PRESCRIBING INFORMATION *Lenvima® (lenvatinib)*

Please refer to the Summary of Product Characteristics (SPC) before prescribing. ***Presentation:*** 4mg and 10mg hard capsules. ***Indication:*** Monotherapy treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI). ***Dose and administration:*** For oral use. Should be initiated and supervised by a health care professional experienced in the use of anticancer therapies. 24 mg once daily at about the same time each day, with or without food. Swallow the capsules whole with water or dissolve in water or apple juice without breaking or crushing - see SPC for guidelines. If dose missed, and it cannot be taken within 12 hours, skip dose and take next dose at normal time. 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:*** Mild to moderate adverse reactions (e.g., Grade 1 or 2) generally do not warrant interruption of lenvatinib, unless intolerable despite optimal management. Severe (e.g., Grade 3) or intolerable adverse reactions require interruption of lenvatinib until improvement of the reaction to Grade 0-1 or baseline. For lenvatinib related toxicities, upon resolution/improvement of an adverse reaction to Grade 0-1 or baseline, resume treatment at a reduced dose of lenvatinib: First dose reduction: 20 mg once daily; second dose reduction 14 mg once daily and third dose reduction 10 mg once daily. Consider further dose reductions on individual basis as limited data on doses below 10 mg once daily. 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 severe reaction (e.g., Grade 3). ***Special populations:*** Patients of age ≥75 years, of Asian race, with comorbidities or body weight <60 kg 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 adjustment of starting dose required in patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. In patients with severe (Child-Pugh C) hepatic impairment, starting dose is 14 mg once daily. Adjust dose further based on individual tolerability. *Patients with renal impairment:* No adjustment of starting dose is required in patients with mild or moderate renal impairment. In patients with severe renal impairment starting dose is 14 mg taken once daily. Adjust dose further based on individual tolerability. Use of lenvatinib in patients with end-stage renal disease is not recommended. *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. 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+. 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. In the case of hepatotoxicity, renal impairment, renal failure, 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. Monitor for clinical symptoms or signs of cardiac decompensation, as dose interruptions, adjustments or discontinuation may be necessary. 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. 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 DTC and hepatocellular carcinoma patients. *Very common (≥1/10):* urinary tract infection, thrombocytopenia, leukopenia, neutropenia, hypothyroidism, hypocalcaemia, hypokalaemia, 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 blood bilirubin, hypoalbuminaemia, increased alanine aminotransferase, increased aspartate aminotransferase, palmar-plantar erythrodysaesthesia syndrome, rash, alopecia, back pain, arthralgia, myalgia, pain in extremity, musculoskeletal pain, proteinuria, fatigue, asthenia, peripheral oedema. *Common (≥1/100 to <1/10):* lymphopenia, increased blood thyroid stimulating hormone , dehydration, hypomagnesaemia, hypercholesterolaemia, cerebrovascular accident, myocardial infarction, cardiac failure, prolonged electrocardiogram qt, decreased ejection fraction, pulmonary embolism, anal fistula, flatulence, increased lipase, increased amylase, hepatic failure, hepatic encephalopathy, increased blood alkaline phosphatase, hepatic function abnormal, increased gamma-glutamyltransferase, cholecystitis, hyperkeratosis, renal failure cases, renal impairment, increased blood creatinine, 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, 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) number:*** 4mg capsules: EU/1/15/1002/001; 10mg capsules: EU/1/15/1002/002 ***MA holder:*** Eisai GmbH ***Further information from:*** Eisai Ltd., Mosquito Way, Hatfield, Hertfordshire, AL10 9SN, UK ***Date of preparation:*** November 2020 UK-LENA-20-00167

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for the MHRA Yellow Card in the Google Play or Apple App Store, or Ireland: www.hpra.ie. Adverse events should also be reported to Eisai Ltd on +44 (0)845 676 1400/ +44 (0)208 600 1400 or EUmedinfo@eisai.net