TEMOZOLOMIDE AND RADIOTHERAPY

Treatment of high-grade glioma (WHO grades 3 and 4), given after surgical resection to patients with performance status 1 or 0, and followed by up to 6 cycles of temozolomide monotherapy
Use in GBM NICE approved 2007

Drug/Dosage: **Temozolomide** 75mg/m^2 PO once daily**, 7 days per week**, during radiotherapy (RT)

Radiotherapy: *Standard RT (generally < 70 years and fit):*
2Gy/fraction, given daily on weekdays only over 6 weeks, to a total of 60Gy

Elderly patients (> 65 years, or < 65 years but less fit):
40Gy in 15 fractions (2.67Gy/#), given daily on weekdays only, over 3 weeks

Grade 3 astrocytoma:
59.4Gy in 33 fractions (1.8Gy/#), given daily on weekdays only, over 6½ weeks

Radiotherapy should commence within 30 – 90 minutes of the daily temozolomide dose

Administration: Temozolomide is available as 5mg, 20mg, 100mg, 140mg, 180mg and 250mg capsules. To be taken on an empty stomach, swallowed whole with a glass of water, 30 – 90 minutes before radiotherapy appointment time.

Other Drugs: PCP prophylaxis (first-line co-trimoxazole 480mg bd Mon, Wed and Fri; second-line inhaled pentamidine) throughout chemo-radiotherapy. This may be discontinued on the last day of radiotherapy.

Frequency: a single course, of the same length as the planned radiotherapy

4 weeks after chemo-radiotherapy completed, to start adjuvant temozolomide monotherapy. **Please refer to Temozolomide protocol for further information regarding monotherapy.**

Main Toxicities: myelosuppression; ovarian failure; infertility

Anti-emetics: mildly emetogenic

Regular Investigations: FBC, LFTs & U&E weekly

Dose Modifications

Haematological Toxicity:	Neutrophils 0.5 - 1.5 x 10^9/l or Platelets 30 - 100 x 10^9/l	Interrupt temozolomide therapy for 1 week. Continue with RT. Repeat FBC after a week and, if within normal parameters, re-start temozolomide at full dose.
	Neutrophils < 0.5 x 10^9/l or Platelets < 30 x 10^9/l	Discontinue concurrent temozolomide permanently. Continue with RT alone.

Renal Impairment: No dose reduction is routinely required in patients with renal impairment but, if severe impairment, confirm dosage requirements with Consultant.

Hepatic Impairment: No dose reduction is routinely required in patients with hepatic impairment but discuss with Consultant and consider the following:

- Hepatic injury, including fatal hepatic failure, has been reported in patients treated with temozolomide. If abnormal LFTs at baseline, the benefit/risk should be considered prior to initiating temozolomide, including the potential for fatal hepatic failure.
- For patients who develop significant liver function abnormalities after treatment has started, discuss the benefit/risk of continuing treatment with the Consultant. Liver toxicity may occur several weeks or more after the last treatment with temozolomide.

Reference:

Stupp, R et al; NEJM 2005; 352 (10): 987 – 996
Van Den Bent et al; JCO 2016; 34 (suppl); abstract LBA2000 (astrocytoma)
Perry, J et al; JCO 2016; 34 (suppl); abstract LBA2 (elderly/frail)