

Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Aug-2024
Document Type: USP Monographs
DocId: GUID-8B2B4B9B-295B-428B-A8BD-F8629BDF376E_10_en-US
DOI: https://doi.org/10.31003/USPNF_M12279_10_01
DOI Ref: 82xe6

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Candesartan Cilexetil and Hydrochlorothiazide Tablets

DEFINITION

Candesartan Cilexetil and Hydrochlorothiazide Tablets contain NLT 90.0% and NMT 110.0% each of the labeled amount of candesartan cilexetil ($C_{33}H_{34}N_6O_6$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$).

IDENTIFICATION

- **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.
- **B.** The UV absorption spectra of the major peaks of the *Sample solution* exhibit maxima and minima at the same wavelengths as those of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

• **PROCEDURE**

Solution A: ▲ [Acetonitrile](#) and [water](#) (10:90). To each liter, add 1.0 mL of [trifluoroacetic acid](#).▲ (USP 1-Aug-2024)

Solution B: ▲ [Acetonitrile](#) and [water](#) (90:10). To each liter, add 1.0 mL of [trifluoroacetic acid](#).▲ (USP 1-Aug-2024)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
4	90	10
6	30	70
15	30	70
17	90	10
20	90	10

Diluent: [Acetonitrile](#) and [water](#) (70:30)

Standard solution: Prepare solutions of [USP Candesartan Cilexetil RS](#) and [USP Hydrochlorothiazide RS](#) in *Diluent* as follows, at concentrations as given in [Table 2](#). Transfer suitable amounts of [USP Candesartan Cilexetil RS](#) and [USP Hydrochlorothiazide RS](#) to a suitable volumetric flask. Add *Diluent* to about 50% of the total volume and sonicate to dissolve. Dilute with *Diluent* to volume.▲ (USP 1-Aug-2024)

Table 2

Tablet Strength Candesartan Cilexetil/Hydrochlorothiazide (mg/mg)	Concentration of ▲ USP Candesartan Cilexetil RS ▲ (USP 1-Aug-2024) (mg/mL)	Concentration of ▲ USP Hydrochlorothiazide RS ▲ (USP 1-Aug-2024) (mg/mL)
16/12.5	0.32	0.25
32/12.5	0.64	0.25
32/25	0.32	0.25

Sample solution: Nominally equivalent to the concentrations as given in [Table 2](#), prepared as follows. Transfer NLT 5 Tablets to a suitable volumetric flask. Add *Diluent* to about 60% of the total volume and sonicate for about 25 min with intermittent shaking. Cool to room temperature and dilute with *Diluent* to volume. Pass through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 282 nm. For *Identification B*, use a diode array detector ▲ in the range of 210–400 nm.▲ (USP 1-Aug-2024)

Column: 4.6-mm × 15-cm; 5-µm packing [L7](#)

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

▲[NOTE—The relative retention times for hydrochlorothiazide and candesartan cilexetil are 0.4 and 1.0, respectively.]▲ (USP 1-Aug-2024)

Suitability requirements

Tailing factor: NMT 2.0 for candesartan cilexetil and hydrochlorothiazide

Relative standard deviation: NMT ▲1.0%▲ (USP 1-Aug-2024) for candesartan cilexetil and hydrochlorothiazide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of candesartan cilexetil (C₃₃H₃₄N₆O₆) and hydrochlorothiazide (C₇H₈ClN₃O₄S₂) in the portion of Tablets taken:

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

r_U = peak response of candesartan cilexetil or hydrochlorothiazide from the *Sample solution*

r_S = peak response of candesartan cilexetil or hydrochlorothiazide from the *Standard solution*

C_S = concentration of [USP Candesartan Cilexetil RS](#) or [USP Hydrochlorothiazide RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of candesartan cilexetil or hydrochlorothiazide in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#).

Medium

For Tablets labeled to contain 16 mg/12.5 mg of candesartan cilexetil/hydrochlorothiazide: 0.35% polysorbate 20 in 0.05 M phosphate buffer, pH 6.5 ▲(dissolve 6.8 g of [potassium phosphate, monobasic](#) in a suitable container containing 500 mL of [water](#); add 3.5 mL of [polysorbate 20](#) and dilute with [water](#) to 1 L; adjust with 2 N sodium hydroxide solution to a pH of 6.5);▲ (USP 1-Aug-2024) 900 mL

For Tablets labeled to contain 32 mg/12.5 mg and 32 mg/25 mg of candesartan cilexetil/hydrochlorothiazide: 0.70% polysorbate 20 in 0.05 M phosphate buffer, pH 6.5 ▲(dissolve 6.8 g of [potassium phosphate, monobasic](#) in a suitable container containing 500 mL of [water](#); add 7.0 mL of [polysorbate 20](#) and dilute with [water](#) to 1 L; adjust with 2 N sodium hydroxide solution to a pH of 6.5);▲ (USP 1-Aug-2024) 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Solution A and Solution B: Prepare as directed in the Assay.

Mobile phase: See [Table 3](#).

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	80	20
3.0	80	20
5.0	30	70

Time (min)	Solution A (%)	Solution B (%)
10.0	30	70
13.0	80	20
16.0	80	20

Standard stock solution A: 0.72 mg/mL of [USP Candesartan Cilexetil RS](#) in [acetonitrile](#). ▲Sonicate to dissolve, if necessary.▲ (USP 1-Aug-2024)

Standard stock solution B: 0.28 mg/mL of [USP Hydrochlorothiazide RS](#) in [acetonitrile](#). ▲Sonicate to dissolve, if necessary.▲ (USP 1-Aug-2024)

Standard solution: Prepare solutions of [USP Candesartan Cilexetil RS](#) and [USP Hydrochlorothiazide RS](#) from *Standard stock solution A* and *Standard stock solution B* in the appropriate *Medium*, at concentrations as given in [Table 4](#). ▲ (USP 1-Aug-2024)

Table 4

Tablet Strength Candesartan Cilexetil/Hydrochlorothiazide (mg/mg)	Concentration of ▲ USP Candesartan Cilexetil RS ▲ (USP 1-Aug-2024) (mg/mL)	Concentration of ▲ USP Hydrochlorothiazide RS ▲ (USP 1-Aug-2024) (mg/mL)
16/12.5	0.018	0.014
32/12.5	0.036	0.014
32/25	0.036	0.028

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 264 nm

Column: 4.6-mm × 15-cm; 5-µm packing [L7](#)

Autosampler temperature: 10°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for candesartan cilexetil and hydrochlorothiazide

Relative standard deviation: NMT 2.0% for candesartan cilexetil and hydrochlorothiazide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of candesartan cilexetil ($C_{33}H_{34}N_6O_6$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) dissolved:

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

r_U = peak response of candesartan cilexetil or hydrochlorothiazide from the *Sample solution*

r_S = peak response of candesartan cilexetil or hydrochlorothiazide from the *Standard solution*

C_S = concentration of [USP Candesartan Cilexetil RS](#) or [USP Hydrochlorothiazide RS](#) in the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) the labeled amount of candesartan cilexetil ($C_{33}H_{34}N_6O_6$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) are dissolved

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**