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Lenvatinib Mesylate

Class: Antineoplastic Agents
- Kinase Inhibitors
- Receptor Tyrosine Kinase Inhibitors
- Tyrosine Kinase Inhibitors
- VEGF Receptor Inhibitors
- VEGFR Inhibitors
- Vascular Endothelial Growth Factor Receptor Inhibitors

VA Class: AN900
Chemical Name: 4-[3-Chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6-quinolinecarboxamide
Molecular Formula: $C_{21}H_{19}ClN_4O_4C_{21}H_{19}ClN_4O_4•CH_4O_3S$
CAS Number: 417716-92-8
Brands: Lenvima

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Introduction

Antineoplastic agent; an inhibitor of multiple receptor tyrosine kinases.[1 2 5 9 10]

Uses for Lenvatinib Mesylate

Differentiated Thyroid Cancer

Treatment of locally recurrent or metastatic, progressive, radioactive iodine (iodine-131)-refractory differentiated thyroid cancer[1 2 10] (designated an orphan drug by FDA for this cancer).[3]

Lenvatinib Mesylate Dosage and Administration

General

Restricted Distribution Program

- Obtain lenvatinib mesylate only through designated specialty pharmacies.[4]
- Contact manufacturer at 855-347-2448 or consult the Lenvima website (**[Web]**) for specific ordering and availability information.[4]

Administration

Oral Administration

Administer orally once daily without regard to meals.[1] Take at the same time each day.[1]

If a dose of lenvatinib is missed, do not take the missed dose within 12 hours of the next dose.[1]

If lenvatinib is used immediately following sorafenib or other antineoplastic agents; potential risk for additive toxicities unless there is an adequate washout period between treatments.[15] In

clinical trials, the minimum washout period was 4 weeks.[15]

Dosage

Available as lenvatinib mesylate; dosage expressed in terms of lenvatinib.[1]

Adults

Differentiated Thyroid Cancer

Oral

24 mg (two 10-mg capsules and one 4-mg capsule) once daily.[1] Continue therapy until disease progression or unacceptable toxicity occurs.[1]

Dosage Modification for Toxicity

Some adverse effects require temporary interruption and/or dosage reduction or discontinuance of therapy.[1] If dosage reduction from 24 mg once daily is necessary, reduce dosage to 20 mg (two 10-mg capsules) once daily.[1] If toxicity recurs on a dosage of 20 mg once daily, reduce dosage to 14 mg (one 10-mg capsule and one 4-mg capsule) once daily.[1] If toxicity recurs on dosage of 14 mg once daily, reduce dosage to 10 mg (one 10-mg capsule) once daily.[1] The manufacturer provides no specific recommendations for further dosage reductions.[1]

Grade 2 or 3 Toxicity or Grade 4 Laboratory Abnormalities

Dosage should be reduced in succession based on the previous dosage level (24 mg, 20 mg, or 14 mg once daily).[1]

Refers to the same or different adverse reaction requiring dosage adjustment.[1]

Table 1. Recommended Dosage Modifications for Persistent and Intolerable Grade 2–3 Adverse Reactions or Grade 4 Laboratory Abnormalities1

Occurrence	Recommended Dosage Modification
First occurrence	Interrupt therapy until toxicity or laboratory abnormality improves to ≤grade 1 or baseline; when resuming therapy, reduce dosage to 20 mg (two 10-mg capsules) once daily[1]
Second occurrence	Interrupt therapy until toxicity or laboratory abnormality improves to ≤grade 1 or baseline; when resuming therapy, further reduce dosage to 14 mg (one 10-mg capsule and one 4-mg capsule) once daily[1]
Third occurrence	Interrupt therapy until toxicity or laboratory abnormality improves to ≤grade 1 or baseline; when resuming therapy, further reduce dosage to 10 mg (one 10-mg capsule) once daily[1]

The manufacturer provides no specific recommendations for further dosage reductions.[1]

Safety of resuming lenvatinib following resolution of grade 4 adverse reactions not established.[1]

Cardiovascular Toxicity

If grade 3 hypertension persists despite optimal antihypertensive therapy, withhold lenvatinib therapy.[1] Once hypertension improves to ≤grade 2, may resume lenvatinib at a reduced dosage.[1] If life-threatening hypertension occurs, discontinue lenvatinib.[1] (See Hypertension under Cautions.)

If grade 3 cardiac dysfunction (i.e., decreased ventricular function, cardiac failure, or pulmonary edema) occurs, withhold lenvatinib therapy.[1] Once the toxicity improves to ≤grade 1 or baseline, may resume lenvatinib at a reduced dosage or discontinue therapy, depending on severity and persistence of the cardiac dysfunction.[1] If grade 4 cardiac dysfunction occurs, discontinue lenvatinib.[1] (See Cardiac Dysfunction under Cautions.)

If ≥grade 3 QT-interval prolongation occurs, withhold lenvatinib therapy.[1] Once the toxicity improves to ≤grade 1 or baseline, may resume lenvatinib at a reduced dosage.[1] (See Prolongation of QT Interval under Cautions.)

Arterial Thromboembolism

If an arterial thromboembolic event occurs, discontinue lenvatinib.[1] (See Arterial Thromboembolic Events under Cautions.)

Hemorrhage

If grade 3 hemorrhage occurs, withhold lenvatinib therapy.[1] Once the hemorrhagic event improves to ≤grade 1 or to baseline, may resume lenvatinib at a reduced dosage or discontinue therapy, depending on severity and persistence of the hemorrhage.[1] If grade 4 hemorrhage occurs, discontinue lenvatinib.[1] (See Hemorrhage under Cautions.)

Nephrotoxicity

If grade 3 or 4 renal impairment or renal failure occurs, withhold lenvatinib therapy.[1] Once the nephrotoxicity improves to ≤grade 1 or to baseline, may resume lenvatinib at a reduced dosage or discontinue therapy, depending on severity and persistence of the toxicity.[1] (See Renal Failure and Impairment under Cautions.)

Hepatotoxicity

If grade 3 or 4 hepatotoxicity occurs, withhold lenvatinib therapy.[1] Once the toxicity improves to ≤grade 1 or to baseline, may resume lenvatinib at a reduced dosage or discontinue therapy, depending on severity and persistence of the hepatotoxicity.[1] (See Hepatic Toxicity under Cautions.)

Proteinuria

Withhold lenvatinib therapy for proteinuria ≥2 g per 24 hours; may resume at a reduced dosage when proteinuria declines below this level.[1]

If nephrotic syndrome occurs, discontinue lenvatinib.[1] (See Proteinuria under Cautions.)

GI Toxicity

If nausea, vomiting, or diarrhea occurs, medical management (e.g., use of antiemetic and/or antidiarrheal agents) is recommended prior to interruption of therapy or dosage reduction of lenvatinib.[1]

If GI perforation or a life-threatening fistula occurs, discontinue lenvatinib.[1] (See GI Perforation and Fistula Formation under Cautions.)

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

If RPLS occurs, withhold lenvatinib therapy.[1] Once the RPLS fully resolves, may resume lenvatinib at a reduced dosage or discontinue therapy, depending on severity and persistence of neurologic symptoms.[1] (See RPLS under Cautions.)

Special Populations

Hepatic Impairment

Severe hepatic impairment (Child-Pugh class C): Reduce dosage to 14 mg (one 10-mg capsule and one 4-mg capsule) once daily.[1] [13]

Mild or moderate hepatic impairment (Child-Pugh class A or B): No dosage adjustment required.[1] [13]

Renal Impairment

Severe renal impairment (Cl_{cr} <30 mL/minute): Reduce dosage to 14 mg (one 10-mg capsule and one 4-mg capsule) once daily.[1]

Mild or moderate renal impairment (Cl_{cr} 30–89 mL/minute): No dosage adjustment required.[1]

End-stage renal disease: Not studied; no specific dosage recommendations.[1]

Geriatric Patients

No specific dosage recommendations.[1]

Cautions for Lenvatinib Mesylate

Contraindications

- Manufacturer states none known.[1]

Warnings/Precautions

Hypertension

Hypertension reported in 73% (grade 3 or 4 in 44%) of lenvatinib-treated patients in the primary efficacy study.[1] [2] Usually develops early during therapy; median time to onset of new or worsening hypertension was 16 days following initiation of therapy.[1] [15]

Assess and control BP prior to initiating and during lenvatinib therapy.[1] Monitor BP following 1 week of therapy, every 2 weeks for the first 2 months, and then at least monthly thereafter.[1] Manage hypertension medically (i.e., with antihypertensive therapy) as needed during therapy.[1]

If grade 3 hypertension occurs, therapy interruption followed by dosage reduction may be necessary.[1] Discontinue lenvatinib if life-threatening hypertension occurs.[1] (See Cardiovascular Toxicity under Dosage and Administration.)

Cardiac Dysfunction

Cardiac dysfunction (i.e., decreased left or right ventricular function, cardiac failure, or pulmonary edema) reported in 7% of lenvatinib-treated patients in the primary efficacy study.[1] Decreased ejection fraction was the most commonly reported finding in these cases.[1]

Monitor for clinical manifestations of cardiac decompensation during therapy.[1]

If grade 3 cardiac dysfunction occurs, therapy interruption followed by dosage reduction or discontinuance of therapy is necessary.[1] Discontinue lenvatinib if grade 4 cardiac dysfunction occurs.[1] (See Cardiovascular Toxicity under Dosage and Administration.)

Arterial Thromboembolic Events

Arterial thromboembolic events (e.g., cerebrovascular accident, TIA, MI) reported.[1] [2] [15]

Discontinue lenvatinib if an arterial thromboembolic event occurs.[1] Safety of resuming lenvatinib following such an event not established.[1] Not evaluated in patients who had an arterial thromboembolic event within the previous 6 months.[1]

Hepatic Toxicity

ALT or AST elevations, acute hepatitis, and hepatic failure (including fatal cases) reported.[1] [2]

Perform liver function tests prior to initiation of therapy, every 2 weeks for the first 2 months of therapy, and then at least monthly thereafter during therapy.[1]

If hepatotoxicity occurs, therapy interruption followed by dosage reduction or discontinuance of therapy may be necessary.[1] Discontinue lenvatinib if hepatic failure occurs.[1] (See Hepatotoxicity under Dosage and Administration.)

Proteinuria

Proteinuria reported in 34% (grade 3 in 11%) of lenvatinib-treated patients in the primary efficacy study.[1] Usually occurs early during therapy.[15]

Monitor for proteinuria prior to initiation of lenvatinib and periodically during therapy.[1] If urine dipstick proteinuria ≥2+ is detected, obtain a 24-hour urine protein.[1] Interrupt lenvatinib therapy for proteinuria ≥2 g per 24 hours; resume therapy at a reduced dosage when proteinuria declines to <2 g per 24 hours.[1] Discontinue lenvatinib if nephrotic syndrome occurs.[1] (See Proteinuria under Dosage and Administration.)

Renal Failure and Impairment

Renal impairment and renal failure reported.[1] [2] Risk factors for developing severe renal impairment include dehydration and hypovolemia secondary to diarrhea and vomiting.[1]

If renal impairment occurs, therapy interruption followed by dosage reduction or discontinuance of therapy may be necessary.[1] (See Nephrotoxicity under Dosage and Administration.)

GI Perforation and Fistula Formation

GI perforation and fistula formation reported in patients receiving lenvatinib or other tyrosine kinase inhibitors.[1] [2] [14] [15] [16]

Discontinue lenvatinib if GI perforation or life-threatening fistula formation occurs.[1]

Prolongation of QT Interval

Prolongation of QT interval reported.[1] [2]

Monitor serum electrolyte concentrations (i.e., potassium, magnesium, calcium) in all patients; correct any electrolyte abnormalities.[1]

Monitor ECGs in patients with congenital long QT syndrome, CHF, or bradyarrhythmias, and in those receiving other drugs known to prolong the QT interval.[1]

If QT-interval prolongation occurs, temporary interruption of therapy followed by dosage reduction may be necessary.[1] (See Cardiovascular Toxicity under Dosage and Administration.)

Hypocalcemia

Hypocalcemia requiring calcium replacement and temporary interruption of therapy and dosage reduction reported.[1] [2]

Monitor blood calcium concentrations at least monthly during therapy; replace calcium as necessary.[1]

If hypocalcemia occurs, interrupt therapy and then reduce dosage or discontinue therapy depending on the presence of ECG changes and severity and persistence of the hypocalcemia.[1] (See Dosage Modification for Toxicity under Dosage and Administration.)

RPLS

RPLS reported in 3 lenvatinib-treated patients (<1%) in clinical trials.[1] [2] RPLS is a neurologic disorder that may manifest with severe headache, seizures, weakness, confusion, blindness, or other visual disturbances; hypertension also may be present.[1] [15] Magnetic resonance imaging (MRI) is necessary to confirm diagnosis.[1]

If RPLS occurs, interrupt therapy until fully resolved.[1] Upon resolution, may resume therapy at a reduced dosage or discontinue therapy, depending on the severity and persistence of the neurologic manifestations.[1] (See Reversible Posterior Leukoencephalopathy Syndrome [RPLS] under Dosage and Administration.)

Hemorrhage

Hemorrhagic events, most commonly epistaxis, reported in 35% of lenvatinib-treated patients in the primary efficacy study.[1] [2] Fatal intracranial hemorrhage reported in 1 of 16 lenvatinib-treated patients who had CNS metastases at baseline in the primary efficacy study.[1]

If grade 3 hemorrhage occurs, interrupt therapy, then reduce dosage or discontinue lenvatinib.[1] Discontinue lenvatinib if grade 4 hemorrhage occurs.[1] (See Hemorrhage under Dosage and Administration.)

Impairment of Thyroid-stimulating Hormone Suppression

Lenvatinib impairs exogenous thyroid suppression.[1] Elevated TSH concentrations observed in 57% of lenvatinib-treated patients with normal TSH concentrations at baseline in the primary efficacy study.[1]

Monitor TSH concentrations monthly; adjust thyroid replacement therapy as needed in patients with differentiated thyroid cancer.[1]

Fetal/Neonatal Morbidity and Mortality

May cause fetal harm; teratogenicity, embryotoxicity, and fetotoxicity demonstrated in animals.[1]

Avoid pregnancy during therapy.[1] Women of childbearing potential should use an effective method of contraception while receiving lenvatinib and for ≥2 weeks after discontinuance of therapy.[1] If used during pregnancy or if patient becomes pregnant while receiving the drug, apprise patients of potential fetal hazard.[1] (See Advice to Patients.)

Impairment of Fertility

Results of animal studies suggest that lenvatinib may impair male and female fertility.[1] [15] Effect on fertility in humans not known.[1] [15]

Specific Populations

Pregnancy

May cause fetal harm.[1] (See Fetal/Neonatal Morbidity and Mortality under Cautions.)

Lactation

Not known whether lenvatinib is distributed into human milk; lenvatinib and its metabolites are distributed into milk in rats.[1] Discontinue nursing.[1]

Pediatric Use

Safety and efficacy not established.[1]

Growth retardation (decreased weight gain, food consumption, and femur and tibia width and/or length), secondary delays in physical development, and reproductive organ immaturity observed in juvenile rats receiving daily oral administration of lenvatinib for 8 weeks.[1]

Geriatric Use

No overall differences in safety and efficacy relative to younger adults.[1] (See Special Populations under Pharmacokinetics: Elimination.)

Hepatic Impairment

Mild or moderate hepatic impairment did not substantially affect systemic exposure of lenvatinib; dosage reduction not necessary.[1 13]

Increased systemic exposure in patients with severe hepatic impairment; dosage reduction recommended.[1 13] (See Hepatic Impairment under Dosage and Administration and also see Special Populations under Pharmacokinetics: Absorption.)

Renal Impairment

Mild or moderate renal impairment did not substantially affect systemic exposure of lenvatinib; dosage adjustment not necessary.[1]

Increased systemic exposure in patients with severe renal impairment; dosage reduction recommended.[1 5] (See Renal Impairment under Dosage and Administration and also see Special Populations under Pharmacokinetics: Absorption.)

Not studied in patients with end-stage renal disease.[1]

Common Adverse Effects

Adverse effects: Hypertension,[1 2] diarrhea,[1 2] fatique,[1 2] arthralgia/myalgia,[1] decreased appetite,[1 2] weight loss,[1 2] nausea,[1 2] stomatitis,[1 2] headache,[1 2] vomiting,[1 2] proteinuria,[1 2] palmar-plantar erythrodysesthesia (hand-foot syndrome),[1 2] abdominal pain,[1] dysphonia,[1 2] constipation,[1] oral pain,[1] cough,[1] rash,[1] peripheral edema.[1]

Laboratory abnormalities: Hypocalcemia,[1] hypokalemia,[1] elevated ALT or AST concentrations,[1] elevated lipase concentrations,[1] elevated S_{cr} concentrations,[1] thrombocytopenia.[1] Hypoalbuminemia, increased alkaline phosphatase, hypomagnesemia, hypoglycemia, hyperbilirubinemia, hypercalcemia, hypercholesterolemia, increased amylase concentrations, hyperkalemia.[1]

Interactions for Lenvatinib Mesylate

Metabolized principally by CYP3A4.[1 5]

Inhibits CYP isoenzymes 2C8, 1A2, 2B6, 2C9, 2C19, 2D6, and 3A and also UGT 1A1 and 1A4.[1] [5] Does not inhibit CYP isoenzymes 2A6 or 2E1 and shows little to no inhibition of UGT1A6, 1A9, or 2B7, or aldehyde oxidase.[1] [5]

Induces CYP3A; does not induce CYP isoenzymes 1A1, 1A2, 2B6, or 2C9, and UGT 1A1, 1A4, 1A6, 1A9, or 2B7.[1]

In vitro, inhibitor of organic anion transporter (OAT) 1, OAT3, organic cation transporter (OCT) 1, OCT2, organic anion transport protein (OATP) 1B1, and bile salt export pump (BSEP); shows little to no inhibition of OATP1B3.[1] [5] Substrate for P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP), but is not a substrate for OAT1, OAT3, OCT1, OCT2, OATP1B1, OATP1B3, or BSEP.[1]

Drugs Affecting Hepatic Microsomal Enzymes and/or Efflux Transport Systems

CYP3A, P-gp, and BCRP inhibitors: Clinically important pharmacokinetic interactions unlikely; dosage adjustment not necessary.[1]

CYP3A and P-gp inducers: Clinically important pharmacokinetic interactions unlikely; dosage adjustment not necessary.[1]

Drugs Metabolized by Hepatic Microsomal Enzymes

Substrates of CYP3A4: Clinically important pharmacokinetic interactions not expected.[1]

Substrates of CYP2C8: Clinically important pharmacokinetic interactions not expected.[1]

Substrates of CYP1A2, 2B6, 2C9, 2C19, or 2D6: Clinically important pharmacokinetic interactions not expected.[1]

Drugs that Prolong QT Interval

Potential pharmacologic interactions (additive effect on QT-interval prolongation).[1] Monitor ECGs during concomitant use; also monitor for and correct any electrolyte abnormalities.[1] (See Prolongation of QT Interval under Cautions.)

Specific Drugs

Drug	Interaction	Comments
Antiarrhythmic agents, class IA (e.g., quinidine, procainamide) and class III (e.g., amiodarone, sotalol)	Possible additive effect on QT-interval prolongation[1]	Periodically monitor ECGs; monitor for and correct electrolyte abnormalities[1] (see Prolongation of QT Interval under Cautions)
Ketoconazole	Ketoconazole increased peak concentrations and AUC of lenvatinib by 19 and 15%, respectively[1] [5]	CYP3A, P-gp, and BCRP inhibitors: No dosage adjustment necessary[1]
Midazolam	Clinically important pharmacokinetic interaction unlikely[1]	

Repaglinide	Clinically important pharmacokinetic interaction unlikely[1]	
Rifampin	Rifampin (single dose) decreased lenvatinib AUC by 18%; peak plasma concentrations were unchanged[1] When administered for 15 days, rifampin increased peak concentrations and AUC of lenvatinib by 33 and 31%, respectively[1]	CYP3A and P-gp inducers: No dosage adjustment necessary[1]

Lenvatinib Mesylate Pharmacokinetics

Absorption

Bioavailability

Following oral administration, peak plasma concentrations usually attained within 1–4 hours.[1]

Systemic exposure and peak plasma concentrations appear to increase in a proportional manner following single or repeated administration of lenvatinib 3.2–32 mg once daily.[1]

Food

Food decreases rate (time to peak concentration delayed by 2 hours) but does not substantially affect extent of absorption.[1]

Special Populations

Total exposure in individuals with mild (Cl_{cr} 60–89 mL/minute) and moderate renal impairment (Cl_{cr} 30–59 mL/minute) similar compared with individuals with normal renal function and was approximately 20% higher in those with severe renal impairment (Cl_{cr} <30 mL/minute).[1,5]

End-stage renal disease: Pharmacokinetics not studied.[1]

Mild (Child-Pugh class A), moderate (Child-Pugh class B), or severe (Child-Pugh class C) hepatic impairment: Dose-adjusted total exposure was 119, 107, or 180% higher, respectively, compared with individuals with normal hepatic function.[1]

Distribution

Extent

Not known whether lenvatinib is distributed into human milk.[1] Lenvatinib and its metabolites distribute into milk in rats at concentrations higher than maternal plasma.[1]

Plasma Protein Binding

98–99%.[1]

Elimination

Metabolism

Primarily metabolized by CYP3A4, aldehyde oxidase, and nonenzymatic processes.[1] [5]

Elimination Route

Eliminated in feces (approximately 64%) and urine (approximately 25%).[1]

Half-life

Approximately 28 hours.[1]

Special Populations

In a pharmacokinetic population analysis, age, gender, and race did not have a substantial effect on apparent clearance.[1]

Stability

Storage

Oral

Capsules

25°C (may be exposed to 15–30°C).[1]

Actions

- Inhibits multiple receptor tyrosine kinases (RTKs),[1] [2] [5] [9] [10] which are involved in the initiation of various cascades of intracellular signaling events that lead to cell proliferation and/or influence processes critical to cell survival and tumor progression (e.g., angiogenesis, metastasis, inhibition of apoptosis).[6] [7] [8]
- Inhibits kinase activities of vascular endothelial growth factor (VEGF) receptors VEGFR-1, VEGFR-2, and VEGFR-3.[1] [2] [5] [9]
- Also inhibits other RTKs involved in pathogenic angiogenesis, tumor growth, and cancer progression, including fibroblast growth factor (FGF) receptors (FGFR1, FGFR2, FGFR3, and FGFR4), platelet-derived growth factor receptor (PDGFR), stem cell factor receptor (c-Kit), and ret proto-oncogene (RET).[1] [2] [5] [9]

Advice to Patients

- Importance of instructing patients to read the manufacturer's patient information before starting lenvatinib therapy and each time their prescription is refilled.[1]
- If a dose is missed by >12 hours, importance of advising patients to skip that dose and take the next dose at the regularly scheduled time.[1]
- Risk of hypertension developing or worsening during therapy.[1] Importance of regular monitoring of BP during treatment.[1] Importance of informing clinician if hypertension occurs.[1]
- Risk of cardiac dysfunction.[1] Importance of immediately informing clinician if symptoms of cardiac dysfunction (e.g., shortness of breath, peripheral edema) occur.[1]
- Risk of arterial thromboembolic events.[1] Advise patients to seek immediate medical attention for new onset chest pain or acute neurologic symptoms consistent with MI or stroke (e.g.,

severe chest pain or pressure, shortness of breath, unilateral numbness or weakness, difficulty talking, severe headache, vision changes, arm, back, neck, or jaw pain).[1]

- Risk of hepatotoxicity.[1] Importance of liver function test monitoring before and during lenvatinib therapy.[1] Importance of immediately reporting any possible manifestations of hepatotoxicity (e.g., jaundice, dark or “tea-colored” urine, light-colored stools).[1]
- Risk of proteinuria and renal impairment or failure.[1] Advise patients that they will be monitored regularly for renal function and proteinuria during lenvatinib therapy.[1]
- Increased risk of GI perforation or fistula formation.[1] Importance of seeking immediate medical attention if severe abdominal pain occurs.[1]
- Increased risk of hemorrhagic events.[1] Advise patient to contact their clinician if bleeding or symptoms of severe bleeding occur.[1]
- Risk of QT-interval prolongation.[1] Importance of informing patients that ECGs and/or serum electrolytes may be monitored during therapy.[1]
- Risk of hypocalcemia.[1] Importance of monitoring calcium concentrations during therapy.[1]
- Risk of RPLS.[1] Importance of contacting clinician promptly if severe headache, seizures, weakness, confusion, or visual disturbances occur during therapy.[1]
- Risk of impairment of exogenous thyroid suppression.[1] Importance of monitoring TSH during therapy.[1]
- Risk of fetal harm.[1] Necessity of advising women of childbearing potential to avoid pregnancy and to use an effective method of contraception during and for ≥2 weeks after discontinuance of therapy.[1] Importance of women informing their clinicians if they are or plan to become pregnant.[1] If pregnancy occurs, advise pregnant women of potential risk to the fetus.[1]
- Importance of advising women to avoid breast-feeding during lenvatinib therapy.[1]
- Importance of informing clinicians of existing or contemplated concomitant therapy, including prescription and OTC drugs, as well as any concomitant illnesses (e.g., cardiovascular disease [including congenital long QT syndrome]).[1]
- Importance of informing patients of other important precautionary information.[1] (See Cautions.)

Preparations

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

*Please refer to the **ASHP Drug Shortages Resource Center** for information on shortages of one or more of these preparations.*

Distribution of lenvatinib mesylate is restricted.[4] (See Restricted Distribution Program under Dosage and Administration.)

Lenvatinib Mesylate

Routes	Dosage Forms	Strengths	Brand Names	Manufacturer
Oral	Capsules	4 mg (of lenvatinib)	Lenvima	Eisai

	10 mg (of lenvatinib)	Lenvima	Eisai
Kit	10 Capsules, Lenvatinib mesylate 10 mg (of lenvatinib) (Lenvima) 5 Capsules, Lenvatinib mesylate 4 mg (of lenvatinib) (Lenvima)	Lenvima 24 mg Daily Dose (available in a package containing 6 blister cards)	Eisai
	10 Capsules, Lenvatinib mesylate 10 mg (of lenvatinib) (Lenvima)	Lenvima 20 mg Daily Dose (available in a package containing 6 blister cards)	Eisai
	5 Capsules, Lenvatinib mesylate 10 mg (of lenvatinib) (Lenvima) 5 Capsules, Lenvatinib mesylate 4 mg (of lenvatinib) (Lenvima)	Lenvima 14 mg Daily Dose (available in a package containing 6 blister cards)	Eisai
	5 Capsules, Lenvatinib mesylate 10 mg (of lenvatinib) (Lenvima)	Lenvima 10 mg Daily Dose (available in a package containing 6 blister cards)	Eisai

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