PAZOPANIB (Votrient)

INDICATION (ICD10) C64

1. First-line treatment option for people with advanced renal cell carcinoma who who have not received prior cytokine therapy and have an ECOG performance status of 0 or 1. (TA215)

REGIMEN

PAZOPAINIB 800mg orally once daily continuously

CYCLE FREQUENCY AND NUMBER OF CYCLES

Until disease progression

ADMINISTRATION

Available as 200mg and 400mg tablets
Swallowed whole with water at least one hour before or two hours after a meal

ANTI-EMETICS

Minimal emetic risk

CONCURRENT MEDICATION REQUIRED

Pazopanib	Moisturiser for hands and feet, to be applied regularly

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.0
Platelets x 10^9/L ≥75
Baseline weight and every cycle
Blood pressure every cycle
Thyroid function baseline then every 3 cycles

MAIN TOXICITES AND ADVERSE REACTIONS

Pazopanib	Gastrointestinal – serious gastrointestinal complications including gastrointestinal perforation have occurred rarely. Haemorrhage – an increased risk of bleeding may occur. Hypertension – treatment induced hypertension, suspend treatment until controlled. Hypothyroidism Mucositis Neutropenia Palmar / plantar syndrome Skin discolouration and depigmentation of the hair and skin

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Pazopanib	Many interactions check carefully

DOSE MODIFICATIONS

Hepatic impairment

Pazopanib

Cases of hepatic failure (including fatalities) have been reported during use of pazopanib.
Mild or moderate hepatic impairment - administration of pazopanib to patients should be undertaken with caution and close monitoring. 800mg pazopanib once daily is the recommended dose in patients with mild abnormalities in serum liver tests (either normal bilirubin and any degree of ALT elevation or elevation of bilirubin up to 1.5xULN regardless of the ALT value).
Moderate hepatic impairment (elevation of bilirubin >1.5-3xULN regardless of the ALT value) - a reduced pazopanib dose of 200mg once daily is recommended.
Severe hepatic impairment (total bilirubin >3xULN regardless of the ALT value) - Pazopanib is not recommended. Exposure at a 200mg dose is markedly reduced, though highly variable, in these patients, with values considered insufficient to obtain a clinically relevant effect.

Dose modifications for drug-induced hepatotoxicity - baseline values of total bilirubin ≤1.5xULN and AST and ALT ≤2xULN

Transaminase elevation between 3 and 8xULN	Continue on pazopanib with weekly monitoring of liver function until transaminases return to grade 1 or baseline.
Transaminase elevation of >8xULN	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 400mg daily and perform serum liver tests weekly for 8 weeks. Following reintroduction of pazopanib, if transaminase elevations >3xULN recur, then pazopanib should be permanently discontinued.
Transaminase elevations >3xULN concurrently with bilirubin elevations >2xULN	Permanently discontinue pazopanib. Patients should be monitored until return to grade 1 or baseline. 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 >3xULN should be managed as per the recommendations outlined for isolated ALT elevations.

Renal impairment

Pazopanib

No dose adjustment is required in patients with CrCl >30ml/min.
Caution is advised in patients with CrCl <30ml/min as there is no data in these patients - discuss with Consultant.

REFERENCES

1. Sternberg, CN et al; JCO 2010; 28: 1061-1068