Indication	Glioblastoma with methylated MGMT promoter post resection in patients aged 18-70yrs of performance status 0-1 only.
Treatment Intent	Radical (radiotherapy given with cycle 1) / Adjuvant
Frequency and number of cycles	Repeat every 42 days. For a maximum of 6 cycles. Patient must have a formal assessment after 3 cycles to determine whether to continue treatment.

Monitoring Parameters pre-treatment	• Consider baseline virology status check for Hep B and CMV.
	• Monitor LFT's, U&E's Glucose and FBC at baseline, day 1 and repeated between day 21-24 of each cycle. If blood counts are still low patient should have repeat bloods on day 29.
	• Chemotherapy nurse review appointment for nadir bloods (day 21-24).
	• If neuts >/= 1.5 and Plts >/= 150 proceed see Table 3.
	• Lung function as clinically indicated.
	• **Hepatic impairment:** (see table 2)
	  ○ Lomustine: Lack of available data in SPC.
	  ○ Temozolomide: Pre-cycle 1 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.
	• **Renal impairment:**
	  ○ See table 1
	• **Haematological Dose Modification:**
	  ○ **Lomustine:**
	  ○ **Dose reductions:** First reduction 75% of initial dose, second reduction 50% of initial dose.
	  ○ Refer to table 3 for dose adjustment guidance.
	  ○ **Temozolomide*:**
	  ○ **Dose levels:**
	  ○ **Reductions:** Dose reduction level one 75mg/m^2, dose reduction level two 50mg/m^2.
	  ○ Refer to table 3 for dose adjustment guidance.
	  ○ **Increases:** Dose increase level one 120mg/m^2, dose increase level two 150mg/m^2 and dose increase level three 200mg/m^2.
	• **Non-haematological toxicity:** If grade 3 or 4 non-haematological toxicity occurs withhold the causative agent.
	• In the event one agent is stopped due to toxicity single agent therapy may be given.
	• If a patient vomits following dosing, no additional dose should be taken that day. The next prescribed dose should be taken at the usual time the following day**.**
	• For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.

References	https://pubmed.ncbi.nlm.nih.gov/30782343/ https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31791-4/fulltext (CeTeG/NOA–09): a randomised, open-label, phase 3 trial paper

	SPC accessed online 20.04.21 The North London Cancer Network Dosage Adjustment for Cytotoxics in Hepatic Impairment 2009, The North London Cancer Network Dosage Adjustment for Cytotoxics in Renal Impairment 2009

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1: Renal impairment guidance

Cr clearance (ml/min)	Lomustine dose	Temozolomide dose
>60	100%	No dose reduction is routinely required in patients with renal impairment
45-60	75%	
30-44	50%	
<30	Not recommended	Not recommended

Table 2: Hepatic impairment guidance

Liver function	Lomustine dose	Temozolomide dose
ALT 80-244 units/l and/or ALP 260 – 650 units/l and/or Bilirubin 32 - 63 µmol/l	No data to guide but generally discontinue and consider pros and cons of changing to chemo following STUPP protocol in concomitant or adjuvant phase only	Delay until LFTs recovered & consultant to assess the benefit / risk of continuing. If decision made to continue, reduce temozolomide to a dose equivalent to 50mg/m^2 /day less than previous cycle. If the same toxicity recurs after the dose reduction, permanently discontinue temozolomide. If prolonged elevation of LFTs, consider liver blood screen and ultrasound.
ALT > 244 units/l and/or ALP > 650 units/l and/or Bilirubin > 63 µmol/l	Permanently discontinue	Permanently discontinue

Table 3: Dose modification in haematological toxicity

Nadir FBC day 21-24		
	Lomustine dose	**Temozolomide dose**
NEUTS>/= 1.5 x 10^9 /l and PLTS>/= 100 x 10^9 /l	Proceed with the next cycle	Proceed with the next cycle Consider dose level increment with next cycle, maximum 200mg/m^2
NEUTS 1-1.4 x 10^9 /l and/or PLTS 25-99 x 10^9 /l	Dose reduce 1 level	Reduce by 1 dose level
NEUTS<1 x 10^9 /l and/or PLTS <25 x 10^9 /l	Permanently discontinue	Reduce by 2 dose levels to 50mg/m^2
	Chemotherapy nurses to inform consultant if patient has any bleeding and recheck bloods in 1 week to ensure platelets increasing. PLT transfusion if PLT <20 and / or bleeding	
Permanently discontinue if NEUTS <1.5 and/or Plts <50 at the dose level of 50mg/m^2 temozolomide		
FBC pre-day 1 of next cycle		
NEUTS >/=1.5 x 10^9 /l and PLTS>150 x 10^9 /l	Proceed	If nadir requirement met consider dose increase by 1 dose level, maximum 200mg/m^2
PLTS 100-149 x 10^9 /l and/or NEUTS 1-1.5x 10^9 /l	Delay until recovery Consider dose reduce 1 level	Delay until recovery If nadir requirement met proceed on recovery but no dose increase.
NEUTS <1 x 10^9 /l and/or PLTS </=99 x 10^9 /l	Delay until recovery then dose reduce. Discontinue if further episode at 50% dose.	Delay until recovery then dose reduce 1 level. Discontinue if further episode at 50mg/m^2 dose.

Repeat every 42 days: first cycle to start with radiotherapy.

TTO	Drug	Dose	Route	Directions
Day 1	**LOMUSTINE**	**100mg/m^2**	PO	Take as a single dose at night on **Day 1 ONLY**. Available as 40mg capsule
	TEMOZOLOMIDE	**100mg/m^2** **(Increase to a maximum of 200mg/m^2 Please see notes above *)**	PO	Take ONCE a day on **DAYS 2 to 6 only.** Take this medicine when your stomach is empty. This means an hour before food or 2 hours after food. Swallow this medicine whole. Do not chew or crush. Available as 5mg, 20mg, 100mg,140mg, 180mg and 250mg capsules
	Ondansetron	8mg	PO	Take BD for 6 days. Take the first dose 30 minutes before taking the Lomustine capsules.
	Domperidone	10mg	PO	Up to TDS PRN. Maximum 30mg day. Do not take for more than 7 days continuously.
	Dexamethasone	6mg	PO	OM for 3/7
	Movicol sachet	1 sachet	PO	Take the contents of ONE sachet dissolved or mixed with water BD as required.