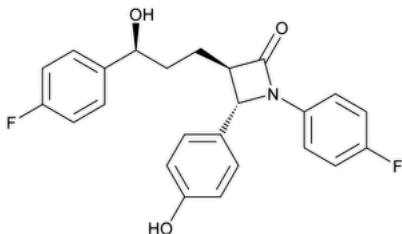


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Ezetimibe



$C_{24}H_{21}F_2NO_3$ 409.43
2-Azetidinone, 1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)-, [3R-[3α(S*),4β]]-;
(3R,4S)-1-(p-Fluorophenyl)-3-[(3S)-3-(p-fluorophenyl)-3-hydroxypropyl]-4-(p-hydroxyphenyl)-2-azetidinone;
(3R,4S)-1-(4-Fluorophenyl)-3-[(S)-3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)-azetidin-2-one CAS RN®: 163222-33-1; UNII:
EOR26LQQ24.

DEFINITION
Ezetimibe contains NLT 98.0% and NMT 102.0% of ezetimibe ($C_{24}H_{21}F_2NO_3$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A or 197M
- **B.** The ratio of the retention time of the ezetimibe peak of the *Sample solution* to that of the *System suitability solution* obtained in *Organic Impurities, Procedure 2* is between 0.97 and 1.03.

ASSAY

Change to read:

PROCEDURE

Solution A: [Water](#)

Solution B: [Acetonitrile](#)

Solution C: [Methanol](#)

Mobile phase: See [Table 1](#). ▲Adjust the percentages of *Solution A* and *Solution B* to achieve a retention time of about 33 min for the ezetimibe peak. The percentage of *Solution C* should remain unchanged.

[NOTE—Ezetimibe and related impurities are sensitive to small variations in *Mobile phase* composition, which may affect resolution and retention characteristics.]▲ (USP 1-Aug-2024)

Table 1

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
0	▲66▲ (USP 1-Aug-2024)	▲24▲ (USP 1-Aug-2024)	10
37	▲66▲ (USP 1-Aug-2024)	▲24▲ (USP 1-Aug-2024)	10
60	40	50	10
70	40	50	10
80	10	80	10
90	10	80	10
90.1	▲66▲ (USP 1-Aug-2024)	▲24▲ (USP 1-Aug-2024)	10

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
100	▲66▲ (USP 1-Aug-2024)	▲24▲ (USP 1-Aug-2024)	10

Diluent: [Acetonitrile](#), [methanol](#), and [water](#) ▲(27:10:63).▲ (USP 1-Aug-2024) Add 1.0 mL of [glacial acetic acid](#) per each liter of the mixture.

Standard solution: 0.25 mg/mL of [USP Ezetimibe RS](#) prepared as follows. Transfer a suitable amount of [USP Ezetimibe RS](#) to a suitable volumetric flask. Dissolve in about 1%–2% of the flask volume of [acetonitrile](#), and dilute with *Diluent* to volume. [NOTE—The *Standard solution* contains a detectable level of o-fluorobenzene isomer (approximately 0.04%) from [USP Ezetimibe RS](#).]

Sample solution: 0.25 mg/mL of Ezetimibe prepared as follows. Transfer a suitable amount of Ezetimibe to a suitable volumetric flask. Dissolve in about 1%–2% of the flask volume of [acetonitrile](#), and dilute with *Diluent* to volume.

Chromatographic system
(See [Chromatography \(621\), System Suitability.](#))

- Mode:** LC
 - Detectors**
 - 0–5 min:** UV 215 nm
 - 5–100 min:** UV 248 nm
 - Column:** 4.6-mm × 15-cm; 5-µm packing [L43](#)
 - Flow rate:** 2 mL/min
 - Injection volume:** 60 µL
- System suitability**
- Sample:** *Standard solution*
 - Suitability requirements**
 - Tailing factor:** NMT 1.5 for ezetimibe
 - Relative standard deviation:** NMT 0.73% for ezetimibe

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of ezetimibe ($C_{24}H_{21}F_2NO_3$) in the portion of Ezetimibe taken:

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

- r_U = peak response of ezetimibe from the *Sample solution*
- r_S = peak response of ezetimibe from the *Standard solution*
- C_S = concentration of [USP Ezetimibe RS](#) in the *Standard solution* (mg/mL)
- C_U = concentration of Ezetimibe in the *Sample solution* (mg/mL)

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

IMPURITIES
• [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%

Change to read:
• **ORGANIC IMPURITIES, PROCEDURE 1**

▲**Solution A, Solution B, Solution C,**▲ (USP 1-Aug-2024) **Mobile phase, Diluent, Standard solution, Sample solution, and Chromatographic system:** Proceed as directed in the Assay.

Sensitivity solution: 0.125 µg/mL of [USP Ezetimibe RS](#) from the *Standard solution* in *Diluent*

System suitability
Samples: *Standard solution* and *Sensitivity solution*
▲[NOTE—The relative retention times in [Table 2](#) are provided as information that could aid in peak assignment.]

Table 2▲ (USP 1-Aug-2024)

Name	Relative Retention Time
Desfluoroaniline analog ^a	0.72
Ezetimibe diastereomers ^b	