RIPRETINIB (Qinlock)

INDICATION (ICD10) C15 - C20, C48.1, C48.2

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (RIP1)

1. Ripretinib for treating metastatic or unresectable gastrointestinal stromal tumours (GIST) after 3 or more kinase inhibitors (imatinib, sunitinib and regorafenib). PS 0, 1 or 2. (TA1146)

REGIMEN

Days 1 to 28	**RIPRETINIB**	150mg	oral	once daily continuously

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression.

ANTI-EMETICS

Low emetic risk (none usually required)

CONCURRENT MEDICATION REQUIRED

Ripretinib	-

ADMINISTRATION

Ripretinib	Available as 50mg tablets. Swallowed whole with or without food

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration

FBC and U&E Neutrophils ≥1.0x10^9/L Platelets ≥50x10^9/L	baseline and every cycle
LFTs	baseline then every 2 weeks for first 2 cycles then every cycle
Serum creatinine (and calculated CrCl)	baseline and every cycle
Hepatitis B exposure (refer to hepatology for lamivudine therapy)	before starting treatment
Blood pressure	Baseline and every cycle
ECHO (ejection fraction)	Baseline and as clinically indicated
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Ripretinib	Arthralgia or myalgia Cardiac toxicity Dermatological effects and phototoxicity Hypertension Left ventricular systolic dysfunction Palmar-plantar erthrodysaethesia Wound healing may be impaired

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

Ripretinib	Strong inhibitors of CYP3A/P-gp (e.g. ketoconazole, erythromycin, clarithromycin, itraconazole, ritonavir, posaconazole, and voriconazole) are to be used with caution and patients should be monitored. Ingestion of grapefruit juice is not recommended. Co-administration with the strong CYP3A inducer rifampicin decreased ripretinib. Concomitant use with strong CYP3A inducers (e.g. carbamazepine, phenytoin, rifampicin, phenobarbital and St. John's wort) and moderate CYP3A inducers (e.g. efavirenz and etravirine) must therefore be avoided. Apalutamide, encorafenib, enzalutamide, ivosidenib, lumacaftor, mitotane, primidone

DOSE MODIFICATIONS
Ripretinib
Starting dose 150mg once daily
Dose reduction 100mg once daily
If patients are unable to tolerate 100mg once daily it should be discontinued

Non-haematological
Ripretinib
Arthralgia or myalgia

Grade 2	• Withhold until grade ≤1 or baseline. If recovered within 7 days, resume at same dose; otherwise resume at reduced dose. • Consider re-escalating if maintained at grade ≤1 or baseline for at least 28 days. • If arthralgia or myalgia recurs, withhold until grade ≤1 or baseline and then resume at a reduced dose regardless of time to improvement.
Grade 3	• Withhold for at least 7 days or until grade ≤1 or baseline (maximum of 28 days). Resume at a reduced dose. • Consider re-escalating if maintained at grade ≤1 or baseline for at least 28 days.

Hypertension

Grade 3	• If symptomatic, withhold until symptoms have resolved and blood pressure is controlled. • If blood pressure is controlled to grade ≤1 or baseline, resume at the same dose; otherwise, resume at reduced dose. • If grade 3 hypertension recurs, withhold until symptoms have resolved and blood pressure is controlled. Resume at a reduced dose.
Grade 4	Permanently discontinue.

Left ventricular systolic dysfunction

Grade 3 or 4	Permanently discontinue.

Other adverse reactions

Grade 3 or 4	• Withhold until grade ≤1 or baseline (maximum 28 days), and then resume at a reduced dose; otherwise permanently discontinue. • Consider re-escalating if no recurrence of the adverse reaction for at least 28 days. • If grade 3 or 4 recurs, permanently discontinue.

Palmar-plantar erythrodysaesthesia syndrome (PPES

Grade 2	• Withhold until grade ≤1 or baseline. If recovered within 7 days, resume at same dose; otherwise resume at reduced dose. • Consider re-escalating if maintained at grade ≤1 or baseline for at least 28 days. • If PPES recurs, withhold until grade ≤1 or baseline and then resume at a reduced dose regardless of time to improvement.
Grade 3	• Withhold for at least 7 days or until grade ≤1 or baseline (maximum 28 days). Resume at a reduced dose. • Consider re-escalating if maintained at grade ≤1 or baseline for at least 28 days.

Hepatic impairment

Ripretinib

No dose adjustment is required in mild hepatic impairment.

Due to insufficient data in moderate or severe impairment there is no dose recommendation.

Monitor closely.

Renal impairment

Ripretinib

No dose adjustment is required in mild or moderate renal impairment.

Due to insufficient data in severe impairment there is no dose recommendation.

REFERENCES

1. SPC

Assessments

	Pre	Cycle 1	Cycle 1 day 15	Cycle 2	Cycle 2 day 15	Cycle 3	Cycle 4	Ongoing
Informed consent	x							
Clinical assessment	x			Pre-C2		x	x	Once stable, alternate cycles
SACT assessment (PS and toxicities)	x	x		x		x	x	Every cycle
FBC	x	x		x			x	Every cycle
U&E & LFTs (including AST and ALP), phosphate & magnesium	x	x	x	x	x	x	x	Every cycle
CrCl	x	x		x			X	Every cycle
Blood pressure	x	x		x		x	x	Every bevacizumab dose
Urinalysis for proteinuria								Every bevacizumab dose
CT scan	x							Every 12 weeks
Weight recorded	x	x		x			x	Every cycle
Height	x	x		x			x	Every cycle