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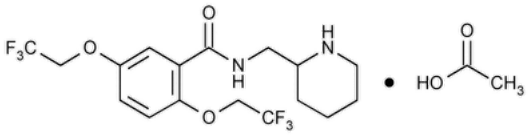
# Flecainide Acetate



$C_{17}H_{20}F_6N_2O_3 \cdot C_2H_4O_2$ 474.39

Benzamide, *N*-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)-, monoacetate;

*N*-(2-Piperidylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)benzamide monoacetate CAS RN®: 54143-56-5; UNII: M8U465Q1WQ.

## DEFINITION

Flecainide Acetate contains NLT 98.0% and NMT 102.0% of flecainide acetate ($C_{17}H_{20}F_6N_2O_3 \cdot C_2H_4O_2$), calculated on the dried basis.

## IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*⟨197⟩:** [Note—Methods described in ⟨197K⟩ or ⟨197A⟩ may be used.]
- **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**

  **Solution:** 130 µg/mL in alcohol

  **Analytical wavelength:** 298 nm

  **Acceptance criteria:** Absorptivities, calculated on the dried basis, do not differ by more than 3.0%.
- **C.** 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:** 0.1 M ammonium acetate in water. Adjust with acetic acid to a pH of 5.4.

  **Solution B:** Acetonitrile

  **Mobile phase:** See *Table 1*.

**Table 1**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 75 | 25 |
| 7.0 | 45 | 55 |
| 12.0 | 45 | 55 |
| 12.1 | 75 | 25 |
| 15.0 | 75 | 25 |

**Diluent:** Acetonitrile and water (25:75)

**Standard solution:** 0.2 mg/mL of USP Flecainide Acetate RS in *Diluent*. Sonication may be needed for complete dissolution.

**Sample solution:** 0.2 mg/mL of Flecainide Acetate in *Diluent*. Sonication may be needed for complete dissolution.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 300 nm

**Column:** 3.0-mm × 15-cm; 3-µm packing L1

**Flow rate:** 0.5 mL/min

**Injection volume:** 10 µL

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 0.73%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of flecainide acetate ($C_{17}H_{20}F_6N_2O_3 \cdot C_2H_4O_2$) in the portion of Flecainide Acetate taken:

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

$r_U$ = peak response of flecainide from the *Sample solution*

$r_S$ = peak response of flecainide from the *Standard solution*

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

$C_U$ = concentration of Flecainide Acetate in the *Sample solution* (mg/mL)

**Acceptance criteria:** 98.0%–102.0% on the dried basis

## OTHER COMPONENTS

• **Content of Acetate**

**Sample solution:** Dissolve about 600 mg of Flecainide Acetate in about 100 mL of dimethylformamide, and stir by mechanical means until dissolved.

**Titrimetric system**

(See *Titrimetry ⟨541⟩*.)

**Mode:** Direct titration

**Titrant:** 0.1 N tetrabutylammonium hydroxide VS

**Endpoint detection:** Potentiometric

**Analysis:** Perform a blank determination and make any necessary correction. Each mL of 0.1 N tetrabutylammonium hydroxide is equivalent to 6.005 mg of acetic acid ($C_2H_4O_2$).

**Acceptance criteria:** 12.4%–12.8% on the dried basis

## IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

• **Organic Impurities**

**Solution A, Solution B, Mobile phase, Diluent,** and **Chromatographic system:** Proceed as directed in the *Assay*.

**System suitability solution:** 0.25 mg/mL of USP Flecainide Acetate RS and 0.1 mg/mL of flecainide acid in *Diluent*

**Sensitivity solution:** 0.001 mg/mL of USP Flecainide Acetate RS in *Diluent*

**Standard solution:** 0.01 mg/mL each of USP Flecainide Acetate RS and USP Flecainide Related Compound A RS in *Diluent*

**Sample solution:** 2.0 mg/mL of Flecainide Acetate in *Diluent*. Sonication may be needed for complete dissolution.

**System suitability**

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

[Note—See *Table 2* for relative retention times.]

**Suitability requirements**

**Resolution:** NLT 5.0 between flecainide acetate and flecainide acid, *System suitability solution*

**Relative standard deviation:** NMT 5.0%, *Standard solution*

**Signal-to-noise ratio:** NLT 50, *Sensitivity solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of flecainide related compound A in the portion of Flecainide Acetate taken:

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

$r_U$ = peak response of flecainide related compound A from the *Sample solution*

$r_S$ = peak response of flecainide related compound A from the *Standard solution*

$C_S$ = concentration of USP Flecainide Related Compound A RS in the *Standard solution* (mg/mL)

$C_U$ = concentration of Flecainide Acetate in the *Sample solution* (mg/mL)

Calculate the percentage of each specified or unspecified impurity in the portion of Flecainide Acetate taken:

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

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

$r_S$ = peak response of flecainide acetate from the *Standard solution*

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

$C_U$ = concentration of Flecainide Acetate in the *Sample solution* (mg/mL)

$F$ = relative response factor (see *Table 2*)

**Acceptance criteria:** See *Table 2*. The reporting threshold is 0.05%.

**Table 2**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Flecainide acid[a] | 0.8 | 0.67 | 0.5 |
| Flecainide | 1.0 | — | — |
| Flecainide related compound A | 1.2 | — | 0.5 |
| Flecainide pyridine analog[b] | 1.6 | 1.0 | 0.5 |
| Any individual unspecified impurity | — | — | 0.10 |
| Total impurities | — | — | 2.0 |

[a] 2,5-Bis(2,2,2-trifluoroethoxy)benzoic acid.

[b] *N*-(Pyridin-2-ylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)benzamide.

## SPECIFIC TESTS

• **Loss on drying** ⟨731⟩

**Analysis:** Dry under vacuum at a pressure not exceeding 5 mm of mercury at 60° for 2 h.

**Acceptance criteria:** NMT 0.5%

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

***Change to read:***

• **USP Reference standards** ⟨11⟩

USP Flecainide Acetate RS

USP Flecainide Related Compound A RS

3-[2,5-Bis(2,2,2-trifluoroethoxy)phenyl]-1,5,6,7,8,8a-hexahydroimidazo[1,5-*a*]pyridine hydrochloride.

$C_{17}H_{18}F_6N_2O_2 \cdot HCl$ ▲432.79▲ (CN 1-Aug-2024)

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| FLECAINIDE ACETATE | Documentary Standards Support | SM22020 Small Molecules 2 |

**Chromatographic Database Information:** Chromatographic Database

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