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Dofetilide

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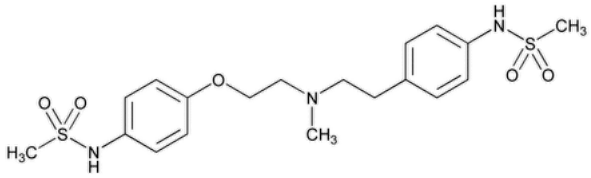

$C_{19}H_{27}N_3O_5S_2$ 441.56

Methanesulfonamide, *N*-[4-[2-[methyl[2-[4-[(methylsulfon yl)amino]phenoxy]ethyl]amino]ethyl]phenyl]-;

▲*N*-{4-[2-(Methyl{2-[4-(methylsulfonamido)phenoxy]ethyl}amino)ethyl]phenyl}methanesulfonamide▲ (ERR 1-Nov-2022) CAS RN®: 115256-11-6; UNII: R4Z9X1N2ND.

DEFINITION

Dofetilide contains NLT 97.0% and NMT 103.0% of $C_{19}H_{27}N_3O_5S_2$, calculated on the anhydrous, solvent-free basis.

IDENTIFICATION

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

Potassium hydroxide solution: 0.56 g/mL of potassium hydroxide

Buffer: 1.36 g of monobasic potassium phosphate and 5 mg of ascorbic acid in 1 L of water. Adjust with *Potassium hydroxide solution* to a pH of 7.0.

Mobile phase: Acetonitrile and *Buffer* (1:3)

System suitability solution: 25 µg/mL of USP Dofetilide RS and 0.5 µg/mL of USP Dofetilide Related Compound A RS in *Mobile phase*

Standard solution: 25 µg/mL of USP Dofetilide RS in *Mobile phase*

Sample solution: 25 µg/mL of Dofetilide in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 3.9-mm × 15-cm; 4-µm packing L7

Temperature: 30°

Flow rate: 1 mL/min

Injection size: 50 µL

System suitability

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

Suitability requirements

Resolution: NLT 8.0 between dofetilide and dofetilide related compound A, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{19}H_{27}N_3O_5S_2$ in the portion of Dofetilide taken:

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

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

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

C_S = concentration of dofetilide in the *Standard solution* (µg/mL)

C_U = concentration of Dofetilide in the *Sample solution* (µg/mL)

Acceptance criteria: 97.0%–103.0% on the anhydrous and solvent-free basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.1%

Organic Impurities

- **Procedure**

Buffer: 0.78 g/L of ammonium acetate. Adjust with glacial acetic acid to a pH of 5.0 ± 0.1.

Diluent: Acetonitrile and *Buffer* (3:22)

Solution A: *Buffer*

Solution B: Methanol

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	88	12
5	88	12
25	70	30
30	70	30

System suitability solution: 1.25 µg/mL each of USP Dofetilide RS and USP Dofetilide Related Compound A RS in *Diluent*

Standard solution: 1.25 µg/mL of USP Dofetilide RS in *Diluent*

Diluted standard solution: 0.125 µg/mL of USP Dofetilide RS in *Diluent* from the *Standard solution*

Sample solution: 0.25 mg/mL of Dofetilide in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 3.9-mm × 15-cm; 5-µm packing L1

Temperature: 30°

Flow rate: 1 mL/min

Injection size: 50 µL

System suitability

Samples: *System suitability solution* and *Diluted standard solution*

System suitability requirements

Resolution: NLT 5.0 between dofetilide and dofetilide related compound A, *System suitability solution*

Column efficiency: NLT 35,000 theoretical plates for the dofetilide peak, *System suitability solution*

Tailing factor: NMT 1.5 for the dofetilide peak, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Diluted standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

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

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

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

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

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

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

Topic/Question	Contact	Expert Committee
DOFETILIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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