North West Coast
Strategic Clinical Networks

# Chemotherapy Protocol

**DRUG REGIMEN:**
Lenvatinib

**Indication for use:**
Advanced or unresectable hepatocellular carcinoma (HCC) who have received no prior therapy
(Check NHS England funding criteria on Blueteq)

**Regimen:**

**Adults weighing 60 kg or more (actual body weight)**

Lenvatinib (Lenvima)12 mg PO once daily until disease progression or unacceptable toxicity

**Adults weighing less than 60 kg (actual body weight)**

Lenvatinib (Lenvima) 8 mg PO once daily until disease progression or unacceptable toxicity

**Investigation prior to initiating treatment**
CT Scan
FBC, U&E, LFTs
Bone Profile
Coag
Cholesterol
ECG
Blood pressure
Urinalysis
TFTs
Performance status

**Cautions**
Monitor closely in patients with mild-moderate hepatic impairment (Child-Pugh A,B), not recommended in patients with severe hepatic impairment (Child-Pugh C)
Not recommended in patients with severe renal impairment

**Investigations and consultations prior to each cycle**
FBC, U&E, LFTs
Bone Profile
Cholesterol
Blood pressure
TFTs

**Acceptable levels for treatment to proceed (if outside these levels defer one week or contact consultant)**
Hb > 9
LFTs normal
Plts > 100
WCC and differential with normal range
U&E within normal range

**Side Effects**
Diarrhoea, hypertension, fatigue, decreased appetite, weight decreased, vomiting, nausea, proteinuria, stomatitis, headache, dysphonia, palmar-plantar erythrodysaesthesia syndrome (PPE), peripheral oedema, hypercholesterolemia, renal failure and impairment, arterial thromboembolisms

**Dose Modification Criteria**

Optimal medical management (i.e. treatment or therapy) for nausea, vomiting, and diarrhoea should be initiated prior to any lenvatinib therapy interruption or dose reduction; however, gastrointestinal toxicity should be actively treated in order to reduce the risk of development of renal impairment or renal failure

Severe (e.g., Grade 3) or intolerable adverse reactions require interruption of the combination of medicines until improvement of the reaction to Grade 0-1 or baseline.

For toxicities thought to be related to lenvatinib (see Table 1), upon resolution/improvement of an adverse reaction to Grade 0-1 or baseline, treatment should be resumed at a reduced dose of lenvatinib as suggested in Table 2.

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).

Grades are based on the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE).

**Table 1 Adverse reactions requiring dose modification of 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. |
| | 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 |

**Table 1 Adverse reactions requiring dose modification of lenvatinib**

| Adverse reaction | Severity | Action | Dose reduce and resume lenvatinib |
|---|---|---|---|

*Grade 4 laboratory abnormalities judged to be non-life-threatening, may be managed as severe reactions (e.g., Grade 3)

**Table 2 Dose modifications from recommended lenvatinib daily dose**

| Dose level | Daily dose (≥60kg) | Daily dose (<60kg) |
|---|---|---|
| Recommended daily dose | 12mg | 8mg |
| First dose reduction | 8mg | 4mg |
| Second dose reduction | 4mg | 4mg every other day |
| Third dose reduction | 4mg every other day | Discontinue |

**Specific Information on Administration**

Lenvatinib is for oral use. The capsules should be taken at about the same time each day, with or without food. The capsules can be swallowed whole with water. Caregivers should not open the capsule, in order to avoid repeated exposure to the contents of the capsule.

Alternatively, the lenvatinib capsules may be added without breaking or crushing them to a tablespoon of water or apple juice in a small glass to produce a suspension. The capsules must be left in the liquid for at least 10 minutes and stirred for at least 3 minutes to dissolve the capsule shells. The suspension is to be swallowed. After drinking, the same amount of water or apple juice (one tablespoon) must be added to the glass and swirled a few times. The additional liquid must be swallowed.

Avoid grapefruit or grapefruit juice.

**THIS PROTOCOL HAS BEEN DIRECTED BY DR Mitchell, DESIGNATED LEAD CLINICIAN FOR UPPER GI CANCER**

**RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE**

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