Acceptance criteria
Individual impurities: See *Impurity Table 1*.
Total impurities: See *Impurity Table 1*.

Impurity Table 1

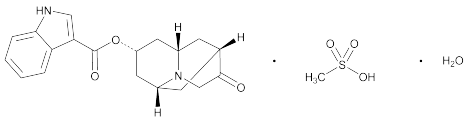
Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Dofetilide related compound A[a]	0.9	1.04	0.5
Dofetilide	1.0	—	—
Any other individual unspecified impurity	—	1.00[b]	0.1
Total impurities	—	—	0.5

[a] *N*-[4-(2-(2-[4-(Methanesulfonamido)phenoxy]ethylamino)ethyl)phenyl] methanesulfonamide.
[b] Unless otherwise determined.

SPECIFIC TESTS
- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 1.0%

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Dofetilide RS
  USP Dofetilide Related Compound A RS
  N-[4-(2-{2-[4-(Methanesulfonamido)phenoxy] ethylamino}ethyl)phenyl]methanesulfonamide.
  427.54

Dolasetron Mesylate



$C_{19}H_{20}N_2O_3 \cdot CH_4O_3S \cdot H_2O$ 438.50

1*H*-Indole-3-carboxylic acid, octahydro-3-oxo-2,6-methano-2*H*-quinolizin-8-yl ester, (2α,6α,8α,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 [115956-13-3].

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. INFRARED ABSORPTION** ⟨**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 dr yness.
  Acceptance criteria: A red or pink color (presence of methanesulfonic acid) develops in the white residue.

ASSAY
- **PROCEDURE**
  Mobile phase: Acetonitrile, water, and 1 M ammonium formate (450:440:110), adding 0.19 mL of triethylamine to the acetonitrile portion
  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 solution B*, 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.

Dolasetron Mesylate Injection

» Dolasetron Mesylate Injection is a sterile solution, suitable for intravenous administration, containing Dolasetron Mesylate in a buffer solution. It contains not less than 90.0 per cent and not more than 110.0 per cent of the labeled amount of dolasetron mesylate ($C_{19}H_{20}N_2O_3 \cdot CH_4O_3S \cdot H_2O$).

Packaging and storage—Preserve in a single-dose container, protected from light. Store at controlled room temperature.

Labeling—Label it to indicate that it may be diluted with a suitable parenteral vehicle prior to intravenous infusion.

USP Reference standards ⟨11⟩**—**
USP Dolasetron Mesylate RS
USP Endotoxin RS

Identification, *Infrared Absorption* ⟨197K⟩**—**

Test specimen—Transfer a portion of Injection, equivalent to about 100 mg of dolasetron mesylate, to a 150-mL beaker. Add about 20 mL of water and 10 mL of a sodium hydroxide solution (1 in 10). Mix, and allow to stand at room temperature for 30 minutes. Pass through a filtering crucible with fritted disk having a medium porosity, using about 100 mL of water to aid in the transfer. Dry the precipitate in a vacuum oven at 105 ° for 4 hours. Prepare a 1.5% mixture of the dried powder with potassium bromide.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 2.7 USP Endotoxin Units per mg of dolasetron mesylate.

pH ⟨791⟩: between 3.2 and 3.8.

Particulate matter ⟨788⟩: meets the requirements for small-volume injections.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

Mobile phase—Proceed as directed in the *Assay* under *Dolasetron Mesylate.*

System suitability preparation—Dissolve accurately weighed quantities of USP Dolasetron Mesylate RS and indole-3-carboxylic acid in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having known concentrations of about 0.1 mg per mL and 0.02 mg per mL, respectively.

Standard preparation—Dissolve an accurately weighed quantity of USP Dolasetron Mesylate RS in *Mobile phase* to obtain a solution having a known concentration of about 0.1 mg per mL.

Assay preparation—Using a "to contain" pipet, transfer 2.5 mL of Injection to a 50-mL volumetric flask. Rinse the pipet with several portions of *Mobile phase*, and collect the rinses in the same flask. Dilute with *Mobile phase* to volume, and mix. Pipet 5.0 mL of this solution into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—Prepare as directed in the *Assay* under *Dolasetron Mesylate.* Chromatograph the *System suitability preparation*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between indole-3-carboxylic acid and dolasetron mesylate is not less than 4; and the tailing factor for the dolasetron mesylate peak is not more than 1.8. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of