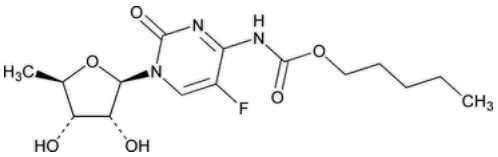
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-A9DECD41-10E1-4DBF-B935-ACADA67ADAC5_4_en-US
DOI: https://doi.org/10.31003/USPNF_M12330_04_01
DOI Ref: lh8x3

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 CAS RN®: 154361-50-9; UNII: 6804DJ8Z9U.

DEFINITION

Capecitabine contains NLT 98.0% and NMT 102.0% of $C_{15}H_{22}FN_3O_6$, calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

Sample: 2 mg of sample in 300 mg of potassium bromide

• **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

• **Procedure**

Diluent: Methanol, acetonitrile, and water (7:1:12)

Solution A: 0.1% mixture of glacial acetic acid in water

Solution B: Methanol, acetonitrile, and *Solution A* (7:1:12)

Solution C: Methanol, acetonitrile, and *Solution A* (16:1:3)

Mobile phase: See the gradient table below.

Time (min)	Solution B (%)	Solution C (%)
0	100	0
5	100	0
20	49	51
30	49	51
31	100	0
40	100	0

[Note—The following solutions may be sonicated if necessary.]

System suitability solution: 0.6 µg/mL each of USP Capecitabine RS, USP Capecitabine Related Compound A RS, USP Capecitabine Related Compound B RS, and USP Capecitabine Related Compound C RS in *Diluent*

Standard solution: 0.6 mg/mL of USP Capecitabine RS in *Diluent*

Sample solution: 0.6 mg/mL of Capecitabine in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Autosampler temperature: 5°

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—For the purpose of peak identification, the approximate relative retention times are given in *Impurity Table 1.* The relative retention times are measured with respect to capecitabine.]

Suitability requirements

Resolution: NLT 1.0 between capecitabine related compound A and capecitabine related compound B, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{15}H_{22}FN_3O_6$ in the portion of Capecitabine taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

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

IMPURITIES

INORGANIC IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%

ORGANIC IMPURITIES

- **PROCEDURE**

Diluent, Solution B, Solution C, System suitability solution, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay.*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Capecitabine taken:

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

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

r_S = peak response for capecitabine from the *Standard solution*

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

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

F = relative response factor for an impurity, from *Impurity Table 1*

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 1.5%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Capecitabine related compound A	0.18	1.05	0.3
Capecitabine related compound B	0.19	0.81	0.3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
2',3'-Di-*O*-acetyl-5'-deoxy-5-fluorocytidine	0.36	0.89	0.1
5'-Deoxy-5-fluoro-N4-(2-methyl-1-butyloxycarbonyl)cytidine + 5'-Deoxy-5-fluoro-N4-(3-methyl-1-butyloxycarbonyl)cytidine	0.95	1.01	0.5
Capecitabine	1.00	1.00	—
[1-[5-Deoxy-3-*O*-(5-deoxy-β-D-ribofuranosyl)-β-D-ribofuranosyl]-5-fluoro-2-oxo-1,2-dihydropyrimidin-4-yl]-carbamic acid pentyl ester	1.06	1.00	0.3
[1-[5-Deoxy-2-*O*-(5-deoxy-β-D-ribofuranosyl)-β-D-ribofuranosyl]-5-fluoro-2-oxo-1,2-dihydropyrimidin-4-yl]-carbamic acid pentyl ester	1.09	1.00	0.2
Capecitabine related compound C	1.11	0.91	0.3
[1-[5-Deoxy-3-*O*-(5-deoxy-α-D-ribofuranosyl)-β-D-ribofuranosyl]-5-fluoro-2-oxo-1,2-dihydropyrimidin-4-yl]-carbamic acid pentyl ester	1.20	1.00	0.3
2',3'-Di-*O*-acetyl-5'-deoxy-5-fluoro-N4-(pentyloxycarbonyl)cytidine	1.37	0.85	0.1
Individual unspecified impurity	—	1.00	0.1

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation* ⟨781S⟩**:** +96.0° to +100.0°

  Sample solution: 10 mg/mL, on the anhydrous and solvent-free basis, in methanol, at 20°
- **Water Determination,** *Method Ic* ⟨921⟩**:** NMT 0.3%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

USP Capecitabine RS

USP Capecitabine Related Compound A RS

5'-Deoxy-5-fluorocytidine.

$C_9H_{12}FN_3O_4$ 245.21

USP Capecitabine Related Compound B RS

5'-Deoxy-5-fluorouridine.

$C_9H_{11}FN_2O_5$ 246.19

USP Capecitabine Related Compound C RS

2',3'-*O*-Carbonyl-5'-deoxy-5-fluoro-N^4-(pentyloxycarbonyl)cytidine.

$C_{16}H_{20}FN_3O_7$ 385.34

Topic/Question	Contact	Expert Committee
CAPECITABINE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 35(4)

Current DocID: GUID-A9DECD41-10E1-4DBF-B935-ACADA67ADAC5_4_en-US

DOI: https://doi.org/10.31003/USPNF_M12330_04_01

DOI ref: lh8x3