER DETERMINATION,** *Method Ia*⟨921⟩**:** Between 3.5% and 4.7%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers, protected from light.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Dolasetron Mesylate RS

USP Dolasetron Mesylate Related Compound A RS

Hexahydro-8-hydroxy-2,6-methano-2*H*-quinolizin-3 (4*H*)-one, hydrochloride.

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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