For the **first-line treatment of patients** with **uHCC**

See a **spectrum** of **results** with **LENVIMA®**

- LENVIMA achieved noninferiority vs sorafenib for OS[1]
- 13.6-month median OS was achieved with LENVIMA vs 12.3 months with sorafenib (HR: 0.92 [95% CI: 0.79-1.06])[1*]
  - Number of events: 351 (73%) with LENVIMA vs 350 (74%) with sorafenib
- LENVIMA did not demonstrate a statistically significant improvement in OS vs sorafenib[1]
- LENVIMA achieved statistical superiority in secondary endpoints PFS and ORR[1]
- 7.3-month median PFS vs 3.6 months with sorafenib (HR: 0.64 [95% CI: 0.55-0.75]; *P*<0.001)[1†]
- 41% ORR vs 12% with sorafenib (95% CI: 36%-45% vs 95% CI: 10%-16%; *P*<0.001)[1†]
  - Complete response: 2.1% (n=10) with LENVIMA vs 0.8% (n=4) with sorafenib[†]
  - Partial response: 38.5% (n=184) with LENVIMA vs 11.6% (n=55) with sorafenib[†]

uHCC=unresectable hepatocellular carcinoma; OS=overall survival; HR=hazard ratio; CI=confidence interval; PFS=progression-free survival; ORR=objective response rate; mRECIST=modified Response Evaluation Criteria In Solid Tumors.
*Based on stratified Cox-model. The noninferiority margin for the HR of LENVIMA vs sorafenib is 1.08.
†Based on a masked independent imaging review according to mRECIST.[2]

INDICATION

LENVIMA is indicated for the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC).

SELECTED SAFETY INFORMATION

Warnings and Precautions

Hypertension. In DTC, hypertension occurred in 73% of patients on LENVIMA (44% grade 3-4). In RCC, hypertension occurred in 42% of patients on LENVIMA + everolimus (13% grade 3). Systolic blood pressure ≥160 mmHg occurred in 29% of patients, and 21% had diastolic blood pressure ≥100 mmHg. In HCC, hypertension occurred in 45% of LENVIMA-treated patients (24% grade 3). Grade 4 hypertension was not reported in HCC.

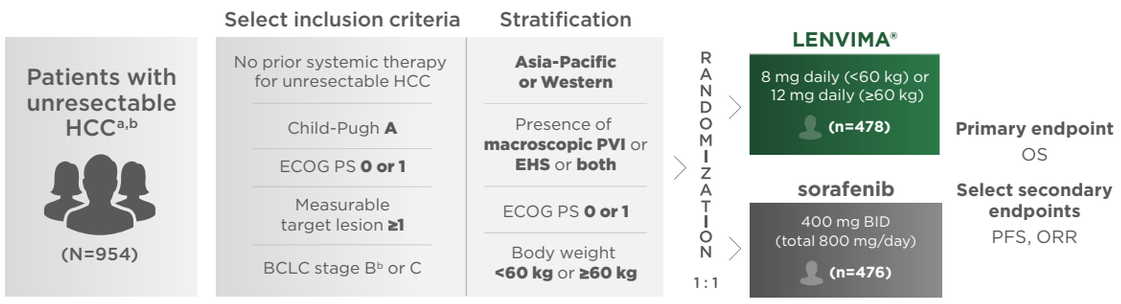
Serious complications of poorly controlled hypertension have been reported. Control blood pressure prior to initiation. Monitor blood pressure after 1 week, then every 2 weeks for the first 2 months, and then at least monthly thereafter during treatment. Withhold and resume at reduced dose when hypertension is controlled or permanently discontinue based on severity.

Please see additional Selected Safety Information throughout and full Prescribing Information.

LENVIMA® (lenvatinib) capsules 10 mg and 4 mg

REFLECT is the first-ever, positive, head-to-head **phase 3 trial** against sorafenib in first-line unresectable HCC[1,2]

A large, phase 3, multicenter, randomized, open-label, noninferiority trial[1-3]



[a]Eligible patients had unresectable HCC, with diagnoses confirmed histologically or cytologically, or confirmed clinically in accordance with American Association for the Study of Liver Diseases criteria.
[b]Ineligible for local liver-directed therapy.

- The REFLECT trial included 217 patients (23%) with hepatitis C and 479 patients (50%) with hepatitis B[2]
- Patients with ≥50% liver occupation, obvious bile duct invasion, or main portal vein invasion were excluded from the trial[2]
- mRECIST and RECIST 1.1 were used for independent assessment of PFS and ORR. Secondary endpoints were tested for superiority[2]
  - mRECIST for HCC criteria measure the sum of viable (enhancement in the arterial phase) tumor diameters and may more accurately measure response in HCC liver lesions than RECIST 1.1[4,5]

SELECTED SAFETY INFORMATION
Warnings and Precautions
Cardiac Dysfunction. Serious and fatal cardiac dysfunction can occur with LENVIMA. Across clinical trials in 799 patients with DTC, RCC, and HCC, grade 3 or higher cardiac dysfunction occurred in 3% of LENVIMA-treated patients. Monitor for clinical symptoms or signs of cardiac dysfunction. Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

Please see additional Selected Safety Information throughout and full Prescribing Information.

Median OS of 13.6 months[1]

LENVIMA® achieved noninferiority primary endpoint vs sorafenib in the REFLECT trial[1]

Overall survival	LENVIMA n=478	sorafenib n=476
Median OS in months (95% CI)	**13.6 (12.1-14.9)**	12.3 (10.4-13.9)
Hazard ratio (95% CI)[c]	0.92 (0.79-1.06)	

- Number of events: 351 (73%) with LENVIMA vs 350 (74%) with sorafenib[1]
- LENVIMA did not demonstrate a statistically significant improvement in OS vs sorafenib[1]

LENVIMA achieved statistical superiority in secondary endpoints PFS and ORR[1]

- 7.3-month median PFS vs 3.6 months with sorafenib (HR: 0.64 [95% CI: 0.55-0.75]; *P*<0.001)*
- 41% ORR vs 12% with sorafenib (95% CI: 36%-45% vs 95% CI: 10%-16%; *P*<0.001)*
  - Complete response: 2.1% (n=10) with LENVIMA vs 0.8% (n=4) with sorafenib*
  - Partial response: 38.5% (n=184) with LENVIMA vs 11.6% (n=55) with sorafenib*

REFLECT=A Multicenter, **R**andomized, Open-Label, Phase 3 Trial to Compare the **EF**ficacy and Safety of **LE**nvatinib (E7080) Versus Sorafenib in First-Line Treatment of Subjects With Unrese**C**table Hepa**T**ocellular Carcinoma; HCC=hepatocellular carcinoma; ECOG PS=Eastern Cooperative Oncology Group performance status; BCLC=Barcelona Clinic Liver Cancer; PVI=portal vein invasion; EHS=extrahepatic spread; BID=twice daily; OS=overall survival; PFS=progression-free survival; ORR=objective response rate; mRECIST=modified Response Evaluation Criteria In Solid Tumors; RECIST=Response Evaluation Criteria In Solid Tumors; CI=confidence interval; HR=hazard ratio.

[c]Based on stratified Cox-model. The noninferiority margin for the HR of LENVIMA vs sorafenib is 1.08.
*Based on a masked independent imaging review according to mRECIST.[2]

SELECTED SAFETY INFORMATION
Warnings and Precautions
Arterial Thromboembolic Events. Among patients receiving LENVIMA or LENVIMA + everolimus, arterial thromboembolic events of any severity occurred in 2% of patients in RCC and HCC and 5% in DTC. Grade 3-5 arterial thromboembolic events ranged from 2% to 3% across all clinical trials. Permanently discontinue following an arterial thrombotic event. The safety of resuming after an arterial thromboembolic event has not been established, and LENVIMA has not been studied in patients who have had an arterial thromboembolic event within the previous 6 months.

LENVIMA® (lenvatinib) capsules 10 mg and 4 mg

DOUBLE THE MEDIAN PFS: More time patients had without their disease progressing

Statistically superior PFS per independent radiology review (mRECIST)[1]

- Number of events: 311 (65%) with LENVIMA vs 323 (68%) with sorafenib[1]
- mRECIST for HCC criteria measure the sum of viable (enhancement in the arterial phase) tumor diameters and may more accurately measure response in HCC liver lesions than RECIST 1.1[4,5]

PFS=progression-free survival; mRECIST=modified Response Evaluation Criteria In Solid Tumors; CI=confidence interval; HR=hazard ratio; HCC=hepatocellular carcinoma; RECIST=Response Evaluation Criteria In Solid Tumors.

SELECTED SAFETY INFORMATION
Warnings and Precautions
Hepatotoxicity. Across clinical studies enrolling 1,327 LENVIMA-treated patients with malignancies other than HCC, serious hepatic adverse reactions occurred in 1.4% of patients. Fatal events, including hepatic failure, acute hepatitis and hepatorenal syndrome, occurred in 0.5% of patients. In HCC, hepatic encephalopathy occurred in 8% of LENVIMA-treated patients (5% grade 3-5). Grade 3-5 hepatic failure occurred in 3% of LENVIMA-treated patients; 2% of patients discontinued LENVIMA due to hepatic encephalopathy, and 1% discontinued due to hepatic failure.

Monitor liver function prior to initiation, then every 2 weeks for the first 2 months, and at least monthly thereafter during treatment. Monitor patients with HCC closely for signs of hepatic failure, including hepatic encephalopathy. Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

Please see additional Selected Safety Information throughout and full Prescribing Information.

MORE THAN TRIPLE THE ORR: More patients with a response

Statistically superior ORR per independent radiology review (mRECIST)[1]

41% of patients with a response to LENVIMA vs 12% with a response to sorafenib[1]

- Tumor assessment was based on mRECIST for HCC criteria, which measures the sum of viable (enhancement in the arterial phase) tumor diameters and may more accurately measure response in HCC liver lesions than RECIST 1.1[3-5]

ORR=objective response rate; mRECIST=modified Response Evaluation Criteria In Solid Tumors; CI=confidence interval; CR=complete response; PR=partial response; HCC=hepatocellular carcinoma; RECIST=Response Evaluation Criteria In Solid Tumors.

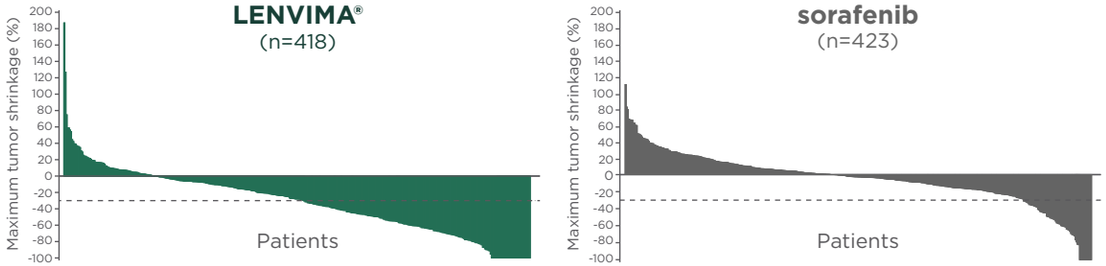
SELECTED SAFETY INFORMATION
Warnings and Precautions
Renal Failure or Impairment. Serious including fatal renal failure or impairment can occur with LENVIMA. Renal impairment was reported in 14% and 7% of LENVIMA-treated patients in DTC and HCC, respectively. Grade 3-5 renal failure or impairment occurred in 3% of patients with DTC and 2% of patients with HCC, including 1 fatal event in each study. In RCC, renal impairment or renal failure was reported in 18% of LENVIMA + everolimus–treated patients (10% grade 3).

Initiate prompt management of diarrhea or dehydration/hypovolemia. Withhold and resume at reduced dose upon recovery or permanently discontinue for renal failure or impairment based on severity.

LENVIMA® (lenvatinib) capsules 10 mg and 4 mg

Post hoc exploratory analysis: Maximum tumor shrinkage

Tumor assessment was based on mRECIST per independent imaging review[3]



- Maximum tumor shrinkage is defined as the percentage change from baseline to post-baseline nadir. These figures and *n* numbers only include patients with both baseline and at least 1 post-baseline target lesion assessment[3]

Limitations: The post hoc exploratory analysis only included patients with both baseline and at least 1 post-baseline target lesion assessment. Maximum tumor shrinkage of target lesion alone does not determine response. The two treatment arms cannot be compared and no conclusions can be drawn.

mRECIST=modified Response Evaluation Criteria In Solid Tumors.

SELECTED SAFETY INFORMATION
Warnings and Precautions
Proteinuria. In DTC and HCC, proteinuria was reported in 34% and 26% of LENVIMA-treated patients, respectively. Grade 3 proteinuria occurred in 11% and 6% in DTC and HCC, respectively. In RCC, proteinuria occurred in 31% of patients receiving LENVIMA + everolimus (8% grade 3). Monitor for proteinuria prior to initiation and periodically during treatment. If urine dipstick proteinuria ≥2+ is detected, obtain a 24-hour urine protein. Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

Please see additional Selected Safety Information throughout and full Prescribing Information.

Adverse reactions (ARs) with LENVIMA®

- The most common ARs (≥20%) observed in patients taking LENVIMA were hypertension (45%), fatigue (44%), diarrhea (39%), decreased appetite (34%), arthralgia/myalgia (31%), decreased weight (31%), abdominal pain (30%), palmar-plantar erythrodysesthesia syndrome (27%), proteinuria (26%), dysphonia (24%), hemorrhagic events (23%), hypothyroidism (21%), and nausea (20%)[1]
- The most common serious ARs (≥2%) observed in the LENVIMA arm were hepatic encephalopathy (5%), hepatic failure (3%), ascites (3%), and decreased appetite (2%)[1]

Most common grade 3-4 (≥5%) ARs in either arm[1]

	LENVIMA n=476	sorafenib n=475
Hypertension[a]	24%	15%
Decreased weight	8%	3%
Fatigue[b]	7%	6%
Proteinuria[c]	6%	2%
Decreased appetite	5%	1%
Palmar-plantar erythrodysesthesia syndrome	3%	11%

REFLECT was not designed to demonstrate a statistically significant reduction in AR rates for LENVIMA vs sorafenib.[1]

REFLECT=A Multicenter, **R**andomized, Open-Label, Phase 3 Trial to Compare the **EF**ficacy and Safety of **LE**nvatinib (E7080) Versus Sorafenib in First-Line Treatment of Subjects With Unrese**C**table Hepa**T**ocellular Carcinoma.
[a]Includes increased diastolic blood pressure, increased blood pressure, hypertension, and orthostatic hypertension.
[b]Includes asthenia, fatigue, lethargy, and malaise.
[c]Includes proteinuria, increased urine protein, and protein urine present.

SELECTED SAFETY INFORMATION
Warnings and Precautions
Diarrhea. Of the 737 LENVIMA-treated patients in DTC and HCC, diarrhea occurred in 49% (6% grade 3). In RCC, diarrhea occurred in 81% of LENVIMA + everolimus–treated patients (19% grade 3). Diarrhea was the most frequent cause of dose interruption/reduction, and diarrhea recurred despite dose reduction. Promptly initiate management of diarrhea. Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

LENVIMA® (lenvatinib) capsules 10 mg and 4 mg

Starting dose and dose modifications

Recommended dosage reductions of LENVIMA® for ARs[1]

	Starting dose	1st dosage reduction to	2nd dosage reduction to	3rd dosage reduction to
Patients <60 kg (<132 lb)	**8 mg** Once daily (two 4-mg capsules)	**4 mg** Once daily (one 4-mg capsule)	**4 mg** Once ***every other*** day (one 4-mg capsule)	**Discontinue therapy**
Patients ≥60 kg (≥132 lb)	**12 mg** Once daily (three 4-mg capsules)	**8 mg** Once daily (two 4-mg capsules)	**4 mg** Once daily (one 4-mg capsule)	**4 mg** Once ***every other*** day (one 4-mg capsule)

Capsules pictured are not actual size.

- Promptly initiate management of diarrhea[1]
- The most common ARs (≥5%) resulting in dose reduction or interruption of LENVIMA were fatigue (9%), decreased appetite (8%), diarrhea (8%), proteinuria (7%), hypertension (6%), and palmar-plantar erythrodysesthesia syndrome (5%)[1]

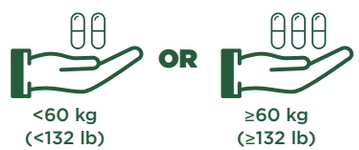
AR=adverse reaction.

For additional management strategies, please visit **www.LENVIMA.com/hcp**

SELECTED SAFETY INFORMATION
Warnings and Precautions
Fistula Formation and Gastrointestinal Perforation. Of the 799 patients treated with LENVIMA or LENVIMA + everolimus in DTC, RCC, and HCC, fistula or gastrointestinal perforation occurred in 2%. Permanently discontinue in patients who develop gastrointestinal perforation of any severity or grade 3-4 fistula.

Please see additional Selected Safety Information throughout and full Prescribing Information.

Once a day. Every day. With or without food[1]



Orally, at the same time each day based on weight

With or without food

Swallowed whole with water

Continue LENVIMA® until disease progression or unacceptable toxicity.[1]

Hepatic impairment[1]

- No dose adjustment is recommended for patients with HCC and mild hepatic impairment (Child-Pugh A)
- There is no recommended dose for patients with HCC and moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment

Renal impairment[1]

- No dose adjustment is recommended for patients with mild (creatinine clearance 60-89 mL/min) or moderate (creatinine clearance 30-59 mL/min) renal impairment
- There is no recommended dose of LENVIMA for patients with HCC and severe renal impairment
- LENVIMA has not been studied in patients with end-stage renal disease

Missed doses of LENVIMA[1]

- LENVIMA should be taken at the same time each day
- If a dose is missed and cannot be taken within 12 hours, skip that dose and take the next dose at the usual time of administration

LENVIMA may be dissolved in a small glass of liquid[1]

- Put capsules into 1 tablespoon of water or apple juice without breaking or crushing
- Leave capsules in water or apple juice for ≥10 minutes. Stir for ≥3 minutes
- After drinking mixture, add 1 tablespoon of water or apple juice to the glass, swirl contents, and swallow water or apple juice

HCC=hepatocellular carcinoma.

LENVIMA® (lenvatinib) capsules 10 mg and 4 mg

Doses available in convenient blister packs

Each blister card contains a 5-day supply of LENVIMA® capsules

12-mg daily dose

8-mg daily dose

Available strength:
LENVIMA 4-mg capsules

- 12-mg and 8-mg blister packs facilitate initial prescriptions
- 8-mg and 4-mg blister packs help you and patients implement dose modifications
- For instance, if reducing from 12 mg to 8 mg, instruct your patient to take two 4-mg capsules instead of three until current prescription runs out, then prescribe your patient the 8-mg pack

Prescribing LENVIMA® (starting doses and/or modified doses)

12-mg dose	8-mg dose	4-mg dose
Three 4-mg caps (12 mg total) PO once daily x 30 days (#90 caps)	Two 4-mg caps (8 mg total) PO once daily x 30 days (#60 caps)	One 4-mg cap PO once daily x 30 days (#30 caps)

SELECTED SAFETY INFORMATION
Warnings and Precautions
QT Interval Prolongation. In DTC, QT/QTc interval prolongation occurred in 9% of LENVIMA-treated patients and QT interval prolongation of >500 ms occurred in 2%. In RCC, QTc interval increases of >60 ms occurred in 11% of patients receiving LENVIMA + everolimus and QTc interval >500 ms occurred in 6%. In HCC, QTc interval increases of >60 ms occurred in 8% of LENVIMA-treated patients and QTc interval >500 ms occurred in 2%.

Monitor and correct electrolyte abnormalities at baseline and periodically during treatment. Monitor electrocardiograms in patients with congenital long QT syndrome, congestive heart failure, bradyarrhythmias, or those who are taking drugs known to prolong the QT interval, including Class Ia and III antiarrhythmics. Withhold and resume at reduced dose upon recovery based on severity.

SELECTED SAFETY INFORMATION
Warnings and Precautions
Hypocalcemia. In DTC, grade 3-4 hypocalcemia occurred in 9% of LENVIMA-treated patients. In 65% of cases, hypocalcemia improved or resolved following calcium supplementation with or without dose interruption or dose reduction. In RCC, grade 3-4 hypocalcemia occurred in 6% of LENVIMA + everolimus–treated patients. In HCC, grade 3 hypocalcemia occurred in 0.8% of LENVIMA-treated patients. Monitor blood calcium levels at least monthly and replace calcium as necessary during treatment. Withhold and resume at reduced dose upon recovery or permanently discontinue depending on severity.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS). Across clinical studies of 1,823 patients who received LENVIMA as a single agent, RPLS occurred in 0.3%. Confirm diagnosis of RPLS with MRI. Withhold and resume at reduced dose upon recovery or permanently discontinue depending on severity and persistence of neurologic symptoms.

Please see additional Selected Safety Information throughout and full Prescribing Information.

LENVIMA® (lenvatinib) capsules 10 mg and 4 mg

SELECTED SAFETY INFORMATION

Warnings and Precautions

Hemorrhagic Events. Serious including fatal hemorrhagic events can occur with LENVIMA. In DTC, RCC, and HCC clinical trials, hemorrhagic events, of any grade, occurred in 29% of the 799 patients treated with LENVIMA as a single agent or in combination with everolimus. The most frequently reported hemorrhagic events (all grades and occurring in at least 5% of patients) were epistaxis and hematuria. In DTC, grade 3-5 hemorrhage occurred in 2% of LENVIMA-treated patients, including 1 fatal intracranial hemorrhage among 16 patients who received LENVIMA and had CNS metastases at baseline. In RCC, grade 3-5 hemorrhage occurred in 8% of LENVIMA + everolimus–treated patients, including 1 fatal cerebral hemorrhage. In HCC, grade 3-5 hemorrhage occurred in 5% of LENVIMA-treated patients, including 7 fatal hemorrhagic events. Serious tumor-related bleeds, including fatal hemorrhagic events, occurred in LENVIMA-treated patients in clinical trials and in the postmarketing setting. In postmarketing surveillance, serious and fatal carotid artery hemorrhages were seen more frequently in patients with anaplastic thyroid carcinoma (ATC) than other tumors. Safety and effectiveness of LENVIMA in patients with ATC have not been demonstrated in clinical trials.

Consider the risk of severe or fatal hemorrhage associated with tumor invasion or infiltration of major blood vessels (eg, carotid artery). Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

Impairment of Thyroid Stimulating Hormone Suppression/Thyroid Dysfunction. LENVIMA impairs exogenous thyroid suppression. In DTC, 88% of patients had baseline thyroid stimulating hormone (TSH) level ≤0.5 mU/L. In patients with normal TSH at baseline, elevation of TSH level >0.5 mU/L was observed post baseline in 57% of LENVIMA-treated patients. In RCC and HCC, grade 1 or 2 hypothyroidism occurred in 24% of LENVIMA + everolimus–treated patients and 21% of LENVIMA-treated patients, respectively. In patients with normal or low TSH at baseline, elevation of TSH was observed post baseline in 70% of LENVIMA-treated patients in HCC and 60% of LENVIMA + everolimus–treated patients in RCC.

Monitor thyroid function prior to initiation and at least monthly during treatment. Treat hypothyroidism according to standard medical practice.

Impaired Wound Healing. Impaired wound healing has been reported in patients who received LENVIMA. Withhold LENVIMA for at least 1 week prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of LENVIMA after resolution of wound healing complications has not been established.

Osteonecrosis of the Jaw (ONJ). ONJ has been reported in patients receiving LENVIMA. Concomitant exposure to other risk factors, such as bisphosphonates, denosumab, dental disease, or invasive dental procedures, may increase the risk of ONJ.

Perform an oral examination prior to treatment with LENVIMA and periodically during LENVIMA treatment. Advise patients regarding good oral hygiene practices and to consider having preventive dentistry performed prior to treatment with LENVIMA and throughout treatment with LENVIMA.

Avoid invasive dental procedures, if possible, while on LENVIMA treatment, particularly in patients at higher risk. Withhold LENVIMA for at least 1 week prior to scheduled dental surgery or invasive

SELECTED SAFETY INFORMATION

Warnings and Precautions

Osteonecrosis of the Jaw (ONJ). (cont'd) dental procedures, if possible. For patients requiring invasive dental procedures, discontinuation of bisphosphonate treatment may reduce the risk of ONJ.

Withhold LENVIMA if ONJ develops and restart based on clinical judgement of adequate resolution.

Embryo-fetal Toxicity. Based on its mechanism of action and data from animal reproduction studies, LENVIMA can cause fetal harm when administered to pregnant women. In animal reproduction studies, oral administration of lenvatinib during organogenesis at doses below the recommended clinical doses resulted in embryotoxicity, fetotoxicity, and teratogenicity in rats and rabbits. Advise pregnant women of the potential risk to a fetus, and advise females of reproductive potential to use effective contraception during treatment with LENVIMA and for at least 30 days after the last dose.

Adverse Reactions

In HCC, the most common adverse reactions (≥20%) observed in LENVIMA-treated patients were hypertension (45%), fatigue (44%), diarrhea (39%), decreased appetite (34%), arthralgia/myalgia (31%), decreased weight (31%), abdominal pain (30%), palmar-plantar erythrodysesthesia syndrome (27%), proteinuria (26%), dysphonia (24%), hemorrhagic events (23%), hypothyroidism (21%), and nausea (20%). The most common serious adverse reactions (≥2%) were hepatic encephalopathy (5%), hepatic failure (3%), ascites (3%), and decreased appetite (2%). Adverse reactions led to dose reductions or interruption in 62% of patients. The most common adverse reactions (≥5%) resulting in dose reductions were fatigue (9%), decreased appetite (8%), diarrhea (8%), proteinuria (7%), hypertension (6%), and palmar-plantar erythrodysesthesia syndrome (5%). Treatment discontinuation due to an adverse reaction occurred in 20% of patients. The most common adverse reactions (≥1%) resulting in discontinuation of LENVIMA were fatigue (1%), hepatic encephalopathy (2%), hyperbilirubinemia (1%), and hepatic failure (1%).

Use in Specific Populations

Because of the potential for serious adverse reactions in breastfed infants, advise women to discontinue breastfeeding during treatment and for at least 1 week after the last dose. LENVIMA may impair fertility in males and females of reproductive potential.

No dose adjustment is recommended for patients with mild (CLcr 60-89 mL/min) or moderate (CLcr 30-59 mL/min) renal impairment. LENVIMA concentrations may increase in patients with DTC or RCC and severe (CLcr 15-29 mL/min) renal impairment. Reduce the dose for patients with RCC or DTC and severe renal impairment. There is no recommended dose for patients with HCC and severe renal impairment. LENVIMA has not been studied in patients with end-stage renal disease.

No dose adjustment is recommended for patients with HCC and mild hepatic impairment (Child-Pugh A). There is no recommended dose for patients with HCC with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment.

References: 1. LENVIMA [package insert]. Woodcliff Lake, NJ: Eisai Inc. **2.** Kudo M, Finn RS, Qin S, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. *Lancet*. 2018;391(10126):1163-1173. **3.** Data on file. Eisai Inc. **4.** Takada J, Hidaka H, Nakazawa T, et al. Modified response evaluation criteria in solid tumors is superior to response evaluation criteria in solid tumors for assessment of responses to sorafenib in patients with advanced hepatocellular carcinoma. *BMC Res Notes*. 2015;8:609. **5.** Lencioni R, Llovet JM. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. *Semin Liver Dis*. 2010;30(1):52-60.

For the **first-line treatment of patients** with **uHCC**

See a **spectrum** of **results** with **LENVIMA®**

LENVIMA achieved its primary endpoint

13.6-MONTH MEDIAN OS vs sorafenib (12.3 months)[1]
HR: 0.92 (95% CI: 0.79-1.06)

- Number of events: 351 (73%) with LENVIMA vs 350 (74%) with sorafenib
- LENVIMA achieved noninferiority vs sorafenib for OS. LENVIMA did not demonstrate a statistically significant improvement in OS vs sorafenib

Statistical superiority vs sorafenib in select secondary efficacy endpoints[1,2]

DOUBLE THE MEDIAN PFS, 7.3 months vs 3.6 months with sorafenib[1]*
HR: 0.64 (95% CI: 0.55-0.75); *P*<0.001

MORE THAN TRIPLE THE ORR, 41% vs 12% with sorafenib[1]*
95% CI: 36%-45% vs 95% CI: 10%-16%; *P*<0.001

- Complete response: 2.1% (n=10) with LENVIMA vs 0.8% (n=4) with sorafenib
- Partial response: 38.5% (n=184) with LENVIMA vs 11.6% (n=55) with sorafenib

LENVIMA AR profile

- The most common ARs observed in LENVIMA-treated patients (≥20%) were, in order of decreasing frequency, hypertension, fatigue, diarrhea, decreased appetite, arthralgia/myalgia, decreased weight, abdominal pain, palmar-plantar erythrodysesthesia syndrome, proteinuria, dysphonia, hemorrhagic events, hypothyroidism, and nausea

uHCC=unresectable hepatocellular carcinoma; OS=overall survival; HR=hazard ratio; CI=confidence interval; PFS=progression-free survival; ORR=objective response rate; AR=adverse reaction; mRECIST=modified Response Evaluation Criteria In Solid Tumors.
*Based on a masked independent imaging review according to mRECIST.[2]

Visit **www.LENVIMA.com/hcp** to learn more

SELECTED SAFETY INFORMATION
Use in Specific Populations (cont'd)
No dose adjustment is recommended for patients with DTC or RCC and mild or moderate hepatic impairment. LENVIMA concentrations may increase in patients with DTC or RCC and severe hepatic impairment. Reduce the dose for patients with DTC or RCC and severe hepatic impairment.

Please see additional Selected Safety Information throughout and full Prescribing Information.

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