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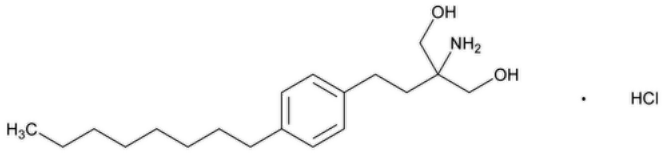
Fingolimod Hydrochloride



$C_{19}H_{33}NO_2 \cdot HCl$ 343.93

1,3-Propanediol, 2-amino-2-[2-(4-octylphenyl)ethyl]-, hydrochloride;

2-Amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride CAS RN®: 162359-56-0.

Fingolimod (free base)

$C_{19}H_{33}NO_2$ 307.48 CAS RN®: 162359-55-9.

DEFINITION

Fingolimod Hydrochloride contains NLT 98.0% and NMT 102.0% of fingolimod hydrochloride ($C_{19}H_{33}NO_2 \cdot HCl$), calculated on an anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

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

• **C.** Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*

ASSAY

• **Procedure**

Solution A: 0.1% phosphoric acid in water

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Acetonitrile (%)
0	80	20
20	5	95
23	5	95
23.1	80	20
33	80	20

Diluent: Acetonitrile and *Solution A* (1:1)

Standard solution: 0.6 mg/mL of USP Fingolimod Hydrochloride RS in *Diluent*

Sample solution: 0.6 mg/mL of Fingolimod Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 3-mm × 15-cm; 3-µm packing L1

Column temperature: 40°

Flow rate: 0.8 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 0.73%

Tailing factor: NMT 5

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fingolimod hydrochloride ($C_{19}H_{33}NO_2 \cdot HCl$) in the portion of Fingolimod Hydrochloride 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 Fingolimod Hydrochloride RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on an anhydrous and solvent-free basis

IMPURITIES

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

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

System suitability solution: 0.6 mg/mL of USP Fingolimod System Suitability Mixture RS in *Diluent*

Standard stock solution: Use the *Standard solution* from the *Assay*.

Standard solution: 0.003 mg/mL of USP Fingolimod Hydrochloride RS from the *Standard stock solution* in *Diluent*

Sensitivity solution: 0.3 µg/mL of USP Fingolimod Hydrochloride RS from the *Standard solution* in *Diluent*

System suitability

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

[Note—The relative retention times of fingolimod and *O*-acetyl fingolimod are about 1.00 and 1.11, respectively.]

Suitability requirements

Resolution: NLT 1.2 between *O*-acetyl fingolimod and fingolimod nonyl homolog; NLT 0.8 between 2-phenethyl fingolimod analog and 3-phenethyl fingolimod analog, *System suitability solution*

Relative standard deviation: NMT 10%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each individual impurity in the portion of Fingolimod Hydrochloride taken:

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

r_U = peak area of each impurity from the *Sample solution*

r_S = peak area of fingolimod hydrochloride from the *Standard solution*

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

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

F = relative response factor for each individual impurity (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 (%)
Fingolimod hexyl homolog	0.82	1.1	0.5
Fingolimod heptyl homolog	0.93	1.0	0.2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Fingolimod	1.00	—	—
Fingolimod nonyl homolog	1.13	1.0	0.2
Fingolimod decyl homolog	1.23	1.0	0.5
3-Phenethyl fingolimod analog	1.97	1.3	0.2
2-Phenethyl fingolimod analog	2.00	1.4	0.2
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** NMT 0.5%

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count is NMT 10^3 cfu/g. The total combined molds and yeasts count is NMT 10^2 cfu/g.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store below 30° in a dry place.

• **USP Reference Standards ⟨11⟩**

USP Fingolimod Hydrochloride RS

USP Fingolimod System Suitability Mixture RS

It contains Fingolimod Hydrochloride and small amounts of the following impurities:

O-Acetyl fingolimod;
2-Amino-2-(hydroxymethyl)-4-(4-octylphenyl)butyl acetate. $C_{21}H_{35}NO_3$ 349.51

Fingolimod decyl homolog;
2-Amino-2-(4-decylphenethyl)propane-1,3-diol. $C_{21}H_{37}NO_2$ 335.53

Fingolimod heptyl homolog;
2-Amino-2-(4-heptylphenethyl)propane-1,3-diol. $C_{18}H_{31}NO_2$ 293.45

Fingolimod hexyl homolog;
2-Amino-2-(4-hexylphenethyl)propane-1,3-diol. $C_{17}H_{29}NO_2$ 279.42

Fingolimod nonyl homolog;
2-Amino-2-(4-nonylphenethyl)propane-1,3-diol. $C_{20}H_{35}NO_2$ 321.51

2-Phenethyl fingolimod analog;
2-Amino-2-[4-octyl-2-(4-octylphenethyl)phenethyl]propane-1,3-diol. $C_{35}H_{57}NO_2$ 523.85

3-Phenethyl fingolimod analog;
2-Amino-2-[4-octyl-3-(4-octylphenethyl)phenethyl]propane-1,3-diol. $C_{35}H_{57}NO_2$ 523.85

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

Topic/Question	Contact	Expert Committee
FINGOLIMOD HYDROCHLORIDE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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