VORASIDENIB (Voranigo)

INDICATION (ICD10) solid tumours

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (VOR1)

1. Vorasidenib for treating grade 2 astrocytoma or oligodendroglioma with IDH1 or IDH2 mutations after surgery (but no other prior anticancer treatments (chemotherapy or radiation). Has been assessed as NOT requiring immediate treatment with chemotherapy OR radiotherapy (i.e. in the absence of vorasidenib, would be suitable for a "watch and wait approach") and does not currently exhibit any of the "high risk" features eg uncontrolled seizures, brain-stem involvement, clinically relevant functional or neurocognitive deficits caused by the tumour or glucocorticoid use for glioma-related signs or symptoms. PS 0 or 1 or if using the Karnofsky/Lansky score, this is 80 or higher.

REGIMEN

VORASIDENIB	40mg	oral	once daily continuously

CYCLE FREQUENCY AND NUMBER OF CYCLES

Continuously until disease progression

ADMINISTRATION

Available as 40mg tablets.
To be taken after at least 2 hours of fasting (water is allowed). Food intake should be avoided for at least 1 hour after taking.

ANTI-EMETICS

Minimal emetic risk

CONCURRENT MEDICATION REQUIRED

Vorasidenib	None required, but may supply loperamide with cycle 1

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E, LFTs every 2 weeks for 2 months then monthly for first 2 years of treatment then as clinically indicated (Consider weekly monitoring for ALT or AST elevations ≤3xULN).
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

Vorasidenib	Diarrhoea LFT abnormalities

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Vorasidenib	Co-administration of vorasidenib with strong or moderate CYP1A2 inhibitors eg fluvoxamine and ciprofloxacin may increase vorasidenib plasma concentrations. Concomitant use of strong or moderate CYP1A2 inhibitors should be avoided and consider alternative therapies. Co-administration of vorasidenib with moderate CYP1A2 inducers eg phenytoin and rifampicin may decrease vorasidenib plasma concentration. Consider alternative therapies that are not moderate CYP1A2 inducers during treatment with vorasidenib. Concomitant use of vorasidenib with smoking tobacco may decrease vorasidenib plasma concentrations which may reduce the anti-tumor activity of vorasidenib. Consider advising that smoking tobacco should be avoided during treatment. Co-administration of vorasidenib with CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP3A4 substrates with narrow therapeutic index eg amitriptyline, alfentanil, carbamazepine, ciclosporin, dosulepin, everolimus, fentanyl, fosphenytoin, ifosfamide, imipramine, phenobarbital, phenytoin, pimozide, quinidine, sirolimus, tacrolimus, tamoxifen, trimipramine, valproic acid, and warfarin may decrease the plasma concentrations of these medicinal products. Concomitant use of substrates of these enzymes with narrow therapeutic index should be avoided. Co-administration of vorasidenib with sensitive substrates of CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP3A4 without narrow therapeutic index eg bupropion, buspirone, celecoxib, darunavir, ibrutinib, midazolam, repaglinide, saquinavir, tipranavir, and triazolam may decrease the plasma concentrations of these medicinal products. Consider alternative therapies that are not sensitive substrates of these enzymes during treatment. Vorasidenib may decrease concentrations of hormonal contraceptives therefore, concomitant use of a barrier method of contraception is recommended during treatment and for at least 3 months after the last dose.

DOSE MODIFICATIONS

Vorasidenib

Starting dose	40mg once daily
First dose reduction	20mg once daily
Second dose reduction	10mg once daily

Non-haematological

Vorasidenib

Hepatotoxicity (elevation of ALT or AST)

Grade 1 ALT or AST increase >ULN to 3xULN *without* concurrent total bilirubin >2xULN	Continue vorasidenib at current dose. Monitor liver enzymes weekly until recovery to <grade 1.
Grade 2 ALT or AST >3 to 5xULN *without* concurrent total bilirubin >2xULN	First Occurrence: Withhold vorasidenib and monitor liver enzymes twice per week until recovery to ≤grade 1 or baseline. • Recovery in ≤28 days, resume vorasidenib at the same dose. • Recovery in >28 days, resume vorasidenib at reduced dose. Recurrence: Withhold vorasidenib and monitor liver enzymes twice per week until recovery to ≤grade 1 or baseline, and resume vorasidenib at reduced dose.
Grade 3 ALT or AST >5 to 20xULN *without* concurrent total bilirubin >2xULN	First Occurrence: Withhold vorasidenib and monitor liver enzymes twice per week until recovery to ≤grade 1 or baseline. • Recovery in ≤28 days, resume vorasidenib at reduced dose. • If not recovered in ≤28 days, permanently discontinue vorasidenib. Recurrence: Permanently discontinue vorasidenib and monitor liver enzymes twice per week until recovery to ≤grade 1 or baseline.
Grade 2 or 3 Any ALT or AST >3 to 20xULN *with* concurrent total bilirubin >2xULN in absence of clear alternative explanation.	Permanently discontinue vorasidenib and monitor liver enzymes twice per week until recovery to ≤grade 1 or baseline.
Grade 4 Any ALT or AST >20xULN	Permanently discontinue vorasidenib and monitor liver enzymes twice per week until recovery to ≤grade 1 or baseline.

Other adverse reactions

Grade 3	First Occurrence: Withhold vorasidenib until recovery to ≤grade 1 or baseline. • Resume vorasidenib at reduced dose. Recurrence: Permanently discontinue vorasidenib.
Grade 4	Permanently discontinue vorasidenib.

Hepatic impairment

Vorasidenib

Should not be used in patients with pre-existing severe hepatic impairment (Child-Pugh class C)

Renal impairment

Vorasidenib

The pharmacokinetics and safety of vorasidenib have not been studied in patients with renal impairment (eGFR ≤40mL/min/1.73m^2) or renal impairment requiring dialysis. Vorasidenib should be used with caution in these patients.

REFERENCES

1. SPC

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
MRI 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