Temozolomide (te-mo-zole-oh-mide)

**Classification**
- Therapeutic: antineoplastics
- Pharmacologic: alkylating agents

**Pregnancy Category** D

**Indications**
Inhibitory: anaplastic astrocytomas progressing despite treatment with a nitrosourea and procarbazine. Newly diagnosed glioblastoma multiforme (with radiation and then alone as maintenance therapy).

**Action**
Temozolomide is not active until converted at physiological pH to MTIC, which alkylates DNA, disrupting its synthesis.

**Therapeutic Effects:**
Death of rapidly replicating cells, especially malignant ones, resulting in regression or slowed tumor growth.

**Pharmacokinetics**
- **Absorption:** Rapidly converted to MTIC, the active metabolite.
- **Distribution:** Unknown.
- **Metabolism and Excretion:** Further metabolism results in the formation of methylhydrazine, which is responsible for most activity.
- **Half-life:** 1.8 hr.

**TIME/ACTION PROFILE (effect on blood counts)**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO/IV (WBC)</td>
<td>unknown</td>
<td>28 days (range 1–44 days)</td>
<td>14 days</td>
</tr>
<tr>
<td>PO/IV (platelets)</td>
<td>unknown</td>
<td>26 days (range 21–40 days)</td>
<td>14 days</td>
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</tbody>
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**Contraindications/Precautions**
- Hypersensitivity to temozolomide or dacarbazine (DTIC);
- OB, Lactation: Pregnancy or lactation.
- Use Cautiously in:
  - Severe hepatic or renal impairment;
  - Geriatric patients and women (q risk of myelosuppression);
  - Active infection;
  - Women (q bone marrow reserve);
  - Other chronic debilitating illness;
  - OB: Patients with childbearing potential;
  - Pedi: Safety not established.

**Adverse Reactions/Side Effects**
- **CNS:** SEIZURES, fatigue, headache, abnormal coordination, amnesia, depression, dizziness, disorientation, mental status changes, weakness.
- **EENT:** Abnormal vision, diplopia.
- **Resp:** Cough.
- **CV:** Peripheral edema.
- **GI:** Hepatotoxicity, nausea, vomiting, abdominal pain, anorexia, constipation, diarrhea, dysphagia, dry mouth, dyspepsia, dysuria, dyspareunia, enteritis, gastritis.
- **Derm:** Pruritus, rash.
- **Endo:** Adrenal hypercorticism.
- **Musculoskeletal:** Arthralgia, myalgia, myopathy.
- **Metabolic:** Weight.
- **MS:** Abnormal gait, back pain.
- **Neuro:** Hemiparesis, myalgia.
- **Misc:** Breast pain (women), fever, injection site reactions, pain at injection site, secondary malignancies (rare).

**Interactions**
- **Drug-Drug:** q bone marrow depression may occur with other antineoplastics or radiation therapy. May q the antibody response to live-virus vaccines and q risk of adverse reactions.

**Route/Dosage**
- **PO, IV (Adults):**
  - Anaplastic astrocytoma—150 mg/m²/day for 5 consecutive days of each 28-day treatment cycle; doses adjusted on the basis of blood counts;
  - Glioblastoma multiforme—75 mg/m²/day for 42 consecutive days concurrently with radiation initially, then starting 4 wk after last dose, maintenance dose of 150 mg/m²/day for 3 consecutive days of each 28-day treatment cycle for 5 cycles; doses adjusted on the basis of blood counts. Concurrent prophylaxis against Pneumocystis jiroveci pneumonia is required during first 42 days of regimen.

**Nursing Implications**
- **Assessment**
  - Monitor patient for seizures. Institute seizure precautions as needed.
  - **Lab Test Considerations:** Monitor CBC with differential and platelet count. Glutaminemia may/may not be concurrent. Phase 1 patient must have an absolute monocyte count (AMC) ≥ 5 × 10⁹/L, a platelet count of ≥ 100 × 10⁹/L, and common toxicity criteria (CTC) non-hematologic toxicity grade ≤ 1 except for nausea or vomiting. Use cautiously in patients with chronic bone marrow depression or radiation therapy.

- **Use Cautiously in:** Severe hepatic or renal impairment; Geriatric patients and women (q risk of myelosuppression); Active infection; Women (q bone marrow reserve); Other chronic debilitating illness; OB: Patients with childbearing potential; Pedi: Safety not established.
alopecia, nausea and vomiting). Obtain CBC weekly. If ANC is <0.5 and platelet count is <100 x 10^9/L or CTC is Grade 2 during any cycle, interrupt therapy until ANC and platelet count have returned to above parameters. If ANC <0.5 x 10^9/L or platelet count is <30 x 10^9/L or CTC is Grade 3 or 4, discontinue therapy. For the Abrasion Phase, see manufacturer’s recommended dosing guidelines. Doxepin is effective as a single-agent but has no demonstrated activity in combination with temozolamide. CBC on Day 22 (21 days after first dose) or within 48 hr of that day, and weekly until ANC is above 1.5 x 10^9/L and platelet count exceeds 100 x 10^9/L or ANC falls to <0.5 x 10^9/L or the platelet count is <50 x 10^9/L during any cycle, the next cycle should be reduced by 50 mg/m^2, but not below 100 mg/m^2, as lowest recommended dose. See manufacturer’s recommendations for specific guidelines. Women and geriatric patients are at greater risk for developing myelosuppression. Nadir for thrombocytopenia usually occurs at 26 days, and for neutropenia usually occurs at 28 days. Recovery usually occurs within 14 days of the nadir.

Potential Nursing Diagnoses
Risk for infection (Adverse Reactions)
Risk for injury (Adverse Reactions)

Implementation
● Prophylactically treat patients with glioblastoma who are receiving concurrent temozolamide and radiotherapy for Pneumocystis jirovecii pneumonia. Continue treatment in patients who develop lymphocytopenia ANC <1.5 x 10^9/L and platelet count exceeds 100 x 10^9/L.

PO:
Administer capsules one at a time with a full glass of water at the same time each day. Take on an empty stomach or at bedtime to reduce nausea and vomiting. Swallow capsules whole; do not chew or open. If capsules are accidentally opened or damaged, avoid inhaling powder or getting on mucous membranes in nose or mouth. May administer antiemetics before or following administration.

IV Administration
● Intermittent Infusion: Bring vial to room temperature before reconstitution. Diluent: Reconstitute with 41 mL or Sterile Water for Injection. Swirl gently; do not shake. Do not dilute further or administer solutions containing particulate matter. Concentration: 2.5 mg/mL. Withdraw 40 mL from each vial to make desired dose and transfer into empty 250 mL PVC infusion bag. Solution is stable for 14 hr at room temperature, including infusion time. Rate: Infuse over 90 min. Flush line before and after infusion.

Patient/Family Teaching
● Instruct patient to take medication as directed, at the same time each day. Capsules should be packaged in 5 separate packets or vials labeled “Day 1,” “Day 2,” “Day 3,” “Day 4,” and “Day 5.” Capsules may be different sizes or colors in each packet. Contact pharmacist or prescriber if there are questions about the packaging.

● Inform patient that antimicrobial medication may be taken if nausea and vomiting occur.

● Instruct patient to avoid health care professional if fever, chills, minimal bleeding or bruising, or fatigue occurs. Caution patient to avoid crowds and persons with known infections. Instruct patient to use a soft toothbrush and electric razor and to be especially careful to avoid falls. Caution patients not to drink alcohol or take medications containing aspirin or NSAIDs, which precipitate gastric bleeding.

● Caution patient not to receive any vaccinations without advice of health care professional.

● Advise patient to use a nonhormonal method of contraception throughout therapy.

● Emphasize the importance of follow-up examination to monitor progress and side effects.

Evaluation/Desired Outcomes
● Slowing of disease progression in patients with refractory astrocytoma and glioblastoma multiforme. Therapy may be continued until disease progresses.

Why was this drug prescribed for your patient?