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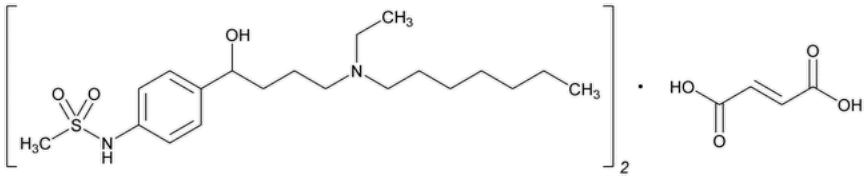
Ibutilide Fumarate



$(C_{20}H_{36}N_2O_3S)_2 \cdot C_4H_4O_4$ 885.23

Methanesulfonamide, *N*-[4-[4-(ethylheptylamino)-1-hydroxybutyl]phenyl]-, (±)-, (*E*)-2-butenedioate (2:1) (salt);
(±)-4'-[4-(Ethylheptylamino)-1-hydroxybutyl]methanesulfonanilide fumarate (2:1) (salt) CAS RN®: 122647-32-9; UNII: 9L5X4M5L6I.
Ibutilide free base CAS RN®: 122647-31-8; UNII: 2436VX1U9B.

DEFINITION

Ibutilide Fumarate contains NLT 98.0% and NMT 102.0% of ibutilide fumarate $[(C_{20}H_{36}N_2O_3S)_2 \cdot C_4H_4O_4]$, calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 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**

Solution A: 2 mL/L of triethylamine in water. Adjust with perchloric acid to a pH of 2.5.

Mobile phase: Acetonitrile and *Solution A* (40:60)

Standard solution: 0.2 mg/mL of USP Ibutilide Fumarate RS in *Mobile phase*. [Note—Sonication may be necessary for complete dissolution.]

Sample solution: 0.2 mg/mL of Ibutilide Fumarate in *Mobile phase*. [Note—Sonication may be necessary for complete dissolution.]

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

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

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

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

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ibutilide fumarate $[(C_{20}H_{36}N_2O_3S)_2 \cdot C_4H_4O_4]$ in the portion of Ibutilide Fumarate taken:

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

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

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

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

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.20%
- **Content of Fumaric Acid**

Solution A, Mobile phase, and **Sample solution:** Proceed as directed in the *Assay*.

Chromatographic system: Proceed as directed in the *Assay*, except use a UV detector at 207 nm.

Standard stock solution: 0.2 mg/mL of USP Fumaric Acid RS in *Mobile phase*. [Note—Sonication may be necessary for complete dissolution.]

Standard solution: 0.02 mg/mL of USP Fumaric Acid RS in *Mobile phase*

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of fumaric acid content in the portion of Ibutilide Fumarate taken:

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

r_U = peak response of fumaric acid from the *Sample solution*

r_S = peak response of fumaric acid from the *Standard solution*

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

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

Acceptance criteria: 12.7%–13.5%

- **Organic Impurities**

Solution A: 2 mL/L of triethylamine in water. Adjust with perchloric acid to a pH of 2.5.

Solution B: Acetonitrile

Diluent: Acetonitrile and *Solution A* (40:60)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
15	60	40
30	30	70
40	30	70
50	60	40
55	60	40

Standard solution: 2 µg/mL of USP Ibutilide Fumarate RS and 3 µg/mL each of USP Ibutilide Related Compound A RS and USP Ibutilide Related Compound B RS in *Diluent*

Sample solution: 2 mg/mL of Ibutilide Fumarate in *Diluent*

Chromatographic system: Proceed as directed in the *Assay*, except use a run time of NLT 2.5 times the retention time of ibutilide for the *Standard solution* and NLT 6.2 times the retention time of ibutilide for the *Sample solution*.

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 5000 theoretical plates for the ibutilide peak

Relative standard deviation: NMT 3.0% for the ibutilide peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ibutilide related compound A, ibutilide related compound B, and any unspecified impurity in the portion of Ibutilide Fumarate taken:

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

r_U = peak response of ibutilide related compound A, ibutilide related compound B, or any other unspecified impurity from the *Sample solution*

r_S = peak response of ibutilide related compound A, ibutilide related compound B, or ibutilide (for calculating any other unspecified impurity) from the *Standard solution*

C_S = concentration of USP Ibutilide Related Compound A RS, USP Ibutilide Related Compound B RS, or USP Ibutilide Fumarate RS (for calculating any unspecified impurity) in the *Standard solution* (mg/mL)

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

Acceptance criteria: See *Table 2*. Disregard the fumaric acid peak and any peak less than 0.01%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Fumaric acid[a]	0.33	—
Ibutilide	1.00	—
Ibutilide related compound B[b]	2.66	0.15
Ibutilide related compound A[c]	3.38	0.15
Any unspecified impurity	—	0.10
Total impurities	—	0.35

[a] This impurity is controlled in the test for *Content of Fumaric Acid*.

[b] *N*-Ethyl-*N*-heptyl-4-hydroxy-4-[4-(methylsulfonamido)phenyl]butanamide.

[c] *N*-Ethyl-*N*-heptyl-4-[4-(methylsulfonamido)phenyl]-4-oxobutanamide.

SPECIFIC TESTS

• **Water Determination,** *Method I* ⟨921⟩**:** NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in air-tight containers, and protect from light. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Fumaric Acid RS

USP Ibutilide Fumarate RS

USP Ibutilide Related Compound A RS

N-Ethyl-*N*-heptyl-4-[4-(methylsulfonamido)phenyl]-4-oxobutanamide.

$C_{20}H_{32}N_2O_4S$ 396.54

USP Ibutilide Related Compound B RS

N-Ethyl-*N*-heptyl-4-hydroxy-4-[4-(methylsulfonamido)phenyl]butanamide.

$C_{20}H_{34}N_2O_4S$ 398.56

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

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

Chromatographic Database Information: Chromatographic Database

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