Indication	For the first-line treatment of advanced renal cell carcinoma.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 30 days Pazopanib is to be continued until loss of clinical benefit or unacceptable toxicity or patient choice to stop treatment, or pazopanib can be stopped for a planned treatment break following the protocol used in the STAR trial; i.e. following 24 weeks of continuous therapy, and if there is no evidence of disease progression on therapy, patients and clinicians may choose to stop treatment for a planned drug free interval/treatment break and then restart sunitinib on disease progression. (Further planned treatments breaks following the same strategy are allowed).
Monitoring Parameters pre-treatment	• **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 (BP)** should be well controlled prior to treatment. Monitor blood pressure (BP) at 1 week, then every 2 weeks for the first 2 months and monthly thereafter. • **ECG** prior to cycle 1 and then as clinically indicated, monitor patients for symptoms of cardiac dysfunction throughout treatment. • **ECHO:** at baseline for at risk patients, then every 6/12 as clinically indicated. • **Thyroid function** must be assessed at baseline then every 12 weeks. • **Monitor FBC and U&E's** at baseline and prior to each cycle or dispensing episode if >28 days dispensed (stable patients only). Maintenance of electrolytes (e.g. calcium, magnesium, potassium) within normal range is recommended. • **LFT's** should be monitored before initiation of treatment with pazopanib and 2 weekly for the first 3 cycles. Thereafter, monitored at each cycle and as clinically indicated. • If neuts <1.0 and/or PLT <50 d/w consultant • **Urine dipstick** each cycle to check for proteinuria. If patient develops nephrotic syndrome- pazopanib to be discontinued • **Hepatic impairment:** o Prior to treatment: In mild or moderate hepatic impairment treatment should be undertaken with caution and close monitoring of tolerability. No dose reduction recommendation in mild hepatic impairment. A dose reduction to 200mg once daily is recommended in moderate hepatic impairment, defined as an elevation of bilirubin >1.5 to 3 x ULN regardless of the ALT value. Pazopanib is not recommended in severe hepatic impairment (defined as total bilirubin > 3 X ULN regardless of any level of ALT). o During treatment: See Table 1 for dose modification guidance • **Renal impairment:** No dose reduction required if CrCl >/=30ml/min, if CrCl <30ml/min d/w consultant. • **Management of adverse reactions and dose adjustments:** • **Dose Modification:** If a dose modification is required it should be in steps of 200mg based on individual tolerability in order to manage adverse reactions. Maximum dose should not exceed 800mg. • **Interstitial lung disease (ILD)/Pneumonitis** which can be fatal, has been reported in association with pazopanib. (Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis and discontinue pazopanib in patients developing ILD or pneumonitis.

	• **Cardiac disorders:** QT prolongation and Torsades de Pointes have been reported. Pazopanib should be used with caution in patients with any relevant cardiac history, or those taking anti-arrhythmics or other medicines that prolong QT. Ensure electrolytes are maintained within the normal range**.** • **Tumour lysis syndrome (TLS)** Cases of TLS have been observed in patients treated with pazopanib. • **Wound healing:** Pazopanib may adversely affect wound healing, pazopanib therapy should be stopped 7 days prior to planned surgery. The decision to resume pazopanib following surgery should be based upon clinical judgment of recovery from surgery. Pazopanib should be discontinued in patients with wound dehiscence. • **Dermatological effects:** Patients should be advised that depigmentation of the hair or skin may occur during treatment with pazopanib. Patients should be advised to moisturize regularly, and cream containing 10% urea is recommended. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** • Avoid concomitant treatment with potent CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, clarithromycin, erythromycin) or inducers (e.g. rifampicin, dexamethasone, phenytoin, carbamazepine). Avoid grapefruit juice throughout the course of treatment. If concomitant use of pazopanib with a strong CYP3A4 inhibitor cannot be avoided the dose of pazopanib should be reduced (see SPC). • Co-administration of pazopanib with medicines that increase gastric pH should be avoided. • Patients on anti-coagulants should be closely monitored (INR/PT). • Concomitant use of pazopanib and simvastatin increases the risk of ALT elevations. • **Missed dose:** If a dose is missed the patient should not take an additional dose, take next dose at usual time. • **Driving and machinery:** Patients should avoid driving or using machines if they feel dizzy, tired or weak. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	KMCC proforma V5 ARIA regimen V1 SPC accessed online 07.10.2024 Novartis Pharmaceuticals UK Ltd

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

Table 1 Dose modifications for drug-induced hepatotoxicity

Liver test values	Dose modification
Transaminase elevation between 3 and 8 x ULN	Continue on pazopanib with weekly monitoring of liver function until transaminases return to Grade 1 or baseline.
Transaminase elevation of >8 x ULN	Interrupt pazopanib until transaminases return to Grade 1 or baseline. If the potential benefit of reinitiating pazopanib treatment is considered to outweigh the risk for hepatotoxicity, then reintroduce pazopanib at a reduced dose of 400 mg daily and perform serum liver tests weekly for 8 weeks. Following reintroduction of pazopanib, if transaminase elevations >3 x ULN recur, then pazopanib should be permanently discontinued.
Transaminase elevations >3 x ULN concurrently with bilirubin elevations >2 x ULN	Permanently discontinue pazopanib. Patients should be monitored until return to Grade 1 or baseline. Pazopanib is a UGT1A1 inhibitor. Mild, indirect (unconjugated) hyperbilirubinaemia may occur in patients with Gilbert's syndrome. Patients with only a mild indirect hyperbilirubinaemia, known or suspected Gilbert's syndrome, and elevation in ALT >3 x ULN should be managed as per the recommendations outlined for isolated ALT elevations.

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**PAZOPANIB**	**800mg**	PO	OD Take without food at least one hour before or two hours after a meal. Swallow whole, do not crush or chew. Do not take with grapefruit juice. Available as 200mg and 400mg tablets. Dispense 30-day supply on initiation of treatment, for patients who are stable on treatment, a maximum of 3 months supply can be dispensed.
	Metoclopramide	10mg	PO	10mg TDS PRN Do not take for more than 5 days continuously. Dispense 28 tablets on cycle 1, then only if specified.
	Loperamide	2mg-4mg	PO	Take two capsules (4mg) initially then one capsule (2mg) after each loose stool when required (max. 8 capsules a day) Dispense 30 capsules on cycle 1, then only if specified.