SUNITINIB (SUTENT®) for mRCC and GIST

NHS Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Cycle length	Drug	Daily Dose	Route	Schedule
Days 1 to 28	6 weeks	**Sunitinib**	50 mg	Oral	ONCE daily

Presented as 12.5mg, 25mg and 50mg hard capsules which may be taken with or without food, swallowed whole with a glass of water.

NUMBER OF DAYS PER CYCLE

One 50mg dose orally, taken daily for four consecutive weeks followed by a two-week rest period to comprise a complete cycle of 6 weeks.

APPROVED INDICATIONS

- First line treatment of metastatic renal cell carcinoma (mRCC) with ECOG performance status of 0 or 1, and adequate haematological, coagulation, hepatic, renal, and cardiac function.
- For patients with unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST) if imatinib treatment has failed because of resistance or intolerance.
- ***Note*** separate protocol exists for pNET.

MONITORING

Blood Pressure: Weekly or twice weekly during the first 6 weeks of treatment (via GP Surgery), then reduced accordingly.
Thyroid Function: Prior to each cycle of sunitinib
FBC, U&Es, LFTs & tumour markers as appropriate prior to each course of chemotherapy.
Scan after 2 cycles

CLINICAL REVIEW

Day 1, Day 14 and Day 28 of First Cycle; Then Day 1 of all other cycles.

NURSE / PHARMACIST LED REVIEW

Each cycle as applicable according to local protocols

ANTI-EMETICS and SUPPORTIVE MEDICINES

Metoclopramide 10 mg three times daily as required
Loperamide 2mg prn (max 16mg in 24 hours) for diarrhoea as required
Emollients (for skin rash) as required

REGIMEN SPECIFIC PRECAUTIONS

- Diarrhoea
- Fatigue
- Nausea & vomiting
- Myelosuppression
- Hypertension
- Left Ventricular Dysfunction
- Hypothyroidism
- Yellow discolouration of urine and skin

Use with caution in patients with pre-existing uncontrolled hypertension, left ventricular dysfunction or arrhythmias or in patients taking concomitant drugs with arrhythmic potential.
Risk of treatment-related tumour haemorrhage

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NOTES

- Drugs that are CYP3A4 inhibitors such as ketoconazole, and to a lesser extent itraconazole, erythromycin, clarithromycin and grapefruit juice may decrease metabolism and increase sunitinib plasma concentrations and should be avoided if possible. The dose of sunitinib may be decreased to 37.5 mg in the presence of strong CYP3A4 inhibitors.
- Drugs that are CYP3A4 inducers such as rifampicin and to a lesser extent dexamethasone, phenytoin, carbamazepine, phenobarbital or Hypericum perforatum (St John's Wort) may increase metabolism and decrease sunitinib plasma concentrations and should be avoided if possible. The dose of sunitinib may be titrated up to 87.5 mg in the presence of strong enzyme inducers in mRCC and GIST.
- Sunitinib may be taken with or without food.

DOSE MODIFICATION

- Dose modifications in 12.5 mg steps (to a minimum of 25mg daily) may be applied based on individual safety and tolerability.
- The licensed schedule is four weeks of treatment followed by a two-week break (4/2 schedule), however improved tolerability has been found with the 2/1 schedule (two weeks of treatment followed by a one-week break) so patients may be switched to this either instead of or as well as a dose-reduction if unacceptable toxicity is experienced.

Haematological toxicity

Dose delay: If ANC < 1.0 or Platelets < 75 until counts recovered

Non-Haematological 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 37.5mg. Dose reduction maintained for ongoing cycle and remainder of therapy.

REFERENCES:

1. NICE, TA169 Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma, 25 March 2009, https://www.nice.org.uk/guidance/ta169
2. NICE, TA179 Sunitinib for the treatment of gastrointestinal stromal tumours, 23 September 2009, https://www.nice.org.uk/guidance/ta179
3. Pfizer. Summary of Product Characteristics – Sutent. Last updated November 2016.
4. Motzer RJ et al., Sunitinib versus Interferon Alfa in Metastatic Renal-Cell Carcinoma, *New England Journal of Medicine*, 356(2), January 11 2007, 115-124
5. Ezz El Din M. Sunitinib 4/2 Versus 2/1 Schedule for Patients With Metastatic Renal Cell Carcinoma: Tertiary Care Hospital Experience. *Clin Genitourin Cancer*. 2017;15:e455-e62.

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DOCUMENT CONTROL

Document Title:	Sunitinib Protocol		
Document No:	CRP08U001	**Current Version:**	1.3
Reviewer:	Chris Beck Chemotherapy Pharmacist Northern Cancer	**Date Approved:**	13.03.18
Approved by:	Steve Williamson Consultant Pharmacist	**Due for Review**	13.03.21
Summary of Changes	1.0a	Original version approved	
	1.1a	Addition of GIST. Improved section on BP and Thyroid Function Monitoring. Revised consultant review.	
	1.2	Protocol reviewed. Typing errors corrected.	
	1.3	Updated to reflect NHS England amendments	
	1.4	Updated with Chemocare parameters. Dose modifications updated, 2/1 schedule added	