Chemotherapy Protocol

Central Nervous System

TEMOZOLOMIDE RT (7 day)

Regimen

- CNS – Temozolomide RT (7 day)

Indication

- First line treatment of newly diagnosed glioblastoma multiforma in conjunction with radiotherapy
- Performance status 0, 1

Toxicity

Drug	Adverse Effect
Temozolomide	Hepatic injury, thrombocytopenia, nausea and vomiting, *Pneumocystis jirovecii* 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 prior to starting treatment and every seven days thereafter
- 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 $1.5x10^9$/L
Platelets	equal to or more than $100x10^9$/L

Consider blood transfusion or erythropoietin according to NICE technology appraisal if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Thereafter

Toxicity	Interrupt temozolomide	Discontinue temozolomide
Neutrophil	0.5 - $1.5x10^9$/L	less than $0.5x10^9$/L
Platelet	10 - $100x10^9$/L	less than $10x10^9$/L

Hepatic Impairment

Toxicity	Action
Bilirubin more than 1.5xULN	Stop temozolomide
ALT more than 2.5xULN	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.

Regimen

7 day cycle for 7 cycles (maximum 49 days)

Drug	Dose	Days	Administration
Temozolomide	75mg/m^2 (maximum 150mg. Note that the maximum dose will be set as 145mg in ARIA to comply with national dose bands)	1-7 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 $2m^{2.}$ This will be set at 145mg in ARIA to comply with the national dose bands.
- Temozolomide therapy should be started on the first day of radiotherapy and stopped on the last day of radiotherapy. It is taken continuously even on days when radiotherapy is not due, for example weekends.
- The maximum number of days of treatment is 49

Administration Information

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

Additional Therapy

Antiemetics

- As take home medication
    - ondansetron 8mg 15 – 30 minutes prior to temozolomide oral
    - domperidone 10mg three times a day when required for the relief of nausea (cycle one only) oral
- Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday
- Gastric protection with a proton pump inhibitor or a H_2 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 – X71.5
- 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 RT (7 day)

Cycle 1 Day 1

Take Home Medicines

1. Temozolomide 75mg/m^2 oral once a day for 7 days oral

2. Ondansetron 8mg once a day 15-30 minutes prior to the temozolomide oral
   Administration Instructions
   An additional 8mg may be taken 12 hours later if required for the relief of nausea and vomiting
   Please supply an original pack (10 tablets) or nearest appropriate equivalent

3. Domperidone 10mg oral three times a day when required oral
   Administration Instructions
   Please supply 30 tablets or nearest original pack size

4. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral
   Administration Instructions
   Please supply sufficient for 49 days of treatment

Cycle 2 - 7

Take Home Medicines

5. Temozolomide 75mg/m^2 oral once a day for 7 days oral

6. Ondansetron 8mg once a day 15-30 minutes prior to the temozolomide oral
   Administration Instructions
   An additional 8mg may be taken 12 hours later if required for the relief of nausea.
   Please supply an original pack (10 tablets) or nearest appropriate equivalent.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	April 2019	The maximum dose of temozolomide changed to 145mg to comply with the national dose bands	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
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.