Lenvima® (lenvatinib mesilate) hepatocellular carcinoma prescribing information for Great Britain (GB), Northern Ireland (NI) and Republic of Ireland (ROI)

Lenvima® (lenvatinib mesilate)
Please refer to the Summary of Product Characteristics (SPC) before prescribing. ***Presentation:*** 4mg and 10mg hard capsules. ***Indication:*** Monotherapy treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC) who have received no prior systemic therapy. ***Dose and administration:*** For oral use. Should be initiated and supervised by a health care professional experienced in the use of anticancer therapies. 8 mg once daily for patients with a body weight of < 60 kg and 12 mg once daily for patients with a body weight of ≥ 60 kg at about the same time each day, with or without food. If dose missed, and it cannot be taken within 12 hours, skip dose and take next dose at normal time. Modify daily dose of lenvatinib as needed according to dose/toxicity management plan. Continue treatment as long as clinical benefit observed or unacceptable toxicity occurs. Initiate medical management for nausea, vomiting, and diarrhoea prior to interruption or dose reduction. Actively treat GI toxicity to reduce risk of renal impairment or failure. ***Dose adjustment:*** Dose adjustments are based only on toxicities observed and not on body weight changes during treatment. Mild to moderate adverse reactions (e.g., Grade 1 or 2) generally do not warrant interruption of lenvatinib, unless intolerable despite optimal management. For persistent and intolerable Grade 2 or Grade 3 toxicities, upon resolution to Grade 0-1 or baseline, resume treatment at a reduced dose of lenvatinib. No dose adjustment required for first occurrence of haematologic toxicity or proteinuria. For ≥60 kg body weight: First occurrence 8mg/day; second occurrence 4 mg/day; third occurrence 4 mg every other day. For <60 kg body weight: First occurrence 4 mg/day; second occurrence 4mg every other day; third occurrence discontinue. Discontinue treatment in case of life-threatening reactions (e.g., Grade 4) except if laboratory abnormality judged to be non-life-threatening, then manage as Grade 3. ***Special populations:*** Patients ≥75 years, of white race or female sex or those with worse baseline hepatic impairment (Child-Pugh A score of 6 compared to score of 5) appear to have reduced tolerability to lenvatinib. *Patients with hypertension:* Control blood pressure prior to treatment and monitor regularly during treatment. *Patients with hepatic impairment:* No dose adjustment of starting dose required for HCC patients with mild hepatic impairment (Child-Pugh A). No dosing recommendation is available for patients with HCC and moderate hepatic impairment (Child-Pugh B) - closely monitor overall safety. Not recommended for HCC patients with severe hepatic impairment (Child-Pugh C). *Patients with renal impairment:* No dose adjustments are required in patients with mild or moderate renal impairment. No dosing recommendation is available for patients with HCC and severe renal impairment. *Elderly population:* No adjustment of starting dose is required. *Paediatric population:* No data in children aged 2 to <18 years. Do not use in children <2 years due to safety concerns identified in animal studies. *Race:* No adjustment of starting dose is required. ***Contra-Indications:*** Hypersensitivity to active substance or any of the excipients. Breast-feeding. ***Special warnings and precautions:*** Control blood pressure prior to treatment with lenvatinib and, if patients are known to be hypertensive, control with stable dose of antihypertensive therapy for at least 1 week prior to treatment with lenvatinib. Start antihypertensive agents as soon as elevated blood pressure is confirmed. Monitor blood pressure after 1 week of treatment with lenvatinib, then every 2 weeks for the first 2 months and monthly thereafter. When necessary, manage hypertension as recommended in SPC. Consider risk of aneurysms and artery dissections prior to treatment in patients with risk factors such as hypertension or history of aneurysm. Monitor urine protein regularly. Interrupt, adjust or discontinue dose if urine dipstick proteinuria ≥2+ is detected. Discontinue in the event of nephrotic syndrome. Closely monitor overall safety in patients with mild or moderate hepatic impairment. Monitor liver function tests before starting treatment, then every 2 weeks for the first 2 months and monthly thereafter during treatment. Monitor patients for worsening liver function including hepatic encephalopathy. In the case of hepatotoxicity, renal impairment, renal failure, cardiac decompensation, signs or symptoms of PRES, bleeding, gastrointestinal perforation or fistula, dose interruptions, adjustments, or discontinuation may be necessary. Discontinue lenvatinib in the event of persistence of Grade 4 diarrhoea despite medical management. Use lenvatinib with caution in patients who have had an arterial thromboembolism within the previous 6 months. Discontinue following an arterial thrombotic event. Women of childbearing potential must use highly effective contraception while taking lenvatinib and for one month after stopping treatment. Consider degree of tumour invasion/infiltration of major blood vessels (e.g. carotid artery) due to potential risk of severe haemorrhage associated with tumour shrinkage/necrosis following lenvatinib therapy. Screen for and treat oesophageal varices in patients with liver cirrhosis before initiating lenvatinib. Do not start lenvatinib in patients with fistulae to avoid worsening and discontinue permanently in patients with oesophageal or tracheobronchial tract involvement and any Grade 4 fistula. Monitor ECGs at baseline and periodically during treatment in all patients particularly those with congenital long QT syndrome, congestive heart failure, bradyarrhythmias, and those taking medicinal products known to prolong the QT interval, including Class Ia and III antiarrhythmics. Withhold lenvatinib in QT interval prolongation greater than 500 ms. Resume lenvatinib at a reduced dose when QTc prolongation is resolved to < 480 ms or baseline. Monitor and correct electrolyte abnormalities before starting treatment. Monitor electrolytes during treatment. Monitor blood calcium levels at least monthly and replace calcium as necessary during treatment. Interrupt or adjust lenvatinib dose as necessary depending on severity, presence of ECG changes, and persistence of hypocalcaemia. Monitor thyroid function before initiation of, and periodically throughout, treatment with lenvatinib. Monitor TSH levels regularly and adjust thyroid hormone administration as required. Consider temporary interruption of lenvatinib in patients undergoing major surgical procedures. Consider dental examination and appropriate preventative dentistry prior to lenvatinib initiation. Avoid invasive dental procedures in patients receiving, or previously treated with, intravenous bisphosphonates. Use with caution in elderly or Asian patients due to reduced tolerability to lenvatinib. Consider washout between lenvatinib and other anti-cancer treatment due to potential risk for additive toxicities. ***Drug Interactions:*** No significant drug-drug interaction expected between lenvatinib and CYP3A4/Pgp substrates. Unknown if lenvatinib reduces effectiveness of hormonal contraceptives. Women using oral hormonal contraceptives should add a barrier method. ***Pregnancy:*** Do not use during pregnancy unless clearly necessary. Women of childbearing potential should avoid becoming pregnant and use highly effective contraception during and for at least one month after treatment. ***Lactation:*** Unknown if excreted in human milk. A risk to newborns or infants cannot be excluded; contraindicated during breast-feeding. ***Fertility:*** Fertility effects in humans are unknown. ***Effects on ability to drive and use machines:*** Use caution when driving or operating machines if experiencing fatigue and/or dizziness. ***Undesirable effects:*** **Consult the SPC for information on all side effects.** The adverse reactions presented in this section are based on the combined safety data of differentiated thyroid cancer and HCC patients. *Very common (≥1/10):* urinary tract infection, thrombocytopenia, lymphopenia, leukopenia, neutropenia, hypothyroidism, increased blood thyroid stimulating hormone, hypocalcaemia, hypokalaemia, hypercholesterolaemia, hypomagnesaemia, decreased weight, decreased appetite, insomnia, dizziness, headache, dysgeusia, haemorrhage, hypertension, hypotension, dysphonia, diarrhoea, gastrointestinal and abdominal pains, vomiting, nausea, oral inflammation, oral pain, constipation, dyspepsia, dry mouth, increased lipase, increased amylase, increased blood bilirubin, hypoalbuminaemia, increased alanine aminotransferase, increased blood alkaline phosphatase, increased gamma-glutamyltransferase, increased aspartate aminotransferase, palmar-plantar erythrodysaesthesia syndrome, rash, alopecia, back pain, arthralgia, myalgia, pain in extremity, musculoskeletal pain, proteinuria, increased blood creatinine, fatigue, asthenia, peripheral oedema. *Common (≥1/100 to <1/10):* dehydration, cerebrovascular accident, myocardial infarction, cardiac failure, prolonged electrocardiogram QT, decreased ejection fraction, pulmonary embolism, anal fistula, flatulence, hepatic failure, hepatic encephalopathy, abnormal hepatic function, cholecystitis, hyperkeratosis, renal failure, renal impairment, increased blood urea, malaise. *Uncommon (≥1/1,000 to <1/100):* perineal abscess, splenic infarction, posterior reversible encephalopathy syndrome, monoparesis, transient ischaemic attack, pneumothorax, pancreatitis, colitis, hepatocellular damage/hepatitis, osteonecrosis of the jaw, nephrotic syndrome, impaired healing. *Frequency not known (cannot be estimated from the available data):* aneurysms and artery dissections, non-gastrointestinal fistula. ***Overdose:*** No specific antidote. In case of suspected overdose, lenvatinib should be withheld and appropriate supportive care given as required. ***Legal Category:*** POM ***Cost: UK NHS list price:*** 4mg capsules pack of 30: £1,437.00; 10mg capsules pack of 30: £1,437.00 ***Marketing authorisation (MA) numbers NI:*** 4mg capsules: EU/1/15/1002/001; 10mg capsules: EU/1/15/1002/002. ***GB:*** 4mg capsules: PLGB 33967/0009; 10mg capsules: PLGB 33967/0008 ***MA holder:*** Eisai GmbH (NI); Eisai Europe Ltd (GB) ***Further information from:*** Eisai Ltd., Mosquito Way, Hatfield, Hertfordshire, AL10 9SN, UK ***Date of preparation***: November 2022 [UK-LENA-22-00177]

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.**or search for the MHRA Yellow Card in the Google Play or Apple App Store, or Republic of Ireland:** www.hpra.ie. **Adverse events should also be reported to Eisai Ltd on +44 (0)208 600 1400 or EUmedinfo@eisai.net**