TEMOZOLOMIDE IRINOTECAN – local funding required

INDICATION (ICD10) C71.6

1. Recurrent and progressive SHH+ medulloblastoma, second line after PCV (unlicensed)

PS 0, 1, 2

REGIMEN

Days 1 to 5	**TEMOZOLOMIDE**	150mg/m^2	oral	once daily (1 hour before irinotecan)
	Premedication 30 minutes prior to irinotecan: Atropine 250mcg subcutaneously			
	IRINOTECAN	50mg/m^2	IV infusion	#ml over 30 minutes

diluent and diluent volume for dose prescribed as per national standardised product specification or licensed dose

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 6 cycles

ADMINISTRATION

Available as various strength capsules

Take on an empty stomach

ANTI-EMETICS

Moderate risk days 1 to 5

CONCURRENT MEDICATION REQUIRED

Irinotecan	Ensure premedication atropine given 30 minutes prior to treatment. Patients who experience delayed diarrhoea on previous cycles may require loperamide 2mg every 2 hours to continue for 12 hours after the last loose stool. This high dose should be discontinued after 48 hours. Consider antibiotic if indicated.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Irinotecan - irritant

Peripheral or central line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs every cycle

Neutrophils x 10^9/L ≥1.5

Platelets x 10^9/L ≥100

Serum creatinine every cycle

Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Irinotecan	Acute cholinergic syndrome (including diarrhea and delayed diarrhoea, abdominal pain, hypotension, dizziness, malaise, increased salivation). Drink large volumes of fluid containing electrolytes and an appropriate antidiarrhoeal therapy - loperamide 4mg initially then 2mg every 2 hours, continuing for 12 hours after the last liquid stool (maximum of 48 hours in total). If acute cholinergic syndrome appears (defined as early diarrhoea and various other signs and symptoms such as sweating, abdominal cramping, myosis and salivation), atropine sulfate (0.25mg subcutaneously) should be administered unless clinically contraindicated
Temozolomide	Myelosuppression, rare protracted aplastic picture can occur Hepatic toxicity – may still occur several weeks after end of treatment Renal impairment

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS (not exhaustive list check SPC/BNF/Stockleys)

Irinotecan	Aprepitant and fosaprepitant increases exposure to irinotecan. Carbamazepine increases exposure to irinotecan, avoid. Enzalutamide, mitotane, phenobarbitone, phenytoin, primidone and rifampicin decreases exposure to irinotecan, avoid.

DOSE MODIFICATIONS

Temozolomide

Dose level -1	Temozolomide dose 100mg/m^2/day	Reduction for prior toxicity
Dose level 0	Temozolomide dose 150mg/m^2/day	Cycle 1 dose

Haematological

Temozolomide
Neutrophils <1.5x10^9/l and platelets <100x10^9/l on day 21 then treatment should be delayed one week and then reduce by one dose level.

Non-haematological

Irinotecan
If patients suffer from severe diarrhoea, which required IV rehydration or neutropenic fever, consider reduction in subsequent cycles, discuss with SpR or Consultant.

Hepatic impairment

Irinotecan

Bilirubin 24-50micromol/L	give 50% dose
Bilirubin >51micromol/L	not recommended

Temozolomide
No need for dose adjustments is expected.

Renal impairment

Irinotecan
Not recommended in renal impairment, use with caution.

Temozolomide
No need for dose adjustments is expected.

REFERENCES

1. Grill, J., et al., Phase II study of irinotecan in combination with temozolomide (TEMIRI) in children with recurrent or refractory medulloblastoma: a joint ITCC and SIOPE brain tumor study. Neuro Oncol, 2013 15(9): p1236-43.
2. Giraud EL, de Lijster B, Krens SD, Desar IME, Boerrigter E, van Erp NP. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Lancet Oncol 2023; 24: e229.

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Every cycle
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E, calcium, magnesium & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
CT scan	X					At cycle 6, Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle