TEMODAR® (temozolomide) for Injection

PHARMACIST:
Dispense enclosed Patient Package Insert to each patient.

PHARMACIST INFORMATION SHEET

What is TEMODAR? *[See Full Prescribing Information, Indications and Usage (1)].*
TEMODAR® (temozolomide) is an alkylating drug for the treatment of adult patients with newly diagnosed glioblastoma multiforme and refractory anaplastic astrocytoma.

How is TEMODAR dosed? *[See Full Prescribing Information, Recommended Dosing and Dose Modification Guidelines (2.1)].*
The daily dose of TEMODAR for a given patient is calculated by the physician, based on the patient's body surface area (BSA) *[see **Table 5** in the Full Prescribing Information, Recommended Dosing and Dose Modification Guidelines (2.1)].* The recommended dose for TEMODAR as an intravenous infusion over 90 minutes is the same as the dose for the oral capsule formulation. Bioequivalence has been established only when TEMODAR for Injection was given over 90 minutes. The dose for subsequent cycles may be adjusted according to nadir neutrophil and platelet counts in the previous cycle and at the time of initiating the next cycle.

Dosing for Patients with Refractory Anaplastic Astrocytoma *[See Full Prescribing Information, Recommended Dosing and Dose Modification Guidelines, Patients with Refractory Anaplastic Astrocytoma (2.1)].*
Dosage of TEMODAR must be adjusted according to nadir neutrophil and platelet counts in the previous cycle and neutrophil and platelet counts at the time of initiating the next cycle. The initial dose is 150 mg/m^2 orally once daily for 5 consecutive days per 28-day treatment cycle. If both the nadir and day of dosing (Day 29, Day 1 of next cycle) absolute neutrophil counts (ANC) are greater than or equal to 1.5 x 10^9/L (1500/µL) and both the nadir and Day 29, Day 1 of next cycle platelet counts are greater than or equal to 100 x 10^9/L (100,000/µL), the TEMODAR dose may be increased to 200 mg/m^2/day for 5 consecutive days per 28-day treatment cycle. During treatment, a complete blood count should be obtained on Day 22 (21 days after the first dose) or within 48 hours of that day, and weekly until the ANC is above 1.5 x 10^9/L (1500/µL) and the platelet count exceeds 100 x 10^9/L (100,000/µL). The next cycle of TEMODAR should not be started until the ANC and platelet count exceed these levels. If the ANC falls to less than 1.0 x 10^9/L (1000/µL) or the platelet count is less than 50 x 10^9/L (50,000/µL) during any cycle, the next cycle should be reduced by 50 mg/m^2, but not below 100 mg/m^2, the lowest recommended dose *[see **Table 4** in the Full Prescribing Information, Recommended Dosing and Dose Modification Guidelines (2.1)].*

Patients should continue to receive TEMODAR until their physician determines that their disease has progressed, or until unacceptable side effects or toxicities occur. Physicians may alter the treatment regimen for a given patient.

Dosing for Patients with Newly Diagnosed Glioblastoma Multiforme *[See Full Prescribing Information, Recommended Dosing and Dose Modification Guidelines, Patients with Newly Diagnosed High Grade Glioma (2.1)].*

Concomitant Phase Treatment Schedule
TEMODAR is administered at 75 mg/m^2 daily for 42 days concomitant with focal radiotherapy (60 Gy administered in 30 fractions), followed by maintenance TEMODAR for 6 cycles. No dose reductions are recommended; however, dose interruptions may occur based on patient tolerance. The TEMODAR dose can be continued throughout the 42-day concomitant period up to 49 days if all of the following conditions are met: absolute neutrophil count greater than or equal to 1.5 x 10^9/L, platelet count greater than or equal to 100 x 10^9/L, common toxicity criteria (CTC) non-hematological toxicity less than or equal to Grade 1 (except for alopecia, nausea, and vomiting). During treatment a complete blood count should be obtained weekly. Temozolomide dosing should be interrupted or discontinued during concomitant phase according to the hematological and non-hematological toxicity criteria as noted in **Table 1** of the Full Prescribing Information under 2.1 Recommended Dosing and Dose Modification Guidelines. *Pneumocystis* pneumonia (PCP) prophylaxis is required during the concomitant administration of TEMODAR and radiotherapy, and should be continued in patients who develop lymphocytopenia until recovery from lymphocytopenia (CTC Grade less than or equal to 1).

Maintenance Phase Treatment Schedule
Four weeks after completing the TEMODAR + RT phase, TEMODAR is administered for an additional 6 cycles of maintenance treatment. Dosage in Cycle 1 (maintenance) is 150 mg/m^2 once daily for 5 days followed by 23 days without treatment. At the start of Cycle 2, the dose can be escalated to 200 mg/m^2, if the CTC non-hematologic toxicity for Cycle 1 is Grade less than or equal to 2 (except for alopecia, nausea, and vomiting), absolute neutrophil count (ANC) is greater than or equal to 1.5 x 10^9/L, and the platelet count is greater than or equal to 100 x 10^9/L. If the dose was not escalated at Cycle 2, escalation should not be done in subsequent cycles. The dose remains at 200 mg/m^2 per day for the first 5 days of each subsequent cycle except if toxicity occurs.

During treatment a complete blood count should be obtained on Day 22 (21 days after the first dose) or within 48 hours of that day, and weekly until the ANC is above 1.5 x 10^9/L (1500/µL) and the platelet count exceeds 100 x 10^9/L (100,000/µL). The next cycle of TEMODAR should not be started until the ANC and platelet count exceed these levels. Dose reductions during the next cycle should be based on the lowest blood counts and worst nonhematologic toxicity during the previous cycle. Dose reductions or discontinuations during the maintenance phase should be applied according to **Tables 2** and **3** in the Full Prescribing Information under 2.1 Recommended Dosing and Dose Modification Guidelines.

How is TEMODAR for Injection prepared? *[See Full Prescribing Information, Preparation and Administration, TEMODAR for Injection (2.2)].*

Care should be exercised in the handling and preparation of TEMODAR. Vials should not be opened. If vials are accidentally opened or damaged, rigorous precautions should be taken with the contents to avoid inhalation or contact with the skin or mucous membranes. The use of gloves and safety glasses is recommended to avoid exposure in case of breakage of the vial. Procedures for proper handling and disposal of anticancer drugs should be considered {1-4}. Several guidelines on this subject have been published.

1. TEMODAR for Injection vials should be stored refrigerated at 2°-8°C (36°-46°F).
2. Bring the vial to room temperature prior to reconstitution with Sterile Water for Injection.
3. Using aseptic technique, reconstitute each vial with 41 mL Sterile Water for Injection. The resulting solution will contain 2.5 mg/mL temozolomide.
4. Vial should be gently swirled and not shaken. Inspect vials, and any vial containing visible particulate matter should not be used. Do not further dilute the reconstituted solution. Upon reconstitution, store at room temperature for up to 14 hours, including infusion time.
5. Using aseptic technique, withdraw up to 40 mL from each vial to make up the total dose and transfer into an empty 250 mL infusion bag.
6. Attach the pump tubing to the bag, purge the tubing and then cap.

How is TEMODAR for Injection administered? *[See Full Prescribing Information, Preparation and Administration, TEMODAR for Injection (2.2)].*
TEMODAR for Injection is administered as an intravenous infusion over 90 minutes. Bioequivalence has been established only when TEMODAR for Injection was given over 90 minutes. TEMODAR for Injection should be administered only by intravenous infusion. Flush the lines before and after each TEMODAR infusion.

TEMODAR for Injection may be administered in the same intravenous line with 0.9% Sodium Chloride injection only.

Because no data are available on the compatibility of TEMODAR for Injection with other intravenous substances or additives, other medications should not be infused simultaneously through the same intravenous line.

What should the patient avoid during treatment with TEMODAR? *[See Full Prescribing Information, Use in Specific Populations, Pregnancy (8.1) and Nursing Mothers (8.3)].*
There are no dietary restrictions for patients taking TEMODAR. TEMODAR may affect testicular function, so male patients should exercise adequate birth control measures. TEMODAR may cause birth defects. Female patients should avoid becoming pregnant while receiving this drug. It is not known whether TEMODAR is excreted into breast milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants and tumorigenicity shown for temozolomide in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of TEMODAR to the mother.

What are the side effects of TEMODAR? *[See Full Prescribing Information, Adverse Reactions (6)].*
Nausea and vomiting are the most common side effects associated with TEMODAR. Noncumulative myelosuppression is the dose-limiting toxicity. Patients should be evaluated periodically by their physician to monitor blood counts.

Other commonly reported side effects reported by patients taking TEMODAR are fatigue, constipation, alopecia, anorexia, headache, and bruising, as well as pain, irritation, itching, warmth, swelling, and redness at the site of infusion.

How is TEMODAR supplied? *[See Full Prescribing Information, How Supplied/Storage and Handling (16)].*
TEMODAR for Injection is supplied in single-use glass vials containing 100 mg temozolomide. TEMODAR is also available as capsules in 5-mg, 20-mg, 100-mg, 140-mg, 180-mg, and 250-mg strengths.

1. OSHA Technical Manual, TED 1-0.15A, Section VI: Chapter 2. Controlling Occupational Exposure to Hazardous Drugs. OSHA, 1999.
2. American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health-Syst Pharm.* 2006; 63:1172-1193.
3. NIOSH Alert: Preventing occupational exposures to antineoplastic and other hazardous drugs in healthcare settings. 2004. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004-165.[3]
4. Polovich, M., White, J. M., & Kelleher, L.O. (eds.) 2005. Chemotherapy and biotherapy guidelines and recommendations for practice (2nd. ed.) Pittsburgh, PA: Oncology.

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MERCK & CO., INC., Whitehouse Station, NJ 08889, USA

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