Temozolomide

Indication
Relapsed CNS lymphoma with palliative intent. (Note: This is an unlicensed indication).

Not recommended to be used with radiotherapy.

Funding must be approved prior to commencing treatment.

ICD-10 codes
Codes with a prefix C85.

Regimen details

Day	Drug	Dose	Route
1 to 5	Temozolomide	150 mg/m^2 (cycle 1) then 200mg/m^2 (cycle 2 onwards)	PO

At the start of cycle 2, the dose is escalated to 200 mg/m^2 if:

- non-haematological toxicity (other than alopecia, nausea and vomiting) for cycle 1 is ≤ grade 2
- neutrophils ≥ 1.5 x 10^9/L
- platelets ≥ 100 x 10^9/L.

Once escalated, the dose remains at 200 mg/m^2 for each subsequent cycle unless toxicity occurs.
For patients who have **not** had any previous chemotherapy, the dose of 200mg/m^2 may be used from cycle 1 onwards.

Patients are likely to be on concurrent steroid therapy at time of starting temozolomide treatment- seek consultant advice regarding dosing of steroid. Patients should be closely monitored for development of PCP infection.

Cycle frequency
28 days

Number of cycles
Until disease progression (usual maximum of 8 cycles)

Administration
Temozolomide hard capsules are available as 5mg, 20mg, 100mg, 140mg, 180mg, and 250mg capsules.
Capsules should be taken on an empty stomach, swallowed whole with a glass of water.
Capsules must **NOT** be opened or chewed.
If vomiting occurs after the dose is administered, a second dose should not be administered that day.

Pre-medication
5HT$_3$-antagonist 30 minutes prior to each temozolomide dose.

Emetogenicity
This regimen has high emetogenic potential.

Additional supportive medication
Laxatives if required.
Antiviral and PCP prophylaxis as per local policy.

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days

Standard limits for administration to go ahead
If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophil count	≥ 1.5 x 10^9/L
Platelet count	≥ 100 x 10^9/L

Dose modifications
- **Haematological toxicity**

Neutrophils		Platelets	Action
≥ 1.5 x 10^9/L	and	≥ 100 x 10^9/L	Continue
1.0 – 1.5 x 10^9/L	and	≥ 100 x 10^9/L	Discuss with consultant
< 1.0 x 10^9/L	or	< 100 x 10^9/L	Delay 1 week and consider reducing dose by 50mg/m^2/day

Temozolomide is to be discontinued if a dose of 100 mg/m^2/day still results in unacceptable toxicity

- **Renal impairment**

No modifications required.

- **Hepatic impairment**

No modifications required. Caution is recommended in patients with severe hepatic impairment.

- **Other toxicities**

Toxicity	Definition	Dose adjustment
Any non-haematological (except alopecia, nausea, vomiting)	Grade 3	Reduce temozolomide by 50mg/m^2/day
	Grade 4	Discontinue treatment

Temozolomide should be discontinued if any ≥ Grade 3 toxicity (except for alopecia, nausea, vomiting) recurs after dose reduction to 100mg/m^2/day.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Thromboembolism
Pneumonitis / dyspnoea
Hypersensitivity and allergic reactions
Myopathy
Teratogenicity
Infertility

- **Frequently occurring side effects**

Nausea and vomiting
Fatigue
Anorexia, weight loss
Constipation or diarrhoea
Rash
Seizures, headache
Arthralgia/myalgia
Myelosuppression
Stomatitis/mucositis
Oedema

- **Other side effects**

Raised liver enzymes
Hearing impairment, tinnitus
Anxiety
Depression
Alopecia
Hyperglycaemia

Significant drug interactions – for full details consult product literature/ reference texts

Sodium valproate - may decrease clearance of temozolomide.

Additional comments

Contra-indicated in patients hypersensitive to dacarbazine (DTIC).

References

- Summary of Product Characteristics Temodal Capsules accessed 22 Feb 2018 via www.medicines.org.uk
- Mankino K *et al*. Salvage treatment with temozolomide in refractory or relapsed primary central nervous system lymphoma and assessment of the MGMT status. J Neurooncol (2012) 106:155–160
- Reni M *et al*. Temozolomide as salvage treatment in primary brain lymphomas. Br J Cancer. (2007) 96(6):864-7

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