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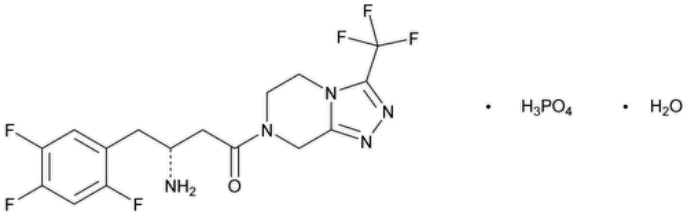
Sitagliptin Phosphate



$C_{16}H_{15}F_6N_5O \cdot H_3PO_4 \cdot H_2O$ 523.33
$C_{16}H_{15}F_6N_5O \cdot H_3PO_4$ 505.31

1,2,4-Triazolo[4,3-*a*]pyrazine, 7-[(3*R*)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, phosphate (1:1) monohydrate;
7-[(*R*)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-*a*]pyrazine monophosphate monohydrate;
(3*R*)-3-Amino-1-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl]-4-(2,4,5-trifluorophenyl)butan-1-one phosphate monohydrate CAS RN®: 654671-77-9; UNII: TS63EW8X6F.

DEFINITION

Sitagliptin Phosphate contains NLT 98.0% and NMT 102.0% of sitagliptin phosphate ($C_{16}H_{15}F_6N_5O \cdot H_3PO_4$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

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

[Note—If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in dehydrated alcohol, evaporate to dryness, and record new spectra using the residues.]

• **B.** Meets the requirements of the test for *Enantiomeric Purity*

• **C. Identification Tests—General ⟨191⟩, *Phosphate*:** A solution containing about 40 mg/mL in water meets the requirements of test *A* of Orthophosphates.

ASSAY

• **Procedure**

Buffer: 1.36 g/L of monobasic potassium phosphate, adjusted with phosphoric acid to a pH of 2.0

Mobile phase: Acetonitrile and *Buffer* (15:85)

Dilute phosphoric acid: Transfer 1 mL of phosphoric acid to a 1-L volumetric flask, and dilute with water to volume.

Diluent: Acetonitrile and *Dilute phosphoric acid* (5:95)

Standard solution: 0.1 mg/mL of USP Sitagliptin Phosphate RS in *Diluent*

Sample solution: 0.1 mg/mL of Sitagliptin Phosphate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 205 nm

Column: 4.6-mm × 15-cm; 5-µm packing L10

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

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Suitability requirements

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of sitagliptin phosphate ($C_{16}H_{15}F_6N_5O \cdot H_3PO_4$) in the portion of Sitagliptin Phosphate taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

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

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer, Mobile phase, Dilute phosphoric acid, Diluent, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: Place 10 mg of Sitagliptin Phosphate and 1 mg of sodium stearyl fumarate into a vial, add 1 mL of water, and tightly seal the vial. Heat at 80° for about 30 h to generate a fumarate adduct of sitagliptin. [Note—The chemical name of fumarate adduct of sitagliptin is 2-[[(*R*)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl]-1-(2,4,5-trifluorophenyl)butan-2-yl]amino]succinic acid.] Transfer the content of the vial into a 100-mL volumetric flask using a small amount of *Diluent*, and dilute with *Diluent* to volume. Mix well by stirring for 1 h. Centrifuge a portion of the solution for 10 min or until the solution is clear, and use the supernatant.

Standard solution: 0.0001 mg/mL of USP Sitagliptin Phosphate RS in *Diluent*

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for sitagliptin and fumarate adduct of sitagliptin are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 1.5 between sitagliptin and fumarate adduct of sitagliptin

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each impurity in the portion of Sitagliptin Phosphate taken:

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

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

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

C_S = concentration of ▲USP Sitagliptin Phosphate RS▲ (ERR 1-Jul-2023) in the *Standard solution* (mg/mL)

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

Acceptance criteria: Disregard any peak below 0.05%.

Any individual impurity: NMT 0.10%

Total impurities: NMT 0.5%

• **Enantiomeric Purity**

Mobile phase: Dehydrated alcohol, chromatographic *n*-heptane, diethylamine, and water (600:400:1:1)

Diluent: Methanol and water (9:1)

System suitability solution: 8 mg/mL of USP Sitagliptin System Suitability Mixture RS in *Diluent*

Sample solution: 8 mg/mL of Sitagliptin Phosphate in *Diluent*

Sensitivity solution: 8 µg/mL of Sitagliptin Phosphate in *Diluent* from the *Sample solution*

Chromatographic system

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

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Mode: LC

Detector: UV 268 nm

Column: 4.6-mm × 25-cm; 5-µm packing L51

Column temperature: 35°

Flow rate: 0.8 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention times for sitagliptin, which is the *R*-enantiomer, and the *S*-enantiomer are 1.0 and 0.9, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the *S*-enantiomer and sitagliptin, *System suitability solution*

Signal-to-noise ratio: NLT 10 for the sitagliptin peak, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of *S*-enantiomer in the portion of Sitagliptin Phosphate taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of the *S*-enantiomer from the *Sample solution*

r_T = sum of the peak responses of the *S*-enantiomer and sitagliptin from the *Sample solution*

Acceptance criteria: NMT 0.5% of the *S*-enantiomer

SPECIFIC TESTS

• **WATER DETERMINATION,** *Method Ia* ⟨921⟩**:** 3.3%–3.7%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at room temperature.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Sitagliptin Phosphate RS

USP Sitagliptin System Suitability Mixture RS

Sitagliptin Phosphate containing *S*-enantiomer.

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

Topic/Question	Contact	Expert Committee
SITAGLIPTIN PHOSPHATE	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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