Edition: BP 2025 (Ph. Eur. 11.6 update)

# Sitagliptin Tablets

General Notices

*(Ph. Eur. monograph 2927)*

**Action and use**

Dipeptidylpeptidase-4 inhibitor; treatment of diabetes mellitus.

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## DEFINITION

Tablets containing *Sitagliptin phosphate monohydrate (2778)*, for human use.

*They comply with the monograph Tablets (0478) and the following additional requirements*.

**Content**

95.0 per cent to 105.0 per cent of the content of sitagliptin ($C_{16}H_{15}F_6N_5O$) stated on the label.

## IDENTIFICATION

*Carry out either tests A, B or tests B, C.*

A. Record the UV spectrum of the principal peak in the chromatograms obtained with the solutions used in the assay, with a diode array detector in the range of 210-400 nm.

*Results* The UV spectrum of the principal peak in the chromatogram obtained with the test solution is similar to the UV spectrum of the principal peak in the chromatogram obtained with reference solution (a).

B. Examine the chromatograms obtained in the assay.

*Results* The principal peak in the chromatogram obtained with the test solution is similar in retention time and size to the principal peak in the chromatogram obtained with reference solution (a).

C. Infrared absorption spectrophotometry (*2.2.24*).

*Preparation* Crush 1 tablet to a powder and homogenise.

*Comparison* *sitagliptin phosphate monohydrate CRS*.

*Results* The spectrum obtained shows absorption maxima at about 1669 $cm^{-1}$, 1513 $cm^{-1}$, 1425 $cm^{-1}$, 1207 $cm^{-1}$, 880 $cm^{-1}$ and 844 $cm^{-1}$, similar to the spectrum obtained with *sitagliptin phosphate monohydrate CRS*. Additional absorption bands may be present.

## TESTS

**Related substances**

Liquid chromatography (2.2.29).

*Solvent mixture* acetonitrile R, 0.1 per cent *V/V* solution of phosphoric acid R (5:95 *V/V*).

*Test solution* To 10 tablets, add a suitable volume of the solvent mixture to obtain a concentration of sitagliptin of 1 mg/mL. Stir vigorously for 1 h. Dilute 2.0 mL of the solution to 25.0 mL with the solvent mixture. Centrifuge a portion of the solution and use the clear supernatant.

*Reference solution (a)* Dissolve 25.0 mg of sitagliptin phosphate monohydrate CRS in the solvent mixture and dilute to 250.0 mL with the solvent mixture.

*Reference solution (b)* Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

*Reference solution (c)* In order to prepare impurity FP-A (fumarate adduct) *in situ*, heat 1 mL of water R and either 1 sitagliptin tablet containing sodium stearyl fumarate as an excipient or 1 mg of sodium stearyl fumarate R and 10 mg of sitagliptin phosphate monohydrate CRS in a tightly closed vial at 80 °C for about 30 h. Dilute to 100 mL with the solvent mixture and stir for 1 h. If using a tablet, dilute with the solvent mixture to obtain a concentration of sitagliptin of 0.08 mg/mL. Centrifuge a portion of the solution and use the clear supernatant.

*Column*:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: end-capped cyanosilyl silica gel for chromatography R (5 µm);

— *temperature*: 30 °C.

*Mobile phase* Mix 15 volumes of acetonitrile R1 and 85 volumes of a 1.36 g/L solution of potassium dihydrogen phosphate R previously adjusted to pH 2.0 with phosphoric acid R.

*Flow rate* 1.0 mL/min.

*Detection* Spectrophotometer at 205 nm.

*Injection* 20 µL of the test solution and reference solutions (b) and (c).

*Run time* 7 times the retention time of sitagliptin.

*Identification of impurities* Use the chromatogram obtained with reference solution (c) to identify the peak due to impurity FP-A.

*Relative retention* With reference to sitagliptin (retention time = about 5.5 min): impurity FP-A = about 1.2.

*System suitability* Reference solution (c):

— resolution: minimum 1.5 between the peaks due to sitagliptin and impurity FP-A.

*Calculation of percentage contents*:

— for each impurity, use the concentration of sitagliptin in reference solution (b).

*Limits*:

— *unspecified impurities*: for each impurity, maximum 0.2 per cent;

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 0.1 per cent.

## Disintegration

[1] (2.9.1).

*Medium* water R.

*Time* 5 min.

## ASSAY

Liquid chromatography (2.2.29) as described in the test for related substances with the following modifications.

*Injection* Test solution and reference solution (a).

*Run time* Twice the retention time of sitagliptin.

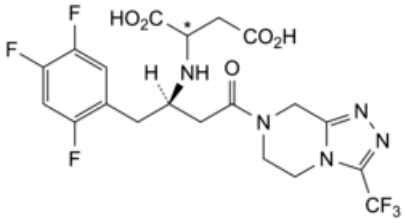
*System suitability* Reference solution (a):

— *repeatability*: maximum relative standard deviation of 1.5 per cent determined on 6 injections.

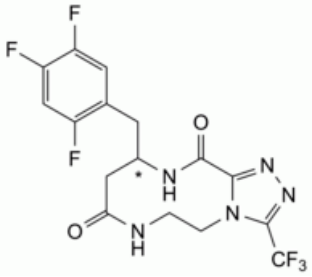
Calculate the percentage content of sitagliptin ($C_{16}H_{15}F_6N_5O$) taking into account the assigned content of *sitagliptin phosphate monohydrate CRS* and applying a conversion factor of 0.806.

## IMPURITIES

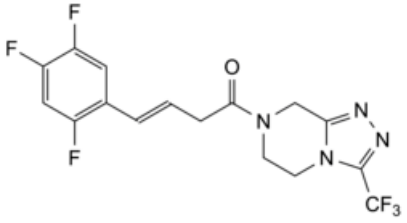
*Other detectable impurities* (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph)*: FP-A, FP-B, FP-C, FP-D, FP-E*.



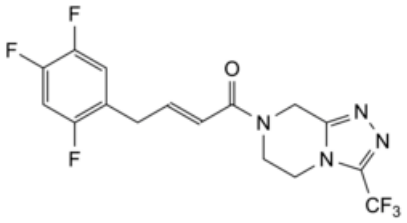
FP-A. 2-[[(2*R*)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl]-1-(2,4,5-trifluorophenyl)butan-2-yl]amino]butanedioic acid,



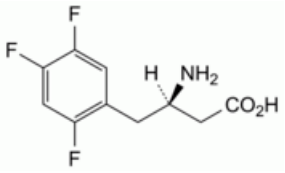
FP-B. 3-(trifluoromethyl)-10-[(2,4,5-trifluorophenyl)methyl]-6,7,10,11-tetrahydro[1,2,4]triazolo[3,4-*c*][1,4,7]triazecine-8,12(5*H*,9*H*)-dione,



FP-C. (3*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,



FP-D. (2*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,



FP-E. (3*R*)-3-amino-4-(2,4,5-trifluorophenyl)butanoic acid.

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[1] The test approved in the marketing authorisation is to be used for routine quality control to confirm batch-to-batch consistency. For more information please consult Ph. Eur. *1. General Notices*.