

Temozolomide and radiotherapy

Indication

Newly diagnosed glioblastoma multiforme (GBM) in adult patients with a WHO performance status of 0 or 2.

(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	Temozolamide	150mg/ m ² once daily	PO
Subsequent adjuvant cycles, C3-7, every 4 weeks			
1-5	Temozolamide	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-HT₃ 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 8 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	$> 1.5 \times 10^9/\text{L}$
Platelet count	$> 100 \times 10^9/\text{L}$
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 $< 1.0 \times 10^9/\text{L}$ **or** platelets $< 100 \times 10^9/\text{L}$, delay 1 week and consider reducing temozolomide by $50\text{mg}/\text{m}^2/\text{day}$. If this happens during RT treatment, continue RT whilst omitting temozolomide for a week.

If platelets $< 50 \times 10^9/\text{L}$ delay 1 week and reduce temozolomide by $50\text{mg}/\text{m}^2/\text{day}$.

Temozolomide is to be discontinued if a dose of $100 \text{ mg}/\text{m}^2/\text{day}$ 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 $50\text{mg}/\text{m}^2/\text{day}$
	Grade 4	Discontinue treatment

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

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
- 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

Date: June 2020
Review: June 2022
VERSION: 14
