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Temozolomide Compounded Oral Suspension

DEFINITION

Temozolomide Compounded Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of temozolomide ($C_6H_6N_6O_2$).

Prepare Temozolomide Compounded Oral Suspension 10 mg/mL as follows (see *Pharmaceutical Compounding—Nonsterile Preparations ⟨795⟩*).

Temozolomide capsules,[a] equivalent to	1 g of temozolomide
Povidone K-30, *USP*	500 mg
Anhydrous Citric Acid, *USP*	25 mg
Purified Water, *USP*	1.5 mL
Vehicle: a 1:1 mixture of Ora-Plus[b] and Ora-Sweet[b] (regular or sugar-free), a sufficient quantity to make	100 mL

[a] Temodar 100-mg capsules, Schering Corporation, Whitehouse, NJ.

[b] Paddock Laboratories, Minneapolis, MN.

Calculate the required quantity of each ingredient for the total amount to be prepared. Empty the required number of *Temozolomide capsules* in a suitable mortar. Add the *Povidone K-30* powder to the mortar, and triturate to a fine powder. [Note—Povidone is critical for physical stability.] Dissolve the *Anhydrous Citric Acid* in *Purified Water*. Add the mixture of *Anhydrous Citric Acid* and *Purified Water* to the mortar to wet the powder. Mix thoroughly to form a uniform paste. Add the *Vehicle* in small portions, and triturate to make a smooth mixture. Add increasing volumes of the *Vehicle* to make a temozolomide liquid that is pourable. Transfer the contents of the mortar, stepwise and quantitatively, to a calibrated bottle. Add enough of the *Vehicle* to bring to final volume, and mix well. It is necessary to wear appropriate personal protective equipment and to perform this procedure in a biologic safety cabinet.

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

ASSAY

• **Procedure**

Solution A: 10 mM ammonium phosphate adjusted to a pH of 3.25

Mobile phase: Methanol and *Solution A* (12:88). Filter and degas.

Standard stock solution: 0.5 mg/mL of USP Temozolomide RS in *Mobile phase*. Transfer the mixture to a centrifuge tube, and centrifuge at 1,500 × g for 10 min. Pass the supernatant through a filter of 0.45-µm pore size, into a glass vial.

Standard solution: 0.1 mg/mL of temozolomide prepared from *Standard stock solution* and *Mobile phase*

Sample solution: Shake thoroughly each bottle of Oral Suspension. Immediately transfer 2.5 mL of Oral Suspension to a 25-mL volumetric flask, and dilute with *Mobile phase* to volume. Vortex the sample for 30 s, centrifuge for 10 min at 1,500 × g, and pass through a membrane filter of 0.22-µm pore size. Pass at least 0.5 mL of sample through the filter before collecting the sample in a vial. Transfer 1.0 mL of the resultant solution to a 10-mL volumetric flask, and dilute with *Mobile phase* to volume to obtain a solution with a nominal concentration of 0.1 mg/mL of temozolomide.

Chromatographic system

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

Mode: LC

Detector: UV 245 nm

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

Flow rate: 1.0 mL/min

Injection volume: 15 µL

System suitability

Sample: *Standard solution*

[NOTE—The retention time for temozolomide is about 7.9 min.]

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0% for replicate injections

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 Oral Suspension 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 Temozolomide RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

• **pH ⟨791⟩:** 3.5–4.5

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Package in tight, light-resistant containers. Store in a refrigerator.

• **BEYOND-USE DATE:** NMT 60 days after the date on which it was compounded, when stored in a refrigerator

• **LABELING:** Label it to indicate that it is to be well shaken before use, and to state the *Beyond-Use Date*.

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Temozolomide RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
TEMOZOLOMIDE COMPOUNDED ORAL SUSPENSION	Brian Serumaga Science Program Manager	CMP2020 Compounding 2020
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CMP2020 Compounding 2020

Chromatographic Database Information: Chromatographic Database

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