SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Temozolomide (TMZ)
CNS

PROTOCOL REF: MPHATEMOZ
(Version No. 3.2)

Approved for use in:

- Newly diagnosed Glioma (after concurrent radiotherapy treatment – see separate protocol) in patients with WHO PS 0-1
- Malignant glioma showing recurrence or progression after standard therapy

Dosage:

Drug	Dose	Route	Frequency
Temozolomide	150mg/m^2	Oral	Once daily for 5 days every 28 days. At Cycle 2, the dose is escalated to 200 mg/m^2, if tolerated

To be given for up to 12 cycles if adjuvant or until progression if recurrent disease

Supportive treatments:

- Ondansetron 8mg – One hour before chemotherapy
- Cyclizine 50mg Tablets – 50mg up to three times a day when required

Administration and counselling points:

Temozolomide is available as 5mg, 20mg, 100mg, 140mg, 180mg and 250mg capsules.

Temozolomide capsules are to be swallowed whole with a glass of water on an empty stomach, 1 hour before or after meals.

For patients unable to swallow capsules, please refer to the information sheet produced by Great Ormond Street Hospital for instructions on how to produce a mixture (available at https://www.gosh.nhs.uk/medical-information-0/medicines-information/temozolomide)

Emetogenic risk:

Mildly emetogenic.

Main toxicities:

Temozolomide		
System Organ Class	Frequency	
Infections and infestations	Common	Infections, herpes zoster, pharyngitis, candidiasis oral
Blood and lymphatic system disorders	Common	Febrile neutropenia, neutropenia, thrombocytopenia, lymphopenia, leukopenia, anaemia
Immune system disorders	Common	Allergic reaction
Endocrine disorders	Common	Cushingoid
Metabolism and nutrition disorders	Very common	Anorexia
	Common	Hyperglycaemia
Psychiatric disorders	Common	Agitation, amnesia, depression, anxiety, confusion, insomnia
Nervous system disorders	Very common	Convulsions, hemiparesis, aphasia/dysphasia, headache
	Common	Ataxia, balance impaired, cognition impaired, concentration impaired, consciousness decreased, dizziness, hypoesthesia, memory impaired, neurologic disorder, neuropathy, paraesthesia, somnolence, speech disorder, taste perversion, tremor
Eye disorders	Common	Hemianopia, vision blurred, vision disorder, visual field defect, diplopia, eye pain
Ear and labyrinth disorders	Common	Deafness, vertigo, tinnitus, earache
Vascular disorders	Common	Haemorrhage, embolism

		pulmonary, deep vein thrombosis, hypertension
Respiratory, thoracic and mediastinal disorders	Common	Pneumonia, dyspnoea, sinusitis, bronchitis, coughing, upper respiratory infection
Gastrointestinal disorders	Very common	Diarrhoea, constipation, nausea, vomiting
	Common	Stomatitis, abdominal pain, dyspepsia, dysphagia
Skin and subcutaneous tissue disorders	Very common	Rash, alopecia
	Common	Erythema, dry skin, pruritus
Musculoskeletal and connective tissue disorders	Common	Myopathy, muscle weakness, arthralgia, back pain, musculoskeletal pain, myalgia
Renal and urinary disorders	Common	Micturition frequency, urinary incontinence
General disorders and administration site conditions	Very common	Fatigue
	Common	Fever, influenza-like symptoms, asthenia, malaise, pain, oedema, oedema peripheral
Investigations	Common	Liver enzymes elevation, weight decreased, weight increased

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details

Interactions:

No studies have been conducted to determine the effect of temozolomide on the metabolism or elimination of other medicinal products. However, since temozolomide does not undergo hepatic metabolism and exhibits low protein binding, it is unlikely that it would affect the pharmacokinetics of other medicinal products. For further details refer to SPC: Temozolomide 20 mg hard capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

Dosing in renal and hepatic impairment:

Renal impairment

No dose adjustment necessary

Hepatic toxicity

Review concurrent medication (particularly anticonvulsants) and consider their effect on liver function. No dose adjustments necessary for mild to moderate hepatic impairment. No data available for patients with severe hepatic impairment. Stop temozolomide if there is a progressive rise in transaminases or rise in bilirubin

Investigations and treatment plan:

	Pre	Cycle 1 Day 1	Cycle 1 Day 15	Cycle 2	Cycle 3	Ongoing
Informed Consent	x					
Clinical Assessment	x	x	x	x	x	Every cycle
SACT Assessment (to include PS and toxicities)	x	x	x	x	x	Every cycle
FBC	x	x	x	x	x	2-weekly for first cycle then every cycle
U&E & LFTs	x	x	x	x	x	2-weekly for first cycle then every cycle
MRI scan	x					Every 3 cycles
Weight recorded	x	x	x	x	x	Every cycle
Height recorded	x					

Dose Modifications and Toxicity Management:

Haematological toxicity (if required):

Proceed on day 1 if-

ANC ≥ 1.5 x 10^9/L	Platelets ≥ 100 x 10^9/L

Delay 1 week on day 1 if-

ANC < 1.5 x 10^9/L	Platelets ≤ 99 x 10^9/L

Dose modifications:

Consider dose reducing by one level in the event of haematological toxicity as per table below.

Dose level	TMZ dose (mg/m^2/day)	Remarks
-1	100	Reduction for prior toxicity
0	150	Dose during cycle 1
1	200	Dose cycles 2-12 in absence of toxicity

Temozolomide should be discontinued if a dose reduction to 100mg/m2 still results in unacceptable toxicity.

Non-haematological toxicities

Temozolomide should be deferred by one week if CTC Grade 3 non-haematological toxicity occurs.

In the event of non-haematological toxicities, consider reducing the dose of temozolomide by one level (as per table above).

If the same Grade 3 non-haematological toxicity occurs despite a dose reduction to 100mg/m2 , temozolomide should be discontinued.

References:

1. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma Stupp R et al NEJM 2005 352:987-996
2. Survival following adjuvant PCV or temozolomide for anaplastic astrocytoma Brandes AA et al Neuro-oncology 2006 253-260
3. Temozolomide chemotherapy alone versus radiotherapy alone for malignant astrocytoma in the elderly: the NOA-08 randomised, phase 3 trial Wick W et al Lancet 2012 13(7):707-715
4. Second line chemotherapy with temozolomide in recurrent oligodendroglioma after PCV chemotherapy: EORTC Brain Tumour Group phase II study 26972 Annals of Oncology 2003 14(4): 599-602
5. Temozolomide 20mg hard capsules, summary of product characteristics, Ranbaxy (UK) Limited a Sun Pharmaceutical Company. Available at: Temozolomide 20 mg hard capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Last updated 15/03/2023.
6. Supplement to: Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; 20: e201–08.

Circulation/Dissemination

Date added into Q-Pulse	7th September 2023
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Version History

Date	Version	Author name and designation	Summary of main changes
As of 6th April 2023	3.2	**Hugh O'Neill**	Updated protocol to new format Updated supportive treatments