Temozolomide and radiotherapy

Indication
Newly diagnosed glioblastoma multiforme (GBM) in adult patients with a WHO performance status of 0 to 2,

or aged 65 years old and over. (NICE TA121)

ICD-10 codes
Codes prefixed with C71.

Regimen details

Day	Drug	Dose	Route
1 to 42	Temozolomide	75 mg/m^2 once daily during the 6 weeks of radiotherapy	PO
4 weeks post completion of RT, C2			
1-5	Temozolomide	150mg/ m^2 once daily	PO
Subsequent adjuvant cycles, C3-13, every 4 weeks			
1-5	Temozolomide	200mg/ m^2 once daily	PO

Cycle frequency
As above

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
Metoclopramide prn during concurrent phase
5-HT_3 antagonist days 1-5 during adjuvant phase

Emetogenicity
This regimen has low emetogenic potential.

Additional supportive medication
PCP prophylaxis: All patients should receive Co-trimoxazole 960mg on alternate days for weeks
Patients who cannot tolerate the above, should receive Pentamidine Isetionate Inhalation 300mg every 4weeks X 3

Antiemetic prior to administration

Capsules not to be chewed or opened, if capsule becomes damaged avoid contact of the powder contents with skin or mucous membrane. If contact does occur wash the affected area.

Capsule sizes are 250mg, 180mg, 140mg, 100mg, 20mg, 5mg. The clinical pharmacist checking the prescription will

round the prescribed dose to the nearest possible using the available capsule sizes

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFT (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
Haemoglobin	≥ 9.5

Dose modifications

No dose reductions will be made in this phase of the patient's treatment. If treatment has to be interrupted, missed doses will be omitted and the radiotherapy continued.

- **Haematological toxicity**

If neutrophils < 1.0 x 10^9/L **or** platelets < 100 x 10^9/L, delay 1 week and consider reducing temozolomide by 50mg/m^2/day. If this happens during RT treatment, continue RT whilst omitting temozolomide for a week.

If 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 and 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**

Thromboembolism
Pneumonitis / dyspnoea
Hypersensitivity and allergic reactions
Myopathy
Hepatic failure
Teratogenicity
Infertility
Opportunistic infections, including PCP, Herpes simplex and oral candidiasis

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Fatigue
Anorexia, weight loss
Constipation, 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 121.
- Summary of Product Characteristics - Temozolomide (MSD) www.medicines.org.uk

THIS PROTOCOL HAS BEEN DIRECTED BY NEURO-ONCOLOGY TEAM

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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