Indication	The treatment of metastatic or inoperable locally advanced differentiated thyroid cancer (papillary or follicular or Hurthle cell type) after radioactive iodine. NB The patient should be naïve to both lenvatinib and sorafenib unless either the patient was previously enrolled in the company's lenvatinib compassionate access scheme or the patient has had to discontinue sorafenib within 3 months of starting sorafenib because of toxicity
Treatment Intent	Palliative treatment
Frequency and number of cycles	Repeat every 28 days Continue until progressive disease, unacceptable toxicity or patient choice Review by the end of the first 8 weeks of treatment
Monitoring parameters pre-treatment	• Monitor FBC, U&Es (in particular potassium, calcium and magnesium) and glucose prior to each cycle. Abnormalities in electrolytes should be corrected before starting treatment. • If neuts <1.0 or platelets <50 d/w consultant. • LFTs should be monitored before cycle 1, then every 2 weeks for the first 2 cycles and then before each cycle. • Thyroid function must be assessed at baseline then every 8 weeks. • Blood pressure (BP) should be well controlled prior to treatment. BP should be monitored after 1 week, then every 2 weeks for the first 2 cycles, and then prior to each cycle. See table 2 for recommended management of hypertension. • ECG prior to cycle 1 and then every 8 weeks. • Urine protein should be monitored prior to each cycle If >/=2+ see table 1. • <u>Hepatic impairment:</u> In patients with severe (Child-Pugh C) hepatic impairment, the recommended starting dose is 14 mg taken once daily. No adjustments necessary in mild or moderate hepatic impairment. • <u>Renal impairment:</u> If CrCl <30ml/min, the recommended starting dose is 14 mg taken once daily. No adjustments necessary if >/=30ml/min. Not recommended in end stage renal disease. <u>Management of adverse reactions and dose adjustments:</u> • Grade 1 or 2 adverse reactions, continue treatment unless adverse events intolerable to the patient despite optimal management. • >/= Grade 3 or intolerable adverse reactions require interruption of treatment until improvement of the reaction to Grade 0-1 or baseline. • See table 1 for management of adverse reactions. • Treatment should be discontinued in case of life-threatening reactions (e.g. Grade 4) with the exception of laboratory abnormalities judged to be non-life-threatening, in which case they should be managed as severe reactions (e.g. Grade 3). • When dose modifications of lenvatinib are required, the 1st dose reduction (DR) should be to 20mg od, the 2nd DR to 14mg od and the 3rd DR to 10mg od (limited data below 10mg). • Gastrointestinal toxicity should be actively managed in order to reduce the risk of development of renal impairment or renal failure.

	Cautions • Monitor for signs or symptoms of cardiac decompensation. • Caution with patients with congenital long QT syndrome, bradyarrhythmias, or congestive heart failure. • Use with caution in patients who have had an arterial thromboembolism within the previous 6 months. • Lenvatinib should not be started in patients with fistula to avoid worsening and lenvatinib should be permanently discontinued in patients with oesophageal or tracheobronchial tract involvement and any Grade 4 fistula. • Lenvatinib may adversely affect the wound healing process as other agents of the same class. • Patients should be advised to be cautious when driving or using machines if they experience fatigue and dizziness Concomitant medication / Drug interactions • Caution in those taking medicinal products known to prolong the QT interval, including Class Ia and III antiarrhythmics. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
Reference(s)	LENVIMA SPC accessed on line 23/02/2018 CCF Formulary October 2017 – Lenvatinib drug monograph

NB For funding information, refer to the SACT funding spreadsheet

Table 1: Adverse reactions related to lenvatinib

Adverse reaction	**Severity**	**Action**	**Dose reduce and resume lenvatinib**
Hypertension	Grade 3 (despite optimal antihypertensive therapy)	Interrupt	Resolves to Grade 0, 1 or 2. See detailed guidance in Table 2
	Grade 4	Discontinue	Do not resume
Proteinuria	≥ 2 gm / 24 hours	Interrupt	Resolves to less than 2 gm / 24 hours.
Nephrotic syndrome	-------	Discontinue	Do not resume
Renal impairment or failure	Grade 3	Interrupt	Resolves to Grade 0-1 or baseline.
	Grade 4*	Discontinue	Do not resume
Cardiac dysfunction	Grade 3	Interrupt	Resolves to Grade 0-1 or baseline.
	Grade 4	Discontinue	Do not resume
PRES/RPLS	Any grade	Interrupt	Consider resuming at reduced dose if resolves to Grade 0-1.
Hepatotoxicity	Grade 3	Interrupt	Resolves to Grade 0-1 or baseline.
	Grade 4*	Discontinue	Do not resume
Arterial thromboembolisms	Any grade	Discontinue	Do not resume
Haemorrhage	Grade 3	Interrupt	Resolves to Grade 0-1.
	Grade 4	Discontinue	Do not resume
GI perforation or fistula	Grade 3	Interrupt	Resolves to Grade 0-1 or baseline.
	Grade 4	Discontinue	Do not resume
Non-GI fistula	Grade 4	Discontinue	Do not resume
QT interval prolongation	>500 ms	Interrupt	Resolves to <480 ms or baseline
Diarrhoea	Grade 3	Interrupt	Resolves to Grade 0-1 or baseline.
	Grade 4 (despite medical management)	Discontinue	Do not resume
*Grade 4 laboratory abnormalities judged to be non-life-threatening, may be managed as severe reactions (e.g., Grade 3)			

Table 2 Recommended management of hypertension associated with lenvatinib

Blood pressure (BP) level	**Recommended action**
Systolic BP ≥140 mmHg up to <160 mmHg or diastolic BP ≥90 mmHg up to <100 mmHg	Continue lenvatinib and initiate antihypertensive therapy, if not already receiving OR Continue lenvatinib and increase the dose of the current antihypertensive therapy or initiate additional antihypertensive therapy
Systolic BP ≥160 mmHg or diastolic BP ≥100 mmHg despite optimal antihypertensive therapy	1. Withhold lenvatinib 2. When systolic BP ≤150 mmHg, diastolic BP ≤95 mmHg, and patient has been on a stable dose of antihypertensive therapy for at least 48 hours, resume lenvatinib at a reduced dose
Life-threatening consequences (malignant hypertension, neurological deficit, or hypertensive crisis)	Urgent intervention is indicated. Discontinue lenvatinib and institute appropriate medical management.

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
	Lenvatinib (Lenvima®)	24mg	po	Swallowed whole with water once a day with or without food. If a patient misses a dose, and it cannot be taken within 12 hours, then that dose should be skipped and the next dose should be taken at the usual time.
	Metoclopramide	10mg	po	up to 3 times a day for 3 days, then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously
	Loperamide	2mg-4mg	po	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if specified.