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Temozolomide for Injection

DEFINITION

Temozolomide for Injection is a sterile, lyophilized mixture of Temozolomide and suitable added substances. It contains NLT 95.0% and NMT 105.0% of the labeled amount of temozolomide ($C_6H_6N_6O_2$).

[CAUTION—Temozolomide is cytotoxic. Great care should be taken to prevent inhaling particles of temozolomide and exposure to the skin.]

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A or 197K

Standard: Dissolve a suitable amount of [USP Temozolomide RS](#) in [methylene chloride](#), using 2 mL of [methylene chloride](#) for each 5 mg of [USP Temozolomide RS](#). Evaporate the [methylene chloride](#) under a stream of nitrogen to dryness, and use the residue.

Sample: Inject 40 mL of [methylene chloride](#) into the vial of Temozolomide for Injection and shake the vial for 30 min using a mechanical shaker. Allow the vial to sit for 15 min or until undissolved solids settle to the bottom. Pass 15 mL of the supernatant through a filter of 0.45- μ m pore size. Discard the first 5 mL and collect the remaining filtrate into a 20-mL scintillation vial. Evaporate the [methylene chloride](#) under a stream of nitrogen to dryness, and use the residue.

Analysis

Samples: *Standard and Sample*

Acceptance criteria: Meets the requirements

- **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

Store the solutions containing temozolomide at 2°–8°.

Solution A: 0.5% (v/v) [glacial acetic acid](#) in [water](#)

Mobile phase: *Solution A* and [methanol](#) (96:4), containing 0.94 g/L of [sodium 1-hexanesulfonate](#) (0.005 M)

System suitability stock solution: 0.2 mg/mL of [USP Temozolomide RS](#) in *Mobile phase*

System suitability solution: Transfer 50 mL of [0.1 N hydrochloric acid](#) and 50 mL of the *System suitability stock solution* to a container. Heat the container at 80° for 4 h. Transfer 10 mL of this solution into a 25-mL volumetric flask and dilute with *Mobile phase* to volume. [NOTE—The preparation forms 2-azahypoxanthine, temozolomide acid, and aminoimidazolecarboxamide.]

Standard solution: 0.1 mg/mL of [USP Temozolomide RS](#) in *Mobile phase* from the *System suitability stock solution*

Sample stock solution: Nominally equivalent to 2.0 mg/mL of temozolomide in [water](#), prepared as follows. Add 40 mL of [water](#) into each of five vials of Temozolomide for Injection and shake manually to dissolve. Combine the solutions from the 5 vials into a 250-mL volumetric flask and dilute with [water](#) to volume.

Sample solution: Nominally equivalent to 0.1 mg/mL of temozolomide in *Mobile phase* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 270 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L1](#)

Autosampler temperature: 2°–8°

Flow rate: 1 mL/min

Injection volume: 75 μ L

System suitability

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

Suitability requirements

Tailing factor: NMT 1.9 for the temozolomide peak, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis**Samples:** *Standard solution* and *Sample solution*Calculate the percentage of the labeled amount of temozolomide ($C_6H_6N_6O_2$) in the portion of Temozolomide for Injection taken:

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

 r_U = peak response of temozolomide from the *Sample solution* r_S = peak response of temozolomide from the *Standard solution* C_S = concentration of [USP Temozolomide RS](#) in the *Standard solution* (mg/mL) C_U = nominal concentration of temozolomide in the *Sample solution* (mg/mL)**Acceptance criteria:** 95.0%–105.0%**PERFORMANCE TESTS**• **UNIFORMITY OF DOSAGE UNITS** (905), **Weight Variation**: Meets the requirements**IMPURITIES****Change to read:**• **ORGANIC IMPURITIES**

Store the solutions containing temozolomide at 2°–8°.

Mobile phase, System suitability stock solution, System suitability solution, and Sample solution: Prepare as directed in the Assay.**Sensitivity solution:** 0.1 µg/mL of [USP Temozolomide RS](#) in *Mobile phase* from the *System suitability stock solution***▲Standard solution:** 1.3 µg/mL of [USP Dacarbazine Related Compound A RS](#) in *Mobile phase*

[NOTE—Dacarbazine related compound A is the hydrochloride salt of aminoimidazolecarboxamide.]▲ (IRA 1-Mar-2021)

Chromatographic system: Proceed as directed in the Assay, except for the *Run time*.**Run time:** NLT 2.5 times the retention time of the temozolomide peak**System suitability****Samples:** *System suitability solution*, *Sensitivity solution*, and ▲*Standard solution*▲ (IRA 1-Mar-2021)**Suitability requirements****Resolution:** NLT 2.5 between the temozolomide and aminoimidazolecarboxamide peaks, *System suitability solution***▲Relative standard deviation:** NMT 5%, *Standard solution*▲ (IRA 1-Mar-2021)**Signal-to-noise ratio:** NLT 10, *Sensitivity solution***Analysis****Samples:** ▲*Standard solution* and▲ (IRA 1-Mar-2021) *Sample solution*

▲Calculate the percentage of aminoimidazolecarboxamide in the portion of Temozolomide for Injection taken:

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

 r_U = peak area of aminoimidazolecarboxamide from the *Sample solution* r_S = peak area of dacarbazine related compound A from the *Standard solution* C_S = concentration of [USP Dacarbazine Related Compound A RS](#) in the *Standard solution* (mg/mL) C_U = nominal concentration of temozolomide in the *Sample solution* (mg/mL) M_{r1} = molecular weight of aminoimidazolecarboxamide (free base of [USP Dacarbazine Related Compound A RS](#)), 126.12

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 M_{r2} = molecular weight of [USP Dacarbazine Related Compound A RS](#) (hydrochloride salt of aminoimidazolecarboxamide), 162.58▲

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(IRA 1-Mar-2021)

Calculate the percentage of ▲any other▲ (IRA 1-Mar-2021) impurity in the portion of Temozolomide for Injection taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$