SUNITINIB (Sutent®)
Pancreatic Neuroendocrine Tumour (pNET)

Background: Sunitinib has been approved by the AWMSG as a treatment option for metastatic, well-differentiated pancreatic neuroendocrine tumours (pNET) with disease progression in adults. Treatment with Sunitinib improved progression free survival compared with placebo in patients with well-differentiated neuroendocrine carcinoma of the pancreas who were receiving best supportive care, including somatostatin analogues if required for symptomatic control.

Patient Group: Patients with unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumours (pNET) with disease progression in adults

Pre-treatment Assessment:
Weight, FBC, U&E, LFTs and Creatinine clearance
TFTs
Baseline ECG
Blood Pressure

Treatment Threshold
WBC ≥ 3 x 10⁹/L
ANC ≥ 1.5 x 10⁹/L
Platelets ≥ 150 x10⁹/L

Regimen Details:
Sunitinib 37.5mg PO once daily (continuously without scheduled rest period)

Taken continuously until disease progression unless unacceptable toxicity
Additional Information:
The first cycle of Sunitinib is **free of charge** under the manufacturers’ patient access scheme.

Administration:
- Tablets should be taken at the same time each day and swallowed whole with some water. Tablets can be taken before or after food.
- Avoid grapefruit juice.

Anti-emetics: Not normally required.

Additional Medication: Loperamide and emollients may be required.

Monitoring and Assessment:
- FBC - monthly
- U&E, LFT creatinine clearance (calculated) – monthly
- TFT - monthly
- BP – weekly for first four weeks then monthly if stable.
- ECG - every 3 to 6 months

Dose Modifications:
Dose modification should be in 12.5 mg increments in a stepwise fashion based on individual tolerability in order to manage adverse reactions. The dose of Sunitinib should not exceed 50 mg. Dose interruptions may be required based on individual safety and tolerability. No specific dose modification is recommended in renal or hepatic impairment (refer to SPC).

Pharmaceutical Care:
- CYP3A4 inducers may increase metabolism of Sunitinib (e.g. dexamethasone, phenytoin, carbamazepine, rifampicin, phenobarbital or herbal preparations containing St. John’s Wort/ *Hypericum perforatum*) and may decrease Sunitinib concentrations. Co-administration should therefore be avoided, or selection of an alternate concomitant medicinal product with no or minimal potential to induce CYP3A4 should be considered. If this is not possible, the dose of Sunitinib may need to be increased in 12.5 mg increments (up to 62.5 mg per day for pNET), based on careful monitoring of tolerability.
- Administration of Sunitinib with potent CYP3A4 inhibitors (e.g. ritonavir, itraconazole, erythromycin, clarithromycin, grapefruit juice) may increase Sunitinib concentrations. Combination with CYP3A4 inhibitors should therefore be avoided, or the selection of an alternate concomitant medicinal product with no, or minimal potential to inhibit CYP3A4 should be considered. If this is not possible, the dose of Sunitinib may need to be reduced to 25 mg daily for pNET, based on careful monitoring of tolerability.
Most Common Toxicities:
- Hypertension
- Myelosuppression +/- bleeding, infection
- Hypothyroidism/Hyperthyroidism
- Stomatitis
- Diarrhoea
- Abdominal pain
- Dyspepsia
- Decreased appetite
- Altered taste
- Nausea and vomiting (mild)
- Headache
- Epistaxis
- Rash
- Skin and hair discolouration/pigmentation
- Dry skin
- Palmar-plantar erythrodysaesthesia syndrome
- Pain in extremities/limb pain
- Fatigue
- Oedema
- Osteonecrosis of the jaw

References:

1. Advice No 1111 Sunitinib for pNET. AWMSG. 
   www.wales.nhs.uk/sites3/page.cfm?orgid=371&pid=24773
   [accessed 20th February 2012]

2. SPC Sutent® Pfizer Ltd www.medicines.org.uk [accessed 20th February 2012]