

Systemic Anti-Cancer Treatment Protocol
Temozolomide with concomitant radiotherapy

**PROTOCOL REF: MPHATEMCR
 (Version No: 1.1)**

Approved for use in:

Adult patients with newly-diagnosed glioblastoma multiforme concomitantly with radiotherapy and subsequently as monotherapy treatment (see separate protocol).

Dosage:

Concomitant temozolomide and radiotherapy

Drug	Dosage	Route	Frequency
Temozolomide	75mg/m ²	oral	Daily for 42 days

Followed by temozolomide monotherapy (see separate protocol), to be reviewed by oncologist 4 weeks after completion of radiotherapy.

Drug	Dosage	Route	Frequency
Temozolomide	150mg/m ²	oral	Once daily for 5 days At Cycle 2, the dose is escalated to 200 mg/m ² , if tolerated, for up to 6 cycles

Supportive treatments:

Moderately emetic:

Ondansetron 8mg daily if required (one hour before temozolomide)

Cyclizine 50mg tablets, three times a day when required

Additional Medication:

PCP prophylaxis, particularly if patients on concurrent corticosteroid (dexamethasone) – co-trimoxazole 960mg PO once a day on Mondays, Wednesdays and Fridays of each

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week which should continue for 4 weeks after last cycle, or until lymphocyte counts return to normal values.

Extravasation risk:

Not applicable

Administration:

Day	Drug	Dose	Route	Frequency
1-21	Temozolomide	75mg/m ²	PO	30 minutes before radiotherapy (or on the morning at weekends) for 21 days
22-42	Temozolomide	75mg/m ²	PO	30 minutes before radiotherapy (or on the morning at weekends) for 21 days
42-49	<i>Temozolomide (optional)</i>	<i>75mg/m²</i>	<i>PO</i>	<i>30 minutes before radiotherapy (or on the morning at weekends) if needed</i>
1 to 70	Co-trimoxazole	960mg	PO	Mondays, Wednesdays and Fridays during treatment and for up to 4 weeks after completion of treatment

During the concomitant phase, temozolomide 75mg/m²/day every day for 42 days, 30 minutes prior to the radiotherapy and in the morning at weekends (non-radiotherapy days). Temozolomide capsules are to be swallowed whole with a glass of water on an empty stomach, 1 hour before or after meals.

Once the radiotherapy is completed, there will be a 4 week treatment free period before the adjuvant cycle commences.

Main Toxicities:

- Myelosuppression (thrombocytopenia and neutropenia)
- Tiredness and weakness (fatigue) during and after treatment

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- Alopecia
- Nausea and vomiting
- Anorexia
- An itchy rash and dry skin – severe allergic rash occurs occasionally and requires discontinuation of temozolomide
- Headaches
- Constipation
- Hepatotoxicity (rare fatal cases have been reported)
- Amenorrhoea, but this may only be temporary
- Loss of fertility
- Pneumocystis carinii pneumonia

Investigations:

	Pre	Wk1	Wk2	Wk3	Ongoing
Medical Assessment	X	X	X	X	Every week
Radiographer / Nursing Assessment		X	X	X	Every week
FBC	X	X	X	X	Once a week
U&E & LFTs	X	X	X	X	Once a week
MRI scan	X				As clinically indicated
Informed Consent	X				
PS recorded	X	X	X	X	
Toxicities documented	X	X	X	X	
Weight recorded	X	X	X	X	Every week

Dose Modifications and Toxicity Management:

Haematological toxicity

During treatment a complete blood count should be obtained weekly.

If radiotherapy is interrupted continue temozolomide (maximum 49 days total)

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Toxicity	TMZ interruption	TMZ discontinuation
Absolute neutrophil count	≥ 0.5 and $\leq 1.5 \times 10^9/L$	$< 0.5 \times 10^9/L$
Platelet count	≥ 10 and $\leq 99 \times 10^9/L$	$< 10 \times 10^9/L$
CTC non-haematological toxicity (except for alopecia, nausea, vomiting)	CTC Grade 2	CTC Grade 3 or 4

Hepatic toxicity

Review concurrent medication – particularly anticonvulsants and consider their effect on LFTs

Stop temozolomide if progressive rise in transaminases or rise in bilirubin

Marrow aplasia

If thrombocytopenia continues after discontinuation of temozolomide with reduction in neutrophil count, then:

- Stop co-trimoxazole
- Repeat FBC daily
- Add daily filgrastim
- Supportive blood product transfusions as necessary
- Contact haematologists for advice in severe cases

References:

<http://www.medicines.org.uk/EMC/medicine/7027/SPC/Temodal+Capsules/>

<http://www.medicines.org.uk/emc/PIL.28687.latest.pdf>

<http://www.cancerresearchuk.org/about-cancer/cancers-in-general/treatment/cancer-drugs/temozolomide>

NICE TA 121 June 2007

Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma

Stupp R et al

NEJM 2005 352:987-996

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