SUNitinib 37.5mg Therapy- 28days

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Treatment of unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumours (pNET) with disease progression in adults	C25	00327a	CDS

* This applies to post 2012 indications

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

The recommended dose of SUNitinib is 37.5mg taken orally, once daily continuously until disease progression or unacceptable toxicity occurs. A treatment cycles consists of 4 weeks of treatment (28 days).

Drug	Dose	Route	Cycle
SUNitinib[a]	37.5mg daily	PO once daily at the same time every day, consistently either with or without food. Swallow whole with a glass of water	Continuous
[a]Commonly available in 12.5mg/25mg/37.5 mg and 50mg hard capsules			
If a dose is missed, the patient should **NOT** be given an additional dose. The patient should take the usual prescribed dose on the following day.			

ELIGIBILITY:

- Indications as above
- ECOG 0-2

EXCLUSIONS:

- Hypersensitivity to SUNitinib, or any of the excipients
- Uncontrolled hypertension
- Pregnancy
- Breastfeeding

CAUTIONS:

- SUNitinib should be used with caution in patients with a known history of QT interval prolongation, patients who are taking antiarrhythmics or medicinal products that can prolong QT interval, or patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances
- Concomitant administration of SUNitinib with potent CYP3A4 inhibitors should be limited because of the possible increase in SUNitinib plasma concentrations
- Significant cardiovascular disease and/or LVEF < 55

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Cardiac assessment as clinically indicated
- Thyroid Function tests
- Blood pressure
- MUGA scan or echocardiogram if clinically indicated or history of cardiac problems

Regular tests:

- FBC, renal and liver profile prior to each cycle
- Thyroid function tests every 12 weeks
- Assess blood pressure at each attendance or appointment
- MUGA scan or echocardiogram as clinically indicated

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant .Dose interruptions may be required based on individual safety and tolerability
- Dose modifications in 12.5 mg steps may be applied based on individual safety and tolerability
  - Dose level -1 : 25mg
  - Dose level +1 : 50mg
- A dose increase to a maximum of 62.5mg should be considered if SUNitinib must be co-administered with a CYP3A4 inducer. If dose is increased, the patient should be monitored carefully for toxicity
- Co-administration of SUNitinib with potent CYP3A4 inhibitors, should be avoided. If this is not possible, the dose of SUNitinib may need to be reduced to a minimum of 25 mg daily for based on careful monitoring of tolerability
- Dose escalation: May increase to +1 dose level if no response after 8 weeks, with grade 1 or lower non-haematologic or grade 2 or lower haematologic treatment related adverse events

Haematological:

Table 1: Dose modification of SUNitinib in haematological toxicity

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose
≥ 1	and	≥ 75	100%
<1	or	< 75	Delay

Renal and Hepatic Impairment:

Table 2: Dose modification of SUNitinib in renal and hepatic impairment

Renal Impairment		Hepatic Impairment	
Renal impairment:	no dose adjustment is needed	Child-Pugh A/B:	no dose adjustment is needed
Haemodialysis:	no initial dose adjustment is needed, increase dose based on sunitinib + active metabolite trough concentration levels	Child-Pugh C:	consider 75% of the original dose, increase if tolerated
Recommendations as per Giraud et al 2023			

Management of adverse events:

Table 3: Dose Modification of SUNitinib for Adverse Events

Adverse reactions	Recommended dose modification
Grade 1-2 reactions*	100%
Grade 3-4	Delay until toxicity resolves to Grade 1. Dose reduce by 1 dose level
Hand foot syndrome (Palmar-plantar erythrodysaesthesia)	Grade 2 or 3: Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles from the 2nd occurrence of a grade 2 reaction and the 1st occurrence of a grade 3 reaction.
Cardiac Toxicity	For asymptomatic decline in LVEF: delay treatment until recovery and consider dose reduction for subsequent cycles. For symptomatic decline in LVEF: Discontinue sunitinib
*With the exception of hand foot syndrome and cardiac toxicity	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti Cancer Therapy (SACT) Induced Nausea and Vomiting- Available on the NCCP website

SUNitinib: Minimal - Low **(Refer to local policy).**

Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS: None required

OTHER SUPPORTIVE CARE:

Anti-diarrhoeal treatment may be required

ADVERSE EFFECTS

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

REGIMEN SPECIFIC COMPLICATIONS

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.
- **Cardiac Toxicity:** Cardiovascular events, including heart failure, cardiomyopathy, and myocardial ischemia and myocardial infarction, some of which were fatal, have been reported in patients treated with SUNitinib. These data suggest that SUNitinib increases the risk of cardiomyopathy. No specific additional risk factors for SUNitinib-induced cardiomyopathy apart from the drug-specific effect have been identified in the treated patients. Use SUNitinib with caution in patients who are at risk for, or who have a history of, these events. Baseline and periodic evaluations of LVEF should also be considered while the patient is receiving SUNitinib.
- In the presence of clinical manifestations of CHF, discontinuation of SUNitinib is recommended. The administration of 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.
- **Hypertension:** Patients should be screened for hypertension and controlled as appropriate. Temporary suspension is recommended in patients with severe hypertension that is not controlled with medical management. Treatment may be resumed once hypertension is appropriately controlled.
- **Aneurysms and artery dissections:** The use of vascular endothelial growth factor (VEGF) pathway inhibitors in patients with or without hypertension may promote the formation of aneurysms and/or artery dissections. Before initiating SUNitinib, this risk should be carefully considered in patients with risk factors such as hypertension or history of aneurysm.
- **Hypothyroidism:** Baseline laboratory measurement of thyroid function is recommended in all patients. Patients with pre- existing hypothyroidism or hyperthyroidism should be treated as per standard medical practice prior to the start of SUNitinib treatment. During SUNitinib treatment, routine monitoring of thyroid function should be performed. Patients who develop thyroid dysfunction should be treated as per standard medical practice. Hypothyroidism has been observed to occur early as well as late during treatment with SUNitinib.
- **Skin and tissue disorders:** Skin discolouration, possibly due to the active substance colour (yellow), is a very common adverse reaction occurring in approximately 30% of patients. Patients should be advised that depigmentation of the hair or skin may also occur during treatment with SUNitinib. Other possible dermatologic effects may include dryness, thickness or cracking of the skin, blisters, or occasional rash on the palms of the hands and soles of the feet. The above reactions were not cumulative, were typically reversible and generally did not result in treatment discontinuation.
- Cases of pyoderma gangrenosum, generally reversible after drug discontinuation, have been reported. Severe cutaneous reactions have been reported, including cases of erythema multiforme (EM) and cases suggestive of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), some of which were fatal. If signs or symptoms of SJS, TEN, or EM (e.g.progressive skin rash often with blisters or mucosal lesions) are present, SUNitinib treatment should be discontinued. If the diagnosis of SJS or TEN is confirmed, treatment must not be re-started. In some cases of suspected EM, patients tolerated the reintroduction of SUNitinib therapy at a lower dose after resolution of the reaction; some of these patients also received concomitant treatment with corticosteroids or

antihistamines.

- **Wound healing:** This treatment may impair wound healing and temporary interruption of treatment is recommended in patients undergoing major surgical procedures.
- **Haemorrhage and tumour bleeding:** Haemorrhagic events, some of which were fatal, reported through post-marketing experience have included gastro-intestinal, respiratory, urinary tract and brain haemorrhages. Patients receiving concomitant treatment with anticoagulants) may be periodically monitored by complete blood counts (platelets), coagulation factors (PT/INR) and physical examination.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for more information.

REFERENCES:

1. Raymond, E et al. SUNitinib malate for the treatment of pancreatic neuroendocrine tumours. N Engl J Med 2011;364;6:501-513.
2. NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
3. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00216-4/fulltext
4. SUNitinib (SUTENT®) Summary of Product Characteristics. Last updated: 27 Nov 2019. Accessed March 2025. Available at: https://www.ema.europa.eu/en/documents/product-information/sutent-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	03/06/2018		Prof Maccon Keane
2	30/05/2018	Updated with new NCCP regimen template and updated interactions	Prof Maccon Keane
3	23/10/2019	Updated adverse effects/regimen specific events regarding aortic aneurysms and dissections as per SmPC update	Prof Maccon Keane
4	13/05/2020	Reviewed. Updated emetogenic potential	Prof Maccon Keane
5	15/09/2025	Reviewed. Title amendment. Addition of cautions section. Updated testing section. Updated renal and hepatic dose modifications to align with Giraud et al 2023. Regimen updated in line with NCCP standardisation. ATC code removed.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.