

SUNITINIB

1. First line use in advanced renal cell carcinoma; NICE approved 2009
(This includes patients intolerant of first line pazopanib, who may be switched to first line sunitinib)
2. Second-line use in adults with Kit (CD 117) +ve unresectable and/or metastatic malignant GIST and who have resistance or intolerance to imatinib; NICE approved 2009
3. Treatment of unresectable or metastatic well-differentiated pancreatic neuroendocrine tumours (pNETs).
For this indication, blueteq registration is required before treatment may start.

Renal cell / GIST: **Sunitinib** initiate at 50mg po od for 4 weeks, followed by 2 weeks rest, to give a complete cycle of 6 weeks*.

If problems with tolerability, or tumour flare during the 2 week rest period, the daily dose may be taken for 2 weeks, followed by a one week rest, and then repeated (called 2/1 schedule)

pNET: **Sunitinib** initiate at 37.5mg po once daily continuously.

Administration: Sunitinib is available as 12.5mg, 25mg and 50mg capsules, which may be taken with or without food at a time of day that suits the patient.
Grapefruit and grapefruit juice should be avoided while on sunitinib.

Frequency: For 6 week cycles, clinical review / toxicity check at the end of week 3 of cycle 1, then just before each cycle.
For continuous use (no breaks), clinical review every 4 weeks, plus toxicity review 2 weeks after starting
To be continued until disease progression or unacceptable adverse events.

Main Toxicities: hand-foot syndrome (foot syndrome may be serious – encourage to moisturise feet and early review to chiropodist); rash; skin discolouration (yellow); diarrhoea / flatulence;
hypertension; myelosuppression; mucositis; hypothyroidism;
fatigue; hair changes

Anti- emetics: mildly emetogenic

Regular: FBC baseline, then before every cycle
Investigations: LFTs & U&Es baseline, then before every cycle
Blood pressure weekly for 1st cycle (ideally via GP, with patient making a record of the readings for the next oncology appointment), then before every cycle
MUGA baseline, only if patient has cardiac history. Repeat if there is suspicion of cardiac toxicity at any point during treatment.
Thyroid function baseline, then every 12 weeks

Comments: Patients should be advised to apply moisturiser to their hands and feet regularly throughout treatment, and to minimise activities that put pressure on feet or hands if they start to develop sore hands or feet. Recommended moisturisers are Udderly Smooth or urea-containing moisturisers e.g. Eucerin.
Also, ensure patient has a supply of metoclopramide (or domperidone), loperamide and Difflam mouthwash, for management of symptoms as required.

Reason for Update: removed continuous sunitinib for rcc or GIST	Approved by Consultant: Dr A Michael
Version: 8	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 7	Date: 14.9.17
Prepared by: S Taylor	Checked by: C Tucker

Wound healing: Sunitinib may adversely affect the wound healing process. Stop sunitinib at least 7 days prior to scheduled surgery¹. The decision to resume sunitinib after surgery should be based on clinical judgement of adequate wound healing.

Interactions: Elimination of sunitinib is mainly through hepatic metabolism. Concomitant use of enzyme inducers (e.g. dexamethasone, phenytoin, St Johns wort) with sunitinib should be avoided, as this may increase the risk of therapeutic failure. N.B. Continuing with the enzyme inducer while increasing the sunitinib dose above 50mg daily is not funded.

Co-administration of sunitinib with enzyme inhibitors (eg itraconazole, erythromycin, grapefruit juice) should also be avoided. If this is not possible, the dose of sunitinib may need to be reduced according to tolerability.

Dose Modifications The daily dose may be reduced in 12.5mg steps, but should not be decreased below 25mg. The daily dose may not be increased above 50mg (or above 37.5mg for continuous use / no breaks), as funding has not been approved for this.

The information in the sections below (haematological and non-haematological toxicities) should be used as a general guide only, and each patient should be considered on their own merits. Note that side effects experienced at a fixed dose may vary in severity and type between cycles. If in doubt, discuss with Consultant.

Haematological Toxicity: Myelosuppression may occur, but often resolves spontaneously without discontinuing treatment. However, if Grade 3 or 4 neutropenia or thrombocytopenia, treat as below:

Neutrophils $0.5 - 0.9 \times 10^9/l$
or
Platelets $10 - 49 \times 10^9/l$ Delay next cycle until above these limits, then continue at the same dose as previous cycle. If more than one delay for this reason, consider reducing the dose by one 12.5mg step on the next cycle.

Neutrophils $< 0.5 \times 10^9/l$
or
Platelets $< 10 \times 10^9/l$ Delay next cycle until neutrophils $\geq 1.0 \times 10^9/l$ and platelets $\geq 50 \times 10^9/l$, then reduce the dose by one 12.5mg step and resume treatment.

Cardiac Toxicity: If hypertension develops, it should be treated (usually by GP) and monitored closely until stabilised. It is not a reason to stop sunitinib, unless patient develops severe hypertension.

In the presence of clinical manifestations of CHF, discontinuation of sunitinib is recommended. Sunitinib should be interrupted and/or the dose reduced in patients without clinical evidence of CHF but with an ejection fraction $< 50\%$, and $> 20\%$ below baseline.

Pancreatic Function: Increases in lipase and amylase activity are often transient and regular monitoring is not required. However, if Grade 4 elevations in amylase or lipase without clinical symptoms of pancreatitis, withhold treatment until toxicity is \leq Grade 3, then continue at the same dose level. If any symptoms of pancreatitis are present, treatment must be discontinued.

Skin Toxicity: Hand-foot syndrome may require a 1-2 week break in treatment until resolved to Grade ≤ 1 if there is ulceration, or if pain relief is required. The patient should be advised to moisturise their hands and feet regularly, and to keep them cool. The patient may also be advised to take care to minimise excessive periods of pressure on their feet, and to make the most of the 2 week breaks to be more active.

Hypothyroidism: Manage according to standard medical practice. Sunitinib treatment may continue.

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Any Other Toxicities: For any other non-haematological Grade 3 toxicity, withhold treatment until toxicity \leq Grade 1, then resume treatment, either at the same dose as previous cycle or with one 12.5mg step dose reduction.
For any other Grade 4 non-haematological toxicity, consider either discontinuing treatment, or resuming with one 12.5mg step reduction once toxicity resolved.
If in doubt, discuss with Consultant.

Hepatic Impairment: Sunitinib and its primary metabolite are mainly metabolised by the liver. However, no dosage adjustment is recommended in patients with mild to moderate hepatic impairment. There is no data available for patients with severe liver impairment.

Renal Impairment: No starting dose adjustment is required for patients with renal impairment (mild-severe) or with end-stage renal disease on haemodialysis.

References: Motzer, RJ et al; NEJM (2007); 356: 115 – 124 (rcc)
Raymond et al; NEJM 2011; 364: 501 – 513 (pNET)
Demetri et al; Lancet 2006: 368; 1329 – 1338 (GIST)
Pyle, L et al; Cancer Nursing Practice 2008; 7 (4): 42 – 46
¹Not specified in SPC, but local agreement

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