Temozolomide (Temodal™)
Recurrent High Grade Gliomas

**Background:** The majority (at least 70%) of malignant gliomas recur locally after initial treatment, usually with very disabling neurological deficit and poor and rapidly deteriorating quality of life. Options for further treatment at this stage are limited and palliative. Temozolomide (Temodal™) is an alkylating agent derived from dacarbazine and first synthesised in 1984. It is indicated for the treatment of patients with malignant glioma showing recurrence or progression after standard therapy (NICE TA 23).

**Patient group:** Patients with recurrent malignant glioma who have failed first-line chemotherapy treatment with other agents (either because of lack of efficacy or because of side effects). WHO grade III or IV, or transformed grade II) confirmed by MRI. Life expectancy > 12 weeks
ECOG PS 0 – 2

**Regimen Details**

**Temozolomide**  
150mg/m² orally once a day (at bedtime) for 5 days (cycle 1)

**Temozolomide**  
200mg/m² orally once a day (at bedtime) for 5 days (from cycle 2 if cycle 1 tolerated)

Repeated every 28 days for 6 cycles.

Supplied as 5mg, 20mg, 100mg, 140mg, 180mg and 250mg capsules

**Pre-treatment assessment:**
Weight, FBC, U&E’s, (LFT’s and creatinine clearance)  
MRI Scan and histology

**General haematological limits:**
Platelets > 100 x 10⁹/L
ANC > 1.5 x 10⁹/L
WBC > 3 x 10⁹/L

**Administration:**
- Temozolomide should be taken on an empty stomach (at least 2 hours since last food).
- The capsules must be swallowed whole with a glass of water and must not be opened or chewed.
Anti-emetics: Highly emetic. Ondansetron 8mg PO BD for 5 days of chemotherapy (pre-temozolomide ondansetron dose should be one hour before) and domperidone 10-20mg QDS PRN.

Additional Medication:
- Consider PCP prophylaxis, particularly if patients on concurrent corticosteroid (dexamethasone) – co-trimoxazole 960mg PO once a day on Mondays, Wednesdays and Fridays of each week which should continue for 4 weeks after last cycle. Patients who cannot tolerate co-trimoxazole should receive prophylactic nebulised pentamidine instead.
- Patients may require treatment for focal seizures (lamotrigine or levetiracetam).

Monitoring and Assessment:
FBC and clinical examination - prior to each cycle of chemotherapy.
U&E, LFTs - prior to each cycle of chemotherapy
MRI Scan – when clinically indicated to assess response

Dose Modifications:

<table>
<thead>
<tr>
<th>Temozolomide dose levels for monotherapy</th>
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</thead>
<tbody>
<tr>
<td>Dose level</td>
</tr>
<tr>
<td>-1</td>
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<tr>
<td>0</td>
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<tr>
<td>1</td>
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</tbody>
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Treatment should be delayed until recovery and then dose reduce as per the table below:

<table>
<thead>
<tr>
<th>Temozolomide dose reduction during monotherapy treatment</th>
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<tbody>
<tr>
<td>Toxicity</td>
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<tr>
<td>ANC</td>
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<tr>
<td>Platelet Count</td>
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<tr>
<td>Non- haematological toxicity</td>
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*Or if the same grade 3 non-haematological toxicity recurs after dose reduction (except alopecia, nausea and vomiting)

NB Avoid altering dexamethasone doses during the temozolomide treatment week as this can make it difficult to determine the cause of any problems (drug side effect or reduced steroid dose).

Pharmaceutical Care:
Monitor INR regularly in patients also taking warfarin (and other coumarin-derived anticoagulants) or consider changing to LMWH.

Co-administration with valproic acid is associated with a small decrease in clearance of temozolomide.

Oral preparation, therefore advise patients to swallow and not open the capsules. If a capsule becomes damaged, avoid contact of the powder contents with skin or mucous membrane. If contact does occur, wash the affected area.

Diminished response to vaccines and avoid use of live vaccines.

Patients whom are also receiving digoxin should have their digoxin levels checked.

Missed doses should be taken as soon as possible only if it is within 12 hours of the planned dose. If the time is greater than 12 hours, omit and take the next dose on time.

Vomiting after a dose – do not repeat the dose.

Most Common Toxicities:
- Myelosuppression +/- infection
- Nausea and vomiting
- Rash
- Alopecia (late onset and may be thinning or patchy hair loss)
- Fatigue
- Constipation
- Convulsions
- Headaches
- Anorexia and weight loss
- Opportunistic infections e.g. PCP
- Dyspnoea and cough
- Blurred vision
- Hearing impairment
- ↑ ALT

References:
3. van den Bent MJ et al. Second-line chemotherapy with temozolomide in recurrent oligodendrogloma after PCV (procarbazine, lomustine and vincristine) chemotherapy: EORTC Brain Tumour Group phase II study 26972
4. Stockley’s Drug Interactions