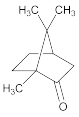
Limit of free undecylenic acid—Transfer 10 g of Calcium Undecylenate, accurately weighed, to a 400-mL beaker, add 250 mL of solvent hexane, and mix for 2 hours using a magnetic stirrer. Filter into a 500-mL flask, evaporate with the aid of a current of air to about 20 mL, and add 100 mL of neutralized alcohol. Add 3 drops of phenolphthalein TS, and titrate with 0.1 N sodium hydroxide VS. Each mL of 0.1 N sodium hydroxide is equivalent to 18.43 mg of $C_{11}H_{20}O_2$: not more than 0.1% is found.

Assay—Boil 40.0 mL of 0.1 N hydrochloric acid VS with about 600 mg of Calcium Undecylenate, accurately weighed, for 10 minutes, or until the undecylenic acid layer is clear, adding water, as necessary, to maintain the original volume. Transfer the mixture, with the aid of water, to a 500-mL separator. Dilute with water to about 75 mL, and extract with two 100-mL portions of solvent hexane. Wash the combined extracts with water until the last washing is neutral to litmus, add the washings to the original water layer. Cool, add 3 drops of methyl orange TS, and titrate the excess hydrochloric acid with 0.1 N sodium hydroxide VS. Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.1 N sodium hydroxide is equivalent to 20.33 mg of $C_{22}H_{38}O_4Ca$.

Camphor



$C_{10}H_{16}O$ 152.23
Bicyclo[2.2.1]heptane-2-one, 1,7,7-trimethyl-.
Camphor.
2-Bornanone [76-22-2].

» Camphor is a ketone obtained from *Cinnamomum camphora* (Linné) Nees et Ebermaier (Fam. Lauraceae) (Natural Camphor) or produced synthetically (Synthetic Camphor).

Packaging and storage—Preserve in tight containers, and avoid exposure to excessive heat.

Labeling—Label it to indicate whether it is obtained from natural sources or is prepared synthetically.

Melting range ⟨741⟩: between 174° and 179°.

Specific rotation ⟨781S⟩: between +41° and +43°, for natural Camphor.

Test solution: 100 mg per mL, in alcohol.
Synthetic Camphor is optically inactive.

Appearance of solution— A 1 in 10 solution in solvent hexane is clear.

Limit of nonvolatile residue—Heat 2.0 g in a tared dish on a steam bath until sublimation is complete. Then dry the residue at 120° for 3 hours, cool, and weigh: the weight of the residue does not exceed 1.0 mg (0.05%).

Halogens—Mix 100 mg of finely divided Camphor with 200 mg of sodium peroxide in a clean, dry, hard glass test tube of about 25-mm internal diameter and 20-cm length. Suspend the tube at an angle of about 45° by means of a clamp placed at the upper end, and gently heat the tube, starting near the upper end, but not heating the clamp, and gradually bringing the heat toward the lower part of the tube until incineration is complete. Dissolve the residue in 25 mL of warm water, acidify with nitric acid, and filter the solution into a comparison tube. Wash the test tube and the filter with two 10-mL portions of hot water, adding the washings to the filtered solution. To the filtrate add 0.50 mL of 0.10 N silver nitrate, dilute with water to 50 mL, and mix: the turbidity does not exceed that produced in a blank test with the same quantities of the same reagents and 0.050 mL of 0.020 N hydrochloric acid (0.035%).

Camphor Spirit

» Camphor Spirit is an alcohol solution containing, in each 100 mL, not less than 9.0 g and not more than 11.0 g of camphor ($C_{10}H_{16}O$).

Camphor	100 g
Alcohol, a sufficient quantity, to make	1000 mL

Dissolve the camphor in about 800 mL of the alcohol, and add alcohol to make 1000 mL. Filter, if necessary.

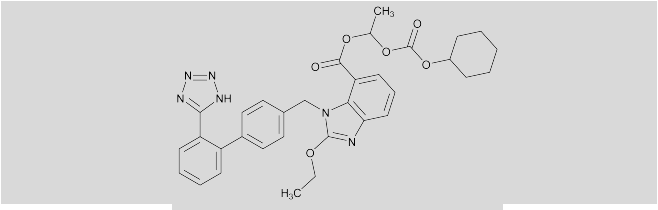
Packaging and storage—Preserve in tight containers.

Alcohol content, *Method II* ⟨611⟩: between 80.0% and 87.0% of C_2H_5OH, the dilution to approximately 2% alcohol being made with methanol instead of with water.

Assay—Transfer 2.0 mL of Camphor Spirit to a suitable pressure bottle containing 50 mL of freshly prepared dinitrophenylhydrazine TS. Close the pressure bottle, immerse it in a water bath, and maintain at about 75° for 16 hours. Cool to room temperature, and transfer the contents to a beaker with the aid of 100 mL of 3 N sulfuric acid. Allow to stand at room temperature for not less than 12 hours, transfer the precipitate to a tared filter crucible, and wash with 100 mL of 3 N sulfuric acid followed by 75 mL of cold water in divided portions. Continue the suction until the excess water is removed, dry the crucible and precipitate at 80° for 2 hours, cool, and weigh. The weight of the precipitate so obtained, multiplied by 0.4581, represents the weight of $C_{10}H_{16}O$ in the specimen taken.

Add the following:

▲Candesartan Cilexetil



$C_{33}H_{34}N_6O_6$
1*H*-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2′-(1*H*-tetrazol-5-yl)[1,1′-biphenyl]-4-yl]methyl]-, 1-[[(cyclohexyloxy)carbonyl]oxy]ethyl ester, (±);
(±)-1-Hydroxyethyl 2-ethoxy-1-[*p*-(*o*-1*H*-tetrazol-5-ylphenyl)benzyl]-7-benzimidazolecarboxylate, cyclohexyl carbonate (ester). 610.66
[145040-37-5].

DEFINITION
Candesartan Cilexetil contains NLT 98.7% and NMT 101.0% of $C_{33}H_{34}N_6O_6$, calculated on anhydrous basis.

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IDENTIFICATION

• **A. Infrared Absorption** ⟨197K⟩**:** If the spectra obtained show differences, proceed with the samples prepared as follows. Separately dissolve a quantity of USP Candesartan Cilexetil RS and Candesartan Cilexetil in alcohol. [NOTE—Heating the solution may be necessary for complete dissolution.] Cool the solution in an ice bath, filter the crystals, and dry at 105°.

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the procedure for *Organic Impurities*.

ASSAY

• **Procedure**

Sample solution: 8.33 mg/mL of Candesartan Cilexetil in glacial acetic acid

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Potentiometric

Titrant: 0.1 N perchloric acid

Analysis: Titrate with 8 mL of 0.1 N perchloric acid VS using a blank determination under the same conditions. Each mL of the *Titrant* is equivalent to 61.07 mg of $C_{33}H_{34}N_6O_6$.

Acceptance criteria: 98.7%–101.0% on the anhydrous basis

IMPURITIES

Inorganic Impurities

• **Residue on Ignition** ⟨281⟩**:** NMT 0.1%, determined from a 1-g sample

Organic Impurities

• **Procedure**

Diluent: Acetonitrile and water (3:2)

Solution A: Acetonitrile, glacial acetic acid, and water (57:1:43)

Solution B: Acetonitrile, glacial acetic acid, and water (90:1:10)

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	100	0
30	0	100

[NOTE—Equilibration for about 10 min may be necessary between injections.]

System suitability solution: 0.04 mg/mL of USP Candesartan Cilexetil RS and 0.125 mg/mL of acenaphthene in *Diluent*

Standard solution: 4 µg/mL of USP Candesartan Cilexetil RS in *Diluent*

Sample solution: 0.4 mg/mL of Candesartan Cilexetil in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1

Flow rate: 0.8 mL/min

Injection size: 10 µL

System suitability

[NOTE—The *Mobile phase* used for testing system suitability is 100% *Solution A* in an isocratic mode.]

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 5.0 between candesartan cilexetil and acenaphthene

Tailing factor: NMT 1.5 for candesartan cilexetil

Relative standard deviation: NMT 3.0% for the candesartan cilexetil peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Candesartan Cilexetil taken:

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

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

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

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

C_U = concentration of Candesartan Cilexetil in the *Sample solution* (mg/mL)

Acceptance criteria

Individual impurities: See *Table 1*.

Total impurities: NMT 0.6%. [NOTE—Calculate the total impurities from the sum of all impurity peaks greater than or equal to 0.05%.]

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Ethyl candesartan[a]	0.4	0.2
Desethyl candesartan cilexetil[b]	0.5	0.3
Candesartan cilexetil	1.0	—
*N*²-Ethyl candesartan cilexetil[c]	2.0	0.2
Any other unknown impurity	—	0.10

[a] Ethyl 1-{[2′-(1*H*-tetrazol-5-yl)biphenyl-4-yl]methyl}-2-ethoxybenzimidazole-7-carboxylate.

[b] ±1-(Cyclohexyloxycarbonyloxy)ethyl 1-{[2′-(1*H*-tetrazol-5-yl)biphenyl-4-yl]methyl}-2-oxobenzimidazole-7-carboxylate.

[c] ±1-(Cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-{[2′-(*N*-ethyl-tetrazol-5-yl) biphenyl-4-yl]methyl}benzimidazole-7-carboxylate.

SPECIFIC TESTS

• **Water Determination,** *Method 1* ⟨921⟩**:** NMT 0.3%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled temperature.

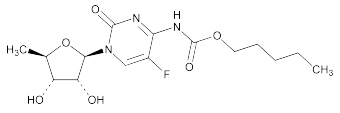
• **USP Reference Standards** ⟨11⟩

USP Candesartan Cilexetil RS

1*H*-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2′-(1*H*-tetrazol-5-yl)[1,1′-biphenyl]-4-yl]methyl]-, 1-[[(cyclohexyloxy)carbonyl]oxy]ethyl ester, (±); (±)-1-Hydroxyethyl 2-ethoxy-1-[*p*-(*o*-1*H*-tetrazol-5-ylphenyl)benzyl]-7-benzimidazolecarboxylate, cyclohexyl carbonate (ester).

610.66▲*USP35*

Capecitabine



$C_{15}H_{22}FN_3O_6$ 359.35

Carbamic acid, [1-(5-deoxy-β-D-ribofuranosyl)-5-fluoro-1,2-dihydro-2-oxo-4-pyrimidinyl]-, pentyl ester;

Pentyl 1-(5-deoxy-β-D-ribofuranosyl)-5-fluoro-1,2-dihydro-2-oxo-4-pyrimidinecarbamate [154361-50-9].

Official from May 1, 2012
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