NHS Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Cycle length	Drug	Daily Dose	Route	Schedule
Days 1 to 21	4 weeks	Tivozanib	1340 micrograms	Oral	ONCE daily

NUMBER OF DAYS PER CYCLE
Tivozanib is given on a 28-day cycle. One 1340 microgram capsule taken daily for 21 days, followed by a 7-day rest period. Treatment is continued until disease progression or unacceptable toxicity.

APPROVED INDICATIONS
First line treatment of advanced renal cell carcinoma (with clear-cell histology) for patients with ECOG performance status of 0 or 1.

EXCLUSION CRITERIA
Brain metastases, unless treated and stable.

MONITORING
- Prior to treatment: BP, Thyroid Function, urine dipstick (for protein), FBC, U&E, LFT's & tumour markers as appropriate.
- Baseline monitoring of QT/QTc interval and periodically during treatment.
- LFTs and blood pressure checked 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&E, LFT's & tumour markers as appropriate

REVIEW BY CLINICIAN
A formal medical review as to whether treatment with tivozanib should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment, and then response monitored periodically as indicated.

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

TOXICITIES
- Diarrhoea
- Hair colour changes
- Stomatitis
- PPE/Hand-foot syndrome
- Hypertension
- Haemorrhage
- Nausea & vomiting
- Anorexia, weight loss
- 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.
- Proteinuria
- PRES (Posterior Reversible Encephalopathy Syndrome)
- Rash
- QT interval prolongation
- Gastrointestinal perforation
- Wound healing complications

EXTRAVASATION Not Applicable

NEUTROPENIA See NCA/ Local Policy

ADMINISTRATION NOTES
Tivozanib is metabolised by CYP3A4 and CYP1A1. CYP3A4 inhibitors are considered unlikely to affect tivozanib treatment, however strong CYP3A4 inducers (such as rifampicin, phenytoin, carbamazepine, phenobarbital and St John's Wort) may reduce levels of tivozanib and this combination should be undertaken with caution.

DOSE MODIFICATION
When dose reduction is necessary, the tivozanib dose can be reduced to 890 micrograms once daily with the normal treatment schedule of 21 days of dosing, followed by a 7-day rest period.

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 890 mcg daily. Dose reduction maintained for ongoing cycle and remainder of therapy.

Renal impairment
No dose adjustment is required in patients with mild or moderate renal. Caution is advised in patients with severe renal impairment due to limited experience and in patients undergoing dialysis as there is no experience of tivozanib in this patient population.

Hepatic impairment
Tivozanib is not recommended in patients with severe hepatic impairment. Patients with moderate hepatic impairment should had their dose reduced to 1340 micrograms on alternate days. No dose adjustment is required in patients with mild hepatic impairment although close monitoring for toxicity is essential.

REFERENCES:

1. Summary of Product Characteristics: Fotivda 1340mcg hard capsules, Eusa Pharma UK, last updated 15 Feb 2018 https://www.medicines.org.uk/emc/product/8996
2. Rini, B.I., Atkins, M.B., Escudier, B.J., Hutson, T.E., Koralewski, P., McDermott, D.F., Pal, S.K., Needle, M.N. and Porta, C., 2017. Tivo-3: A phase 3, randomized, controlled, multi-center, open-label study to compare tivozanib hydrochloride to sorafenib in subjects with refractory advanced renal cell carcinoma (RCC).

DOCUMENT CONTROL

Document Title:	Tivozinib (Fotivda) for first-line mRCC		
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	1.0	First Version.	