LENVATINIB (Lenvima)

INDICATION (ICD10) C73

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)

The treatment of differentiated thyroid cancer after radioactive iodine where all the following criteria are met:

2. Confirmed histological diagnosis of differentiated thyroid carcinoma (papillary or follicular or Hurtle cell type)
3. Either metastatic disease or inoperable locally advanced disease
4. Refractory to radioactive iodine
5. The disease is progressive and is either symptomatic or imminently likely to become symptomatic
6. Treatment naïve to both lenvatinib and sorafenib unless either:a) previously enrolled in the company's lenvatinib compassionate access scheme and all other NHS England treatment criteria are fulfilled ie if treated with previous sorafenib, lenvatinib will only be accepted for NHS funding if the patient was intolerant of sorafenib according to the conditions set out in b) below or b) the patient has had to discontinue sorafenib within 3 months of starting sorafenib because of toxicity (ie there is sorafenib toxicity which cannot be managed by dose delay or dose modification) and there has been no disease progression whilst on sorafenib Note: Sequential use of lenvatinib and then sorafenib is only funded if the patient has to discontinue lenvatinib because of intolerance within 3 months of its start and if the disease has not progressed whilst the patient is on lenvatinib. The use of lenvatinib after disease progression on or after sorafenib is not funded and vice versa.
7. ECOG performance status of 0 or 1 or 2
8. Lenvatinib is to be continued as long as clinical benefit is observed or until there is unacceptable toxicity or patient choice to stop treatment
9. A formal medical review as to whether treatment with lenvatinib should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment
10. No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve)
11. Lenvatinib is to be otherwise used as set out in its Summary of Product Characteristics

REGIMEN

LENVATINIB 24mg orally daily

CYCLE FREQUENCY AND NUMBER OF CYCLES

Continuously until disease progression.

ADMINISTRATION

Available as 4mg and 10mg tablets
Swallowed whole with water once daily with or without food

ANTI-EMETICS

Minimal risk

CONCURRENT MEDICATION REQUIRED

Lenvatinib	Diarrhoea – Loperamide required Skin – apply moisturizer to hands and feet regularly

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC and U&E every cycle
LFTs every 2 weeks for first 2 cycles then every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Creatinine every cycle
Blood pressure every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Lenvatinib	Diarrhoea –Proactive management of diarrhoea including adequate hydration combined with anti-diarrhoeal medicinal products especially within the first 6 weeks of the treatment is important and should start at first signs of diarrhoea. Prolonged QT interval Hypertension Skin – apply moisturizer to hands and feet regularly

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Lenvatinib	-

DOSE MODIFICATIONS

Non-haematological

Management of adverse reactions may require dose interruption, dose reduction, or discontinuation of lenvatinib.
Mild to moderate adverse reactions (eg grade 1 or 2) generally do not warrant interruption, unless intolerable to the patient despite optimal management.
Severe (eg grade 3) or intolerable adverse reactions require interruption of lenvatinib until improvement of the reaction to grade 0-1 or baseline.Treatment should be discontinued in case of life-threatening reactions (eg grade 4) with the exception of laboratory abnormality judged to be non-life-threatening, in which case they should be managed as severe reaction (eg grade 3).
For lenvatinib related toxicities, upon resolution/improvement of an adverse reaction to grade 0-1 or baseline, treatment should be resumed at a reduced dose of lenvatinib.

Recommended daily dose 24mg orally once daily
First dose reduction 20mg orally once daily
Second dose reduction 14mg orally once daily
Third dose reduction 10mg orally once daily

Hypertension

Grade 3 (despite optimal antihypertensive therapy)	Interrupt until resolves to grade 0, 1 or 2.
Grade 4	Discontinue. Do not resume

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 ≤150mmHg, 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.

Proteinuria ≥2gm/24 hours	Interrupt Resolves to less than 2g/24hours
Nephrotic syndrome	Discontinue. Do not resume
Renal impairment or failure, or hepatotoxicity grade 3	Interrupt. Resolves to grade 0-1 or baseline
Renal impairment or failure, or hepatotoxicity grade 4	Discontinue. Do not resume
Cardiac dysfunction, GI perforation or fistula grade 3	Interrupt. Resolves to grade 0-1 or baseline
Cardiac dysfunction, GI perforation or fistula grade 4	Discontinue. Do not resume
Non-GI fistula Grade 4	Discontinue. Do not resume
PRES/RPLS Any grade	Interrupt. Consider resuming at reduced dose if resolves to grade 0-1
Arterial thromboembolisms Any grade	Discontinue. Do not resume
Haemorrhage grade 3	Interrupt. Resolves to grade 0-1
Haemorrhage grade 4	Discontinue. Do not resume
QT prolongation >500ms	Interrupt. Resolves to <480ms or baseline
Diarrhoea grade 3	Interrupt. Resolves to grade 0-1 or baseline
Diarrhoea grade 4 (despite medical management)	Discontinue. Do not resume

Hepatic impairment

Lenvatinib

No adjustment of starting dose is required in HCC patients with mild (Child-Pugh A) hepatic impairment.

There is no dosing recommendation (or funding) for HCC patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment.

Renal impairment
Lenvatinib
No adjustment of starting dose is required on the basis of renal function in patients with mild or moderate renal impairment.
There is no dosing recommendation for HCC patients with CrCl <30ml/min.

REFERENCES
1. SPC