Temozolomide Recurrent Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Indicator
Adult patients with Grade III or IV malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma, showing recurrence or progression after standard therapy.	C71	00342a	CDS

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

A treatment cycle comprises 28 days. Temozolomide is administered orally once daily for the first 5 days followed by a 23 day treatment interruption (total of 28 days) until disease progression or unacceptable toxicity develops

Day	Drug	Dose	Route	Cycle (28 day)
1-5	Temozolomide	[a]200mg/m^2 ONCE daily	PO	Continuous
[a]In patients previously untreated with chemotherapy, temozolomide is administered orally at a dose of 200 mg/m^2 once daily for the first 5 days followed by a 23 day treatment interruption (total of 28 days). In patients previously treated with chemotherapy, the initial dose is 150 mg/m^2 once daily, to be increased in the second cycle to 200 mg/m^2 once daily, for 5 days if there is no haematological toxicity				
Temozolomide hard capsules should be administered in the fasting state. The capsules must be swallowed whole with a glass of water and must not be opened or chewed. If vomiting occurs after the dose is administered, a second dose should not be administered that day				
If a dose is missed, the patient should make up that dose, unless the next dose is due within 12 hours.				

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Adequate renal and hepatic function

EXCLUSIONS:

- Patients with hypersensitivity to temozolomide or any of its listed excipients
- Hypersensitivity to dacarbazine
- Severe myelosuppression
- Creatinine > 1.5 x ULN
- Significant hepatic dysfunction
- Pregnancy or lactation

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- Blood, renal and liver profile
- Glucose
- Virology screen -Hepatitis B (HBsAg, HBcoreAb)

*(Reference Adverse Events/Regimen Specific Complications for information on Hepatitis B reactivation)

Regular tests:

- Blood, renal and liver profile at day 1 of each cycle

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- Dose reductions and discontinuations should be applied according to Tables 1 and 2.

Table 1: Temozolomide dose levels for Monotherapy Treatment

Dose Level	Temozolomide Dose (mg/m^2)	Remarks
-1	100	Reduction for prior toxicity
0	150	Dose during Cycle 1
1	200	Dose during Cycles 2-6 in absence of toxicity

Table 2: Temozolomide dose reduction or discontinuation during monotherapy treatment

Toxicity	Reduce temozolomide by 1 dose level[a]	Discontinue Temozolomide
ANC	< 1 x 10^9/L	See footnote b
Platelets	< 50 x 10^9/L	See footnote b
CTC non-haematological toxicity (except for alopecia, nausea, vomiting)	CTC Grade 3	CTC Grade 4[b]

[a]Temozolomide dose levels are listed in Table 1.

[b] Temozolomide is to be discontinued if:

- dose level -1 (100 mg/m^2) still results in unacceptable toxicity
- the same Grade 3 non-haematological toxicity (except for alopecia, nausea, vomiting) recurs after dose reduction.

Renal and Hepatic Impairment:

Table 3: Dose modification of temozolomide in renal and hepatic impairment

Renal Impairment	Hepatic Impairment
No data are available on the administration of temozolomide in patients with renal impairment. Caution should be exercised when temozolomide is administered in these patients	• The pharmacokinetics of temozolomide were comparable in patients with normal hepatic function and in those with mild or moderate hepatic impairment. • No data are available on the administration of temozolomide in patients with severe hepatic impairment (Child's Class C). • Based on the pharmacokinetic properties of temozolomide, it is unlikely that dose reductions are required in patients with severe hepatic impairment. However, caution should be exercised when temozolomide is administered in these patients.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Moderate - High (**Refer to local policy).**

PREMEDICATIONS: None

OTHER SUPPORTIVE CARE:

Temozolomide can have genotoxic effects. Therefore, men being treated with it should be advised not to father a child up to 6 months after receiving the last dose and to seek advice on cryoconservation of sperm prior to treatment, because of the possibility of irreversible infertility due to therapy with temozolomide.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Opportunistic infections and reactivation of infections**: Opportunistic infections (such as Pneumocystis jirovecii pneumonia) and reactivation of infections (such as HBV, CMV) have been observed during the treatment with Temozolomide.
- **Pneumocystis jirovecii pneumonia (PJP):** There may be a higher occurrence of PJP when temozolomide is administered during a longer dosing regimen. However, all patients receiving temozolomide, particularly patients receiving steroids, should be observed closely for the development of PJP, regardless of the regimen. Cases of fatal respiratory failure have been reported in patients using temozolomide, in particular in combination with dexamethasone or other steroids.
- **Hepatitis B Virus (HBV):** Hepatitis due to HBV reactivation, in some cases resulting in death, has been reported. Experts in liver disease should be consulted before treatment is initiated in patients with positive hepatitis B serology (including those with active disease). During treatment patients should be monitored and managed appropriately.
- **Hepatotoxicity:** Hepatic injury, including fatal hepatic failure, has been reported in patients treated with temozolomide. Baseline liver function tests should be performed prior to treatment initiation. If abnormal, physicians should assess the benefit/risk prior to initiating temozolomide including the potential for fatal hepatic failure. For all patients, liver function tests should be checked after each treatment cycle. For patients with significant liver function abnormalities, physicians should assess the

benefit/risk of continuing treatment. Liver toxicity may occur several weeks or more after the last treatment with temozolomide.

DRUG INTERACTIONS:

- No studies have been conducted to determine the effect of temozolomide on the metabolism or elimination of other medicinal products.
- Since temozolomide does not undergo hepatic metabolism and exhibits low protein binding, it is unlikely that it would affect the pharmacokinetics of other medicinal products
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Temozolomide - L01AX03

REFERENCES:

1. Bower M, Newlands ES, Bleehan NM et al. Multicentre CRC phase II trial of temozolomide in recurrent or progressive high grade glioma. Cancer Chemother Pharmacol 1997;40:484-8.
2. Yung WKA, Prados MD, Yaya-Tur R et al. Multicenter phase II trial of temozolomide in patients with anaplastic astrocytoma or anaplastic oligoastrocytoma at first relapse. J Clin Oncol 1999;17:2762-71.
3. Temodal ® Summary of Product Characteristics Accessed June 2020. Available at https://www.ema.europa.eu/en/documents/product-information/temodal-epar-product-information_en.pdf
4. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V2 2019. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

Version	Date	Amendment	Approved By
1	20/06/2016		Prof Maccon Keane
2	20/06/2018	Updated with new NCCP regimen template and clarified treatment table	Prof Maccon Keane
3	15/07/2020	Regimen review Updated emetogenic potential	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.