Temozolomide and radiotherapy

Indication
Newly diagnosed glioblastoma multiforme (GBM) in adult patients with a WHO performance status of 0 or 1.

(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

Cycle frequency
As above

Number of cycles
A single 6 week course.

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 once daily, 30 minutes prior to temozolomide days 1 to 3 only.
Continued beyond this only if clinically indicated.

Emetogenicity
This regimen has low emetogenic potential.

Additional supportive medication
PCP prophylaxis as per local policy.

Extravasation
N/A

Investigations – pre first cycle

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

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	Weekly during treatment
U+E (including creatinine)	Weekly during treatment
LFT	Weekly during treatment

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

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**

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Action**
0.5-1.5	or	50-100 x 10^9/L	Interrupt temozolomide therapy for 1 week (and continue with radiotherapy). If FBC has recovered after 1 week, resume temozolomide at full dose.
<0.5	or	<50 x 10^9/L	Discontinue treatment (and continue with radiotherapy alone).

- **Renal impairment**

No dose modifications required.

- **Hepatic impairment**

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

- **Other toxicities**

For any grade 2 toxicity, (other than alopecia or nausea and vomiting), withhold temozolomide until recovery. For grade 3-4 toxicity discontinue temozolomide.

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. Accessed 19 Mar 2014 via www.nice.org.uk
- Summary of Product Characteristics - Temozolomide (MSD) Accessed 8 March 2019 via www.medicines.org.uk
- Roger Stupp et al.; Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma; NEJM; Volume 352:987-996

Written/reviewed by: v2 Dr C Herbert (Consultant Oncologist, UHBristol NHS Trust)

Checked by: Sarah Murdoch (Senior Oncology Pharmacist, SW Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Clinical Network)

Date: December 2014 v2 March 2019