Positive Quality Intervention: Temozolomide (Temodar®) for Glioblastoma Multiforme

**Description:** The purpose of this PQI is a summary of the process for initiating and monitoring oral temozolomide therapy in patients with Glioblastoma Multiforme (GBM).

**Background:** GBM is the most common primary malignant brain tumor in adults and comprises 54% of all gliomas with a median survival of 6 to 12 months. Temozolomide is an FDA approved medication used to treat GBM. Temozolomide is a prodrug that is converted into its active alkylating metabolite which causes DNA double strand breaks and apoptosis. Concurrent treatment with temozolomide and radiation followed by a 4 week break, then maintenance temozolomide for 5 days every 28 days for 6 cycles was found to improve 2 year survival from 10.4% (radiation alone) to 26.5% (radiation + temozolomide). Furthermore, patients with MGMT promoter methylated GBM were shown to have a better 18-month overall survival with concurrent temozolomide and radiation (62%) when compared with unmethylated MGMT (8%).

**PQI Process:**
- Screen for Hepatitis B and C prior to starting treatment  
  - Initiate entecavir or tenofovir for history of hep B infection to prevent reactivation
- Ensure appropriate indication and dose, keeping in mind that dose modifications occurred frequently in the clinical trials  
  - Temozolomide 75 mg/m² PO daily during radiation followed by a 4 week break, then 150-200 mg/m² PO daily x 5 every 28 days for 6 cycles
- Concurrent temozolomide with radiation can cause lymphocytopenia therefore ensure appropriate prophylaxis of Pneumocystis Jiroveci with oral trimethoprim-sulfamethoxazole, inhaled pentamidine, atovaquone or dapsone and should be continued until recovery from lymphocytopenia (lymphocyte count at or greater than 0.8 x 10^9/L)
- 5HT3 antagonist should be prescribed for prevention and treatment of nausea and vomiting  
  - Recommend 5HT3 antagonist 30 to 60 minutes prior to temozolomide for prevention of nausea and vomiting
- Monitor pregnancy, CBC (thrombocytopenia, neutropenia, lymphopenia), liver enzymes, pneumocystis

**Dosing Interruption or Discontinuation during Concomitant Radiotherapy and Temozolomide**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Therapy Interruption</th>
<th>Discontinue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute Neutrophil Count</td>
<td>≥ 0.5 x 10⁹/L and &lt; 1.5 x 10⁹/L</td>
<td>&lt; 0.5 x 10⁹/L</td>
</tr>
<tr>
<td>Platelet Count</td>
<td>≥ 10 x 10⁹/L and less &lt; 100 x 10⁹/L</td>
<td>&lt; 10 x 10⁹/L</td>
</tr>
<tr>
<td>Common Toxicity Criteria (CTC) Non-Hematological Toxicity (except for alopecia, nausea, vomiting)</td>
<td>CTC Grade 2</td>
<td>CTC Grade 3 or 4</td>
</tr>
</tbody>
</table>

**Temozolomide Dose Levels for Maintenance Treatment**

<table>
<thead>
<tr>
<th>Dose level</th>
<th>Dose (mg/m²/day)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td>100</td>
<td>Reduction for prior toxicity</td>
</tr>
<tr>
<td>0</td>
<td>150</td>
<td>Dose during Cycle 1</td>
</tr>
<tr>
<td>1</td>
<td>200</td>
<td>Dose during Cycles 2-6 in absence of toxicity</td>
</tr>
</tbody>
</table>

**IMPORTANT NOTICE:** NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, does not provide individual medical advice, and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual’s sole responsibility to seek guidance from a qualified healthcare professional. Updated 8.21.23
Temozolomide Dose Reduction or Discontinuation during Maintenance Treatment

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Reduce Temozolomide by 1 Dose Level</th>
<th>Discontinue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute Neutrophil Count</td>
<td>Less than $1.0 \times 10^9$/L</td>
<td>Discontinue if dose reduction to $&lt; 100$ mg/m$^2$ is required or if the same Grade 3 non-hematological toxicity (except for alopecia, nausea, vomiting) recurs after dose reduction</td>
</tr>
<tr>
<td>Platelet Count</td>
<td>Less than $50 \times 10^9$/L</td>
<td></td>
</tr>
<tr>
<td>CTC Non-Hematological Toxidity (except for alopecia, nausea, vomiting)</td>
<td>CTC Grade 3</td>
<td>CTC Grade 4</td>
</tr>
</tbody>
</table>

**Temozolomide Dose Modification Table**

- **150 mg/m$^2$/day x 5 days (Starting Dose) or 200 mg/m$^2$/day x 5 days**
  - Measure Day 22 ANC and platelets
  - Measure ANC and platelets on Day 29 (Day 1 of next cycle)
  - Based on lowest counts at either Day 22 or Day 29
  - **ANC less than 1000/µL or platelets less than 50,000/µL**
    - Hold until ANC > 1500/µL and platelets > 100,000/µL; reduce dose by 50 mg/m$^2$/d for subsequent cycle
  - **ANC 1000/µL - 1500/µL or platelets 50,000/µL - 100,000/µL**
    - Hold until ANC > 1500/µL and platelets > 100,000/µL; maintain previous dose
  - **ANC > 1500/µL and platelets > 100,000/µL**
    - Increase dose to, or maintain dose at, 200 mg/m$^2$/d x 5d for subsequent cycle

**Patient-Centered Activities:**
- Provide Oral Chemotherapy Education (OCE) Sheet
- Provide Treatment Support Kit (TSK)
- Counsel patient on disease state, treatment regimen, what to expect and verify patient understanding
- Counsel patient on common side effects which include alopecia, constipation, nausea/vomiting, headache, and fatigue
- **Temozolomide may be taken on an empty stomach 1-2 hours before radiation or at bedtime**
- Counsel patient to swallow capsules (may be multiple) whole with a full glass of water
  - May administer on an empty stomach and/or bedtime to reduce nausea/vomiting and consistently take in this manner
  - Do not repeat dose if vomiting occurs after the dose is administered

**References:**
1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers.
2. Temozolomide [prescribing information].