Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Apr-2024
Document Type: USP Monographs
DocId: GUID-6396D7AC-ABBE-49ED-B8F5-C213E832E46B_4_en-US
DOI: https://doi.org/10.31003/USPNF_M4978_04_01
DOI Ref: voje0

Sitagliptin Tablets

DEFINITION

Sitagliptin Tablets contain an amount of sitagliptin phosphate ($C_{16}H_{15}F_6N_5O \cdot H_3PO_4$) equivalent to NLT 95.0% and NMT 105.0% of the labeled amount of sitagliptin ($C_{16}H_{15}F_6N_5O$).

IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **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

Change to read:

- **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)

▲Solution A▲ (IRA 1-Apr-2024) : Transfer 1 mL of phosphoric acid to a 1-L volumetric flask, and dilute with water to volume.

Diluent: Acetonitrile and ▲*Solution A*▲ (IRA 1-Apr-2024) (5:95)

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

Sample stock solution: Nominally 1.0 mg/mL of sitagliptin, prepared as follows. Place 10 Tablets in a suitable volumetric flask, and dilute with *Diluent* to volume. Add a stir bar and stir vigorously for 1 h, ensuring that a vortex is achieved during stirring.

Sample solution: Nominally 0.08 mg/mL of sitagliptin, prepared as follows. Transfer 8.0 mL of the *Sample stock solution* to a 100-mL volumetric flask, and dilute with *Diluent* to volume. Centrifuge a portion of the solution for 10 min or until the solution is clear, and use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 205 nm. For *Identification A* use a diode array detector in the range of 210–400 nm.

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

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT ▲1.0%▲ (IRA 1-Apr-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sitagliptin ($C_{16}H_{15}F_6N_5O$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak ▲response of sitagliptin▲ (IRA 1-Apr-2024) from the *Sample solution*

r_S = peak ▲response of sitagliptin▲ (IRA 1-Apr-2024) from the *Standard solution*

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

C_U = nominal concentration of sitagliptin in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of sitagliptin, 407.32

M_{r2} = molecular weight of anhydrous sitagliptin phosphate, 505.31

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩**

Time: 5 min

Acceptance criteria: Meet the requirements

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer, Mobile phase, ▲Solution A▲ (IRA 1-Apr-2024), Diluent, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution (*Procedure 1* may be used for Tablets containing sodium stearyl fumarate as an excipient in the formulation, and *Procedure 2* may be used for all products.)

Procedure 1: Place 1 Tablet of any potency 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▲, *N*-succinyl sitagliptin.▲ (IRA 1-Apr-2024) Transfer the contents 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. If needed, further dilute with *Diluent* to obtain a solution with a concentration of 0.08 mg/mL of sitagliptin, based on the label claim of the Tablet. Centrifuge a portion of the solution for 10 min or until the solution is clear, and use the supernatant.

Procedure 2: Place 10 mg of USP Sitagliptin Phosphate RS 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▲, *N*-succinyl sitagliptin.▲ (IRA 1-Apr-2024) Transfer the contents 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: 0.0002 mg/mL of USP Sitagliptin Phosphate RS in *Diluent*

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

System suitability

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

▲[Note—The relative retention times in *Table 1* are provided as information that could aid in peak assignment.]

Table 1▲ (IRA 1-Apr-2024)

Name	Relative Retention Time
Sitagliptin acid[a]	0.55
Sitagliptin	1.0
▲*N*-succinyl sitagliptin▲ (IRA 1-Apr-2024) (if present)[b,c]	1.2
Sitagliptin triazecine analog[d]	1.8
Sitagliptin phenylcrotonyl analog[e]	▲4.1▲ (IRA 1-Apr-2024)
Sitagliptin styrylacetyl analog[f]	▲4.7▲ (IRA 1-Apr-2024)

[a] (*R*)-3-Amino-4-(2,4,5-trifluorophenyl)butanoic acid.

[b] 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.

[c] This degradation product may be present only for Tablets containing sodium stearyl fumarate as an excipient in the formulation.

[d] 10-(2,4,5-Trifluorobenzyl)-3-(trifluoromethyl)-6,7,10,11-tetrahydro-[1,2,4]triazolo[3,4-*c*][1,4,7]triazecine-8,12(5*H*,9*H*)-dione.

[e] (*E*)-1-{3-(Trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl}-4-(2,4,5-trifluorophenyl)but-2-en-1-one.

[f] (*E*)-1-{3-(Trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl}-4-(2,4,5-trifluorophenyl)but-3-en-1-one.

Suitability requirements

Resolution: NLT 1.5 between sitagliptin and ▲*N*-succinyl sitagliptin,▲ (IRA 1-Apr-2024) *System suitability solution*

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

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of ▲any degradation product▲ (IRA 1-Apr-2024) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of each ▲degradation product▲ (IRA 1-Apr-2024) from the *Sample solution*

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

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

C_U = nominal concentration of sitagliptin in the *Sample solution* (mg/mL)

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

M_{r1} = molecular weight of sitagliptin, 407.32

M_{r2} = molecular weight of anhydrous sitagliptin phosphate, 505.31

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Sitagliptin acid▲▲ (IRA 1-Apr-2024)	0.65	0.2
▲▲ (IRA 1-Apr-2024)	▲▲ (IRA 1-Apr-2024)	▲▲ (IRA 1-Apr-2024)
▲*N*-succinyl sitagliptin▲ (IRA 1-Apr-2024) (if present)▲▲ (IRA 1-Apr-2024)	1.0	0.2
Sitagliptin triazecine analog▲▲ (IRA 1-Apr-2024)	1.0	0.2
Sitagliptin phenylcrotonyl analog▲▲ (IRA 1-Apr-2024)	▲1.0▲ (IRA 1-Apr-2024)	0.2
Sitagliptin styrylacetyl analog▲▲ (IRA 1-Apr-2024)	▲2.1▲ (IRA 1-Apr-2024)	0.2
Any ▲unspecified degradation product▲ (IRA 1-Apr-2024)	1.0	0.2

Name	Relative Response Factor	Acceptance Criteria, NMT (%)
Total ▲degradation products▲ (IRA 1-Apr-2024)	—	0.6

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩
  USP Sitagliptin Phosphate RS

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

Topic/Question	Contact	Expert Committee
SITAGLIPTIN TABLETS	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:
Pharmacopeial Forum: Volume No. 49(5)

Current DocID: GUID-6396D7AC-ABBE-49ED-B8F5-C213E832E46B_4_en-US

DOI: https://doi.org/10.31003/USPNF_M4978_04_01

DOI ref: voje0