Indication	Monotherapy treatment of metastatic or unresectable gastrointestinal stromal tumours after 3 or more kinase inhibitors, including imatinib, sunitinib and regorafenib.
Treatment Intent	Palliative.
Frequency and number of cycles	28 day cycle. Continue until progressive disease, unacceptable toxicity or patient choice.
Monitoring Parameters	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • **Blood pressure:** must be stable prior to treatment and BP should be monitored prior to each cycle or as clinically indicated. • **ECHO/MUGA** and **ECG** prior to cycle 1 and then as clinically indicated throughout treatment. Baseline left ventricular ejection fraction should be >/= 50% prior to starting treatment. • **Dermatological evaluation** should be performed prior to initiation of treatment and throughout treatment. • **Haematological monitoring and parameters:** • **FBC, CPK, U&Es, LFT's**, **lipase**, **amylase** and **triglycerides** at baseline and at each cycle. • If neuts >/=1.0 and PLT >/=75 proceed with treatment. • **Hepatic impairment:** no recommended dose reduction in mild impairment. No available recommendations in moderate or severe impairment, use at clinician's discretion and monitor closely. • **Renal impairment:** no recommended dose reduction in mild or moderate impairment. Limited data in severe renal impairment (CrCl<30ml/min) use at clinicians' discretion. • **Management of adverse reactions:** o **Wound healing complications:** Ripretinib has the potential to adversely affect wound healing. Treatment with ripretinib is to be withheld for at least 3 days prior to and after minor surgery and at least 5 days prior to and after major surgery. Ripretinib may then be resumed after surgery based on clinical judgement of adequate wound healing. o **Cutaneous squamous cell carcinoma (CuSCC):** CuSCC has been reported in some patients, dermatological monitoring should continue throughout treatment. o **Palmar-Plantar Erythrodysaesthesia Syndrome (PPES) and Phototoxicity:** PPES has been reported in patients treated with ripretinib dose modification or interruption may be required, see table 1. o Patients should be advised to limit excessive use of soap and bathing, use moisturisers and avoid perfumed products. o Patients should be advised to avoid or minimise exposure to direct sunlight, sunlamps, and other sources of ultraviolet radiation. Patients should be advised to wear protective clothing and high SPF sunscreen during treatment. • **Dose Modification:** o Dose interruption or reduction may be required. When dose reduction is necessary the dose should be reduced to 100mg once daily, if 100mg is not tolerated treatment should be discontinued. See table 1 for recommended dose modification for adverse reactions. o If co-administration with a strong CYP3A inducer cannot be avoided ripretinib dose may be increased from 150 mg once daily to 150 mg twice daily. Close monitoring of overall efficacy and safety is recommended in these patients. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** o Concurrent use of strong CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin) and moderate CYP3A4 inducers (e.g., bosentan, efavirenz, etravirine,

	phenobarbital, primidone) should be avoided during treatment. If co-administration with a moderate or strong CYP3A inducer cannot be avoided ripretinib dose modification may be required. There is no SPC recommendation for dose modification when co-administered with a moderate CYP3A4 inducers, see **dose modification** section above for SPC guidance when given with strong CYP3A4 inducers. ○ Co-administration of ripretinib with CYP isoform-selective substrates (e.g. substrates of CYP2C8 such as repaglinide, paclitaxel or CYP3A4 substrates such as cyclosporin or tacrolimus) may increase or decrease their efficacy, when co-administered with substrates with narrow therapeutic index close monitoring is recommended. ○ It is unknown whether ripretinib may reduce the effectiveness of systemically acting hormonal contraceptives, and therefore women using systemically acting hormonal contraceptives should add a barrier method. ○ Co-administration with strong inhibitors of CYP3A/P-gp (e.g. ketoconazole, erythromycin, clarithromycin, itraconazole, ritonavir, posaconazole, and voriconazole) should be used with caution and patients should be monitored. ○ Patients should not drink grapefruit juice or eat grapefruit whilst taking ripretinib. ○ Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. • **Missed dose:** ○ **once a day administration,** if a dose is missed and it cannot be taken within 8 hours of the regular scheduled time, patients should omit the dose and treatment should resume with the next scheduled daily dose. If vomiting occurs after taking a dose, an additional dose should not be taken. ○ **twice daily administration**, if a dose is missed and cannot be taken within 4 hours of the regular scheduled time, the patient should take the missed dose as soon as possible and then take the next dose at the regularly scheduled time. If missed by more than 4 hours of the regular scheduled time, the dose should be omitted and resume the usual dosing schedule. • **Pregnancy and contraception:** Females of reproductive potential and males with female partners of reproductive potential must use effective contraception during treatment and for at least 1 week after the final dose of ripretinib. • **Driving and machinery:** some patients experience fatigue during treatment, if affected patients should be advised this may affect their ability to drive or operate machinery. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	SPC accessed online 08.04.2026 CDF list V1.392 accessed online 08.04.2026

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

Table 1: Recommended dose modifications for adverse reactions

Adverse reaction	**Severity**[a]	**dose modifications**
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.
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.
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.
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.

[a] Graded per National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 (NCI CTCAE v4.03).

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**RIPRETINIB**	**150mg**	PO	OD for 28 days. Take at approximately the same time each day, with or without food. Swallow whole, do not split, crush or chew the tablets. Available as 50mg tablets.
	Metoclopramide	10mg	PO	10mg up to three times a day PRN. Do not take for more than 5 days continuously. Dispense on Cycle 1 only, then only if required