PAZOPANIB (VOTRIENT®)
for 1st line mRCC

Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Cycle length	Drug	Daily Dose	Route	Schedule
Days 1 to 28	4 weeks	Pazopanib	800 mg	Oral	ONCE daily

Presented as 200mg and 400mg capsule-shaped, pink, film-coated tablet
Pazopanib should be taken without food, at least one hour before or two hours after a meal

NUMBER OF DAYS PER CYCLE
Continuous until disease progression

APPROVED INDICATIONS
NICE TA 215
Pazopanib is recommended as a first-line treatment option for people with advanced renal cell carcinoma who have not received prior cytokine therapy and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

ELIGABILITY
Patients with ECOG performance status of 0 or 1, and adequate haematological, coagulation, hepatic, renal, and cardiac function.

MONITORING
- Prior to treatment: BP, Thyroid Function, urine dipstick (for protein), FBC, U&Es, LFTs & tumour markers as appropriate.
- LFTs every two weeks for first two cycles of treatment, then at the start of each cycle thereafter.
- Prior to each subsequent treatment: BP, Thyroid Function, FBC, U&Es, LFTs & tumour markers as appropriate
- CT scan every 3 cycles or as indicated.

REVIEW BY CLINICIAN
Day 14 and Day 28 of Cycle One; Day 28 for each subsequent cycle

NURSE / PHARMACIST LED REVIEW
Each cycle as applicable according to local protocols

ANTI-EMETICS and SUPPORTIVE MEDICINES
Loperamide 2mg prn (max 16mg in 24 hours) for diarrhoea as required
Emollients (for skin rash) as required

REGIMEN SPECIFIC PRECAUTIONS
- Diarrhoea
- Hair colour changes
- Hypertension
- Nausea & vomiting
- Anorexia
- Fatigue
- Taste disturbance or loss of taste
- Abnormal liver function
- Hypothyroidism
- Use with caution in patients with pre-existing uncontrolled hypertension, left ventricular dysfunction or arrhythmias or in patients taking concomitant drugs with arrhythmic potential.
- Pazopanib is contraindicated in people with severe hepatic impairment.
- Proteinuria

EXTRAVASATION Not Applicable

NEUTROPENIA See NCA/ Local Policy

NOTES

- Pazopanib is a substrate for CYP3A4, P-glycoprotein and BCRP (breast cancer resistant protein).
- Drugs that are CYP3A4 inhibitors such as ketoconazole, and to a lesser extent itraconazole, erythromycin, clarithromycin and grapefruit juice may decrease metabolism and increase pazopanib plasma concentrations. Administration of pazopanib with a strong CYP3A4 inhibitor should be avoided, however the dose of pazopanib can be reduced to 400mg daily if the combination cannot be avoided, however increased monitoring for side-effects is advised and further dose reduction to be considered if unacceptable toxicity is encountered.
- Co-administration of pazopanib with a P-gp or BCRP inhibitor will result in an increase in plasma pazopanib concentrations.
- Drugs that are CYP3A4 inducers such as and to a lesser extent dexamethasone, phenytoin, carbamazepine, rifampicin, phenobarbital or Hypericum perforatum (St John's wort) may increase metabolism and decrease pazopanib plasma concentrations and avoidance of these combinations is recommended.
- Administration of pazopanib with a high fat or low-fat meal results in an approximately 2-fold increase in AUC and C_{max}. Therefore, pazopanib should be administered at least 1 hour before or 2 hours after a meal.
- Concomitant administration of pazopanib with esomeprazole decreases the bioavailability of pazopanib by approximately 40% (AUC and C_{max}), and co-administration of pazopanib with medicines that increase gastric pH should be avoided. If the concomitant use of a proton-pump inhibitor (PPI) is medically necessary, it is recommended that the dose of pazopanib be taken without food once daily in the evening concomitantly with the PPI.
- Simvastatin is contraindicated during pazopanib treatment due to increased risk of ALT elevations. Other statins have not been studied however are cautioned as an interaction cannot be excluded.

DOSE MODIFICATION

Pazopanib may be reduced by 200mg increments (e.g. to 600mg, then to 400mg etc).

Haematological toxicity

Dose delay if ANC < 1.0 or Platelets < 100 until counts recovered.

Non-Hematologic Toxicity, e.g. Diarrhoea, Skin Rash

CTC grade 0 - 1	No change.
CTC grade 2	Therapy withheld until toxicity resolves to grade 1. No change in subsequent dose.
CTC grade 3 - 4	Therapy withheld until toxicity resolves to grade 1. Decrease subsequent dose to next dose level (i.e. 200mg dose reduction). Dose reduction maintained for ongoing cycle and remainder of therapy.

Renal impairment

No dose adjustment is required in patients with creatinine clearance > 30 ml/min. Caution is advised in patients with creatinine clearance < 30 ml/min.

Hepatic impairment

- The SPC recommends a reducing pazopanib dose directly to **200 mg once daily*** in in patients with moderate hepatic impairment (defined as an elevation of bilirubin > 1.5 to 3 x ULN regardless of ALT.
- Pazopanib is contraindicated in bilirubin > 3 x ULN.
- Check with prescriber before proceeding if ALT raised above ULN.

REFERENCES:

1. Summary of Product Characteristics – pazopanib. July 2011.
2. Sternberg CN, Davis ID, Mardiak J, et al. Pazopanib in locally advanced or metastatic renal cell carcinoma: results of a randomized phase III trial. J Clin Oncol 2010; 28: 1061-8

DOCUMENT CONTROL

Document Title:	PAZOPANIB (VOTRIENT®) for 1st line mRCC		
Document No:	CRP11-U015	**Current Version:**	1.2
Reviewer:	Chris Beck Chemotherapy Pharmacist Northern Cancer Alliance	**Date Approved:**	13.03.18
Approved by:	Steve Williamson Consultant Pharmacist Northern Cancer Alliance	**Due for Review**	13.03.21
Summary of Changes	1.1	Protocol reviewed and reissued, Antiemetic advice updated	
	1.2	Protocol updated with Chemocare parameters, interactions & monitoring advice updated.	