

## Chemotherapy Protocol

### Central Nervous System

#### TEMOZOLOMIDE (150)

#### Regimen

- CNS – Temozolomide (150)

#### Indication

- First line treatment of newly diagnosed glioblastoma multiforma starting four weeks after treatment with concomitant radiotherapy and temozolomide
- Recurrent or progressive malignant glioma in patients previously treated with chemotherapy
- Performance status 0, 1

#### Toxicity

Drug	Adverse Effect
Temozolomide	Hepatic injury, thrombocytopenia, nausea and vomiting, <i>Pneumocystis jirovecii</i> infection

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

#### Monitoring

##### *Drugs*

- FBC, LFT's, U&E's and glucose on day 22 of the cycle
- Clinical examination including neurological assessment, whole brain imaging and chest x-ray prior to starting treatment

#### Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

### Haematological

Prior to starting treatment the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

During treatment a complete blood count should be obtained on day 22 (21 days after the first dose of temozolomide). Temozolomide can be restarted, at a reduced dose, provided the neutrophils have recovered to  $1 \times 10^9/L$  and platelets  $100 \times 10^9/L$  within seven days of the planned administration date, or administration discontinued according to the tables below.

Toxicity	Reduce dose by $50 \text{mg}/\text{m}^2$	Discontinue temozolomide
Neutrophil	$0.5 - 1 \times 10^9/L$	less than $0.5 \times 10^9/L$
Platelet	$10 - 100 \times 10^9/L$	less than $10 \times 10^9/L$

Temozolomide is to be discontinued if a dose of  $100 \text{mg}/\text{m}^2$  still results in unacceptable toxicity or the same NCI CTC grade 3 non-haematological toxicity (except for alopecia, nausea, vomiting) recurs after dose reduction.

### Hepatic Impairment

Toxicity	Action
Bilirubin more than $1.5 \times \text{ULN}$	Stop temozolomide
ALT more than $2.5 \times \text{ULN}$	Stop temozolomide

### Renal Impairment

Drug	Action
Temozolomide	No dose reductions are required. Caution in severe renal impairment

### Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 2 toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. For toxicity that is NCI-CTC grade 3 or above discontinue treatment, in some situations it may be appropriate to re-start treatment with a reduced dose when symptoms have resolved

## Regimen

When used following concomitant temozolomide and radiotherapy treatment is started four weeks after completing the concomitant phase. The dose in cycle 1 (monotherapy) is 150mg/m<sup>2</sup> once a day for 5 days followed by 23 days without treatment. At the start of cycle 2, the dose is escalated to 200mg/m<sup>2</sup> if the NCI CTC non-haematological toxicity for cycle 1 is less than or equal to grade 2 (except for alopecia, nausea and vomiting) or the absolute neutrophil count is greater than or equal to 1.5x10<sup>9</sup>/L, and the thrombocyte count is greater than or equal to 100x10<sup>9</sup>/L. If the dose is not escalated at cycle 2, escalation should not be done in subsequent cycles. Once escalated, the dose remains at 200mg/m<sup>2</sup> per day for the first 5 days of each subsequent cycle except if toxicity occurs.

### **28 day cycle for 6 cycles**

#### Cycle One

<b>Drug</b>	<b>Dose</b>	<b>Days</b>	<b>Administration</b>
Temozolomide	150mg/m <sup>2</sup> (maximum 300mg)	1-5 inclusive	Oral

#### Cycle Two to Six

<b>Drug</b>	<b>Dose</b>	<b>Days</b>	<b>Administration</b>
Temozolomide	200mg/m <sup>2</sup> (maximum 400mg)	1-5 inclusive	Oral

## Dose

- Temozolomide will be dose banded in accordance with the national dose bands (temozolomide oral)
- The dose of temozolomide will be capped at 2m<sup>2</sup>

## Administration Information

- Temozolomide should be taken on an empty stomach
- Temozolomide to be taken with plenty of water swallowed whole, not chewed

## Additional Therapy

### Antiemetics

- As take home medication
  - ondansetron 8mg 15 – 30 minutes prior to temozolomide oral

- Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday until lymphocytes are above 0.8
- Gastric protection with a proton pump inhibitor or a H<sub>2</sub> antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

#### Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to oral temozolomide.

#### Coding

- Procurement – X70.5, X71.1
- Delivery – X73.1

#### References

- 1.National Institute for Health and Clinical Excellence (2007). NICE TA 121. Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma. DOH: London
- 2.National Institute for Clinical Excellence (2001). NICE TA 23: Guidance on the use of temozolomide for the treatment of recurrent malignant glioma (brain cancer). DOH: London
- 3.Stupp et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 2005; 352: 987-96

## REGIMEN SUMMARY

### Temozolomide (150)

#### Cycle 1

##### Take Home Medicines

1. Temozolomide 150mg/m<sup>2</sup> oral once a day for 5 days oral  
Administration Instructions  
Take on an empty stomach, swallow whole, do not chew
2. Ondansetron 8mg once a day 15-30 minutes prior to the temozolomide oral  
Administration Instructions  
An additional 8mg dose may be taken 12 hours later if required for the treatment of nausea and vomiting  
Please supply an original pack (10 tablets) or nearest appropriate equivalent

#### Cycle 2 - 6

##### Take Home Medicines

3. Temozolomide 200mg/m<sup>2</sup> oral once a day for 5 days oral  
Administration Instructions  
Take on an empty stomach, swallow whole, do not chew
4. Ondansetron 8mg once a day 15-30 minutes prior to the temozolomide oral  
Administration Instructions  
An additional 8mg dose may be taken 12 hours later if required for the treatment of nausea and vomiting  
Please supply an original pack (10 tablets) or nearest appropriate equivalent

## DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Feb 2019	Lymphocyte dose adjustment removed Dose rounding changed to dose bands Disclaimer updated	Donna Kimber Pharmacy Technician	Dr Deborah Wright Pharmacist
1	Oct 2015	None	Dr Deborah Wright Pharmacist	Dr Omar Al Salihi Consultant Clinical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust  
NHS Isle of Wight  
Portsmouth Hospitals NHS Trust  
Salisbury Hospital NHS Foundation Trust  
University Hospital Southampton NHS Foundation Trust  
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.