Temozolomide monotherapy

Indication

Recurrent malignant glioma in patients who have Karnofsky performance status ≥70 (WHO performance status ≤ 2)

(NICE TA23)

Adjuvant monotherapy following Radiotherapy in patients who did not have concurrent RT

ICD-10 codes

Codes prefixed with C71

Regimen details

For patients who have had previous chemotherapy or radiotherapy

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 and 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.
Cap BSA at 2.2 m^2

Cycle frequency

28 days

Number of cycles

Adjuvant – 6 -12 cycles
Advanced disease – up to 12 cycles according to response

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 (5 days)

Emetogenicity
This regimen has high emetogenic potential.

Additional supportive medication
Laxatives if required. Metoclopramide 10mg tds prn.

Extravasation
N/A

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs (including AST)	14 days

Investigations - pre subsequent cycles
FBC, U+E (including creatinine), LFT (including AST)

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**

If neutrophils < 1.5 x 10^9/L **or** platelets < 100 x 10^9/L, delay 1 week and consider reducing temozolomide by 50mg/m^2/day.

If neutrophils < 1.0 x 10^9/L **or** platelets < 50 x 10^9/L delay 1 week and reduce temozolomide 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 dose modifications required.

- **Hepatic impairment**

No dose 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

- **Other side effects**

Raised liver enzymes
Hearing impairment, tinnitus
Anxiety
Depression
Alopecia

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.

References

- National Institute for Health and Clinical Excellence. Technology Appraisal 23.
- National Institute for Health and Clinical Excellence. Technology Appraisal 121.
- Summary of Product Characteristics Temodal Capsules www.medicines.org.uk
- Roger Stupp et al.; Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma; NEJM; Volume 352:987-996

THIS PROTOCOL HAS BEEN DIRECTED BY DR BEAUMONT, DESIGNATED LEAD CLINICIAN FOR NEURO-ONCOLOGY

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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