

For patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.¹

LENVIMA + pembrolizumab

LENVIMA + pembrolizumab:

Unlock this treatment option for appropriate patients with advanced endometrial carcinoma

Indication for LENVIMA + pembrolizumab¹

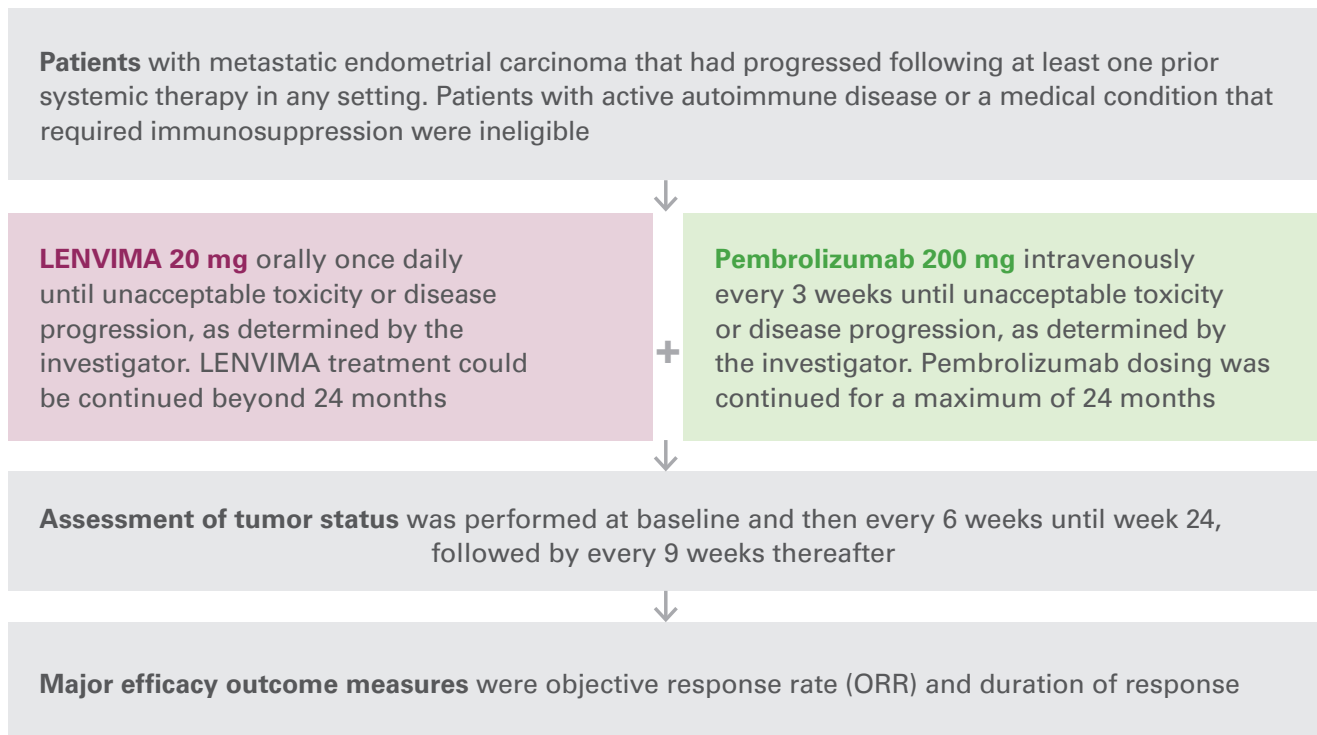
LENVIMA and pembrolizumab, in combination, are indicated for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy, and are not candidates for curative surgery or radiation.

This indication is approved under conditional approval based on waiver of phase III study. Safety monitoring program (SMP) for this indication is required.

Study Design and Patient Baseline Characteristics

Patients in the **LENVIMA + pembrolizumab** clinical trial received at least 1 prior systemic therapy^{1,2}

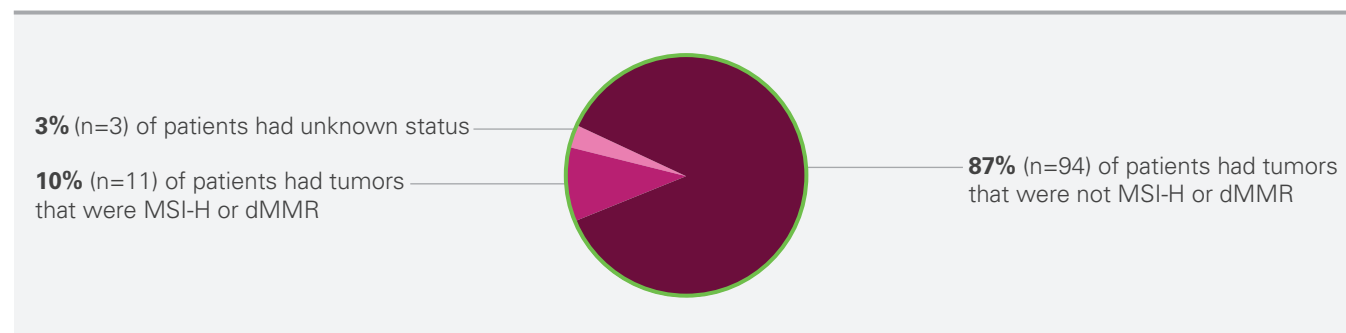
Study 111/KEYNOTE-146 (N=108): A single-arm, multicenter, open-label, multicohort trial



- Clinically stable patients who were considered by the investigator to be deriving clinical benefit were permitted to remain on treatment beyond RECIST-defined disease progression.
- Median study follow-up: 13 months

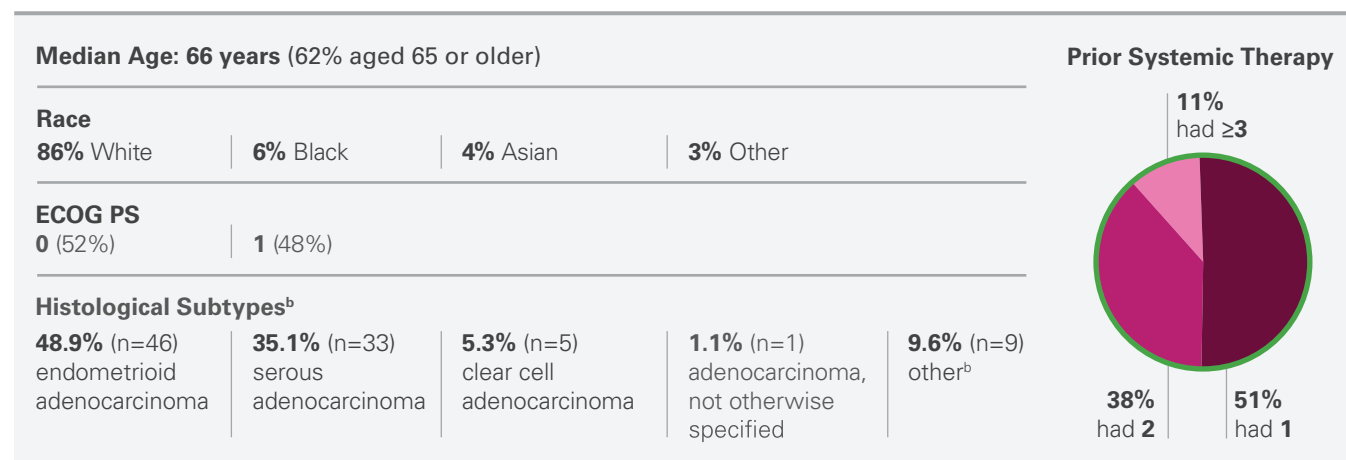
Patient Baseline Characteristics

Tumor MSI-H/dMMR Status (N=108)^{a,1}



^aTumor MSI status was determined using a polymerase chain reaction (PCR) test and tumor MMR status was determined using an immunohistochemistry (IHC) test.

Patient Characteristics (n=94 patients with tumors not MSI-H or dMMR)^{1,2}



^bPredominantly mixed histology.

LENVIMA + pembrolizumab response rates^{1,2,3}

Results in patients (n=94) with advanced endometrial carcinoma that had progressed following prior systemic therapy and that was not MSI-H or dMMR

38.3%
objective response rate
(95% CI, 29%–49%)

10.6% complete response

27.7% partial response

Median duration of response (DOR) had not been reached at time of analysis. Among the 36 responding patients, the DOR ranged from 1.2+ to 33.1+ months.

76% duration of response ≥ 6 months^a

Median follow-up time of 18.7 months.

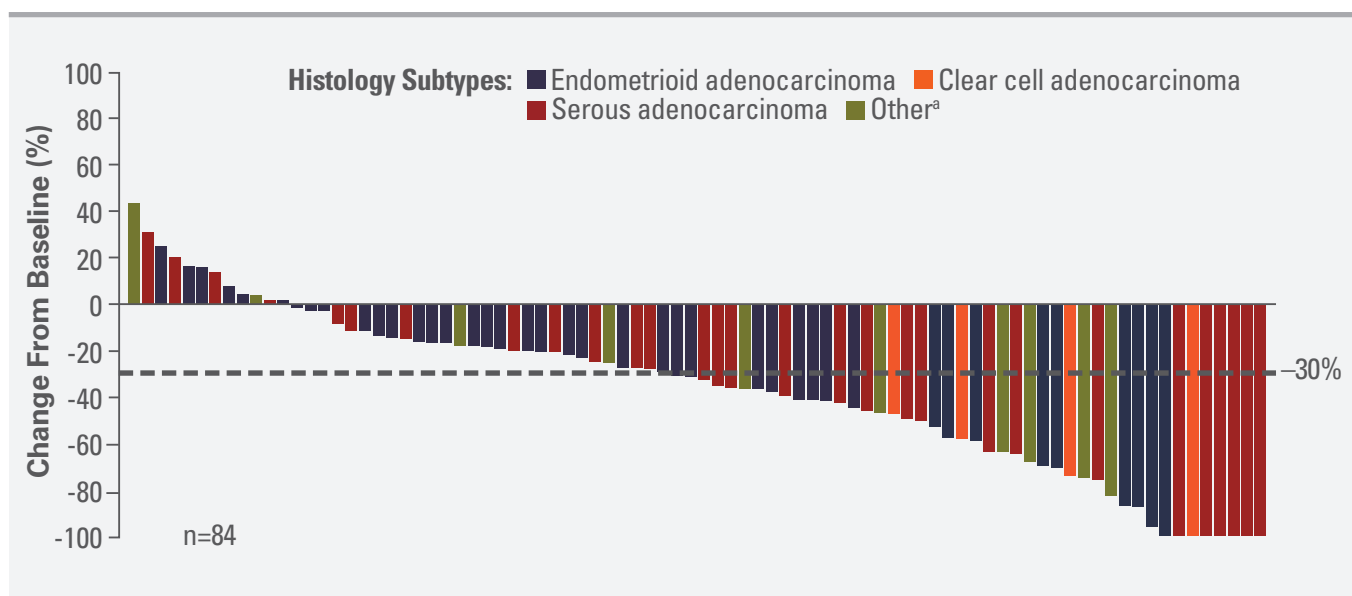
– Overall response and DOR were assessed by independent radiologic review committee (IRC) on RECIST 1.1.

^aBased on Kaplan-Meier estimates: includes 25 patients with responses of 6 months or longer.

Exploratory post hoc analysis: Target lesion shrinkage³

- Figure shows the percentage change in sum of diameters of target lesions at post-baseline nadir (Independent Imaging Review, RECIST 1.1). Target lesion shrinkage does not equal objective response rate.
- Among the 94 patients included in the efficacy analysis, 10 patients did not have the data required for inclusion in the figure (ie, withdrawal of consent, death, or lack of measurable disease).

Limitations: This exploratory post hoc analysis only included the 84 patients with both a baseline and at least one post-baseline target lesion assessment. Maximum tumor shrinkage of target lesion alone does not determine response. No conclusions can be drawn.



^aPredominantly mixed histology.¹

Adverse Events in the Clinical Trial

Adverse events in Study 111⁴

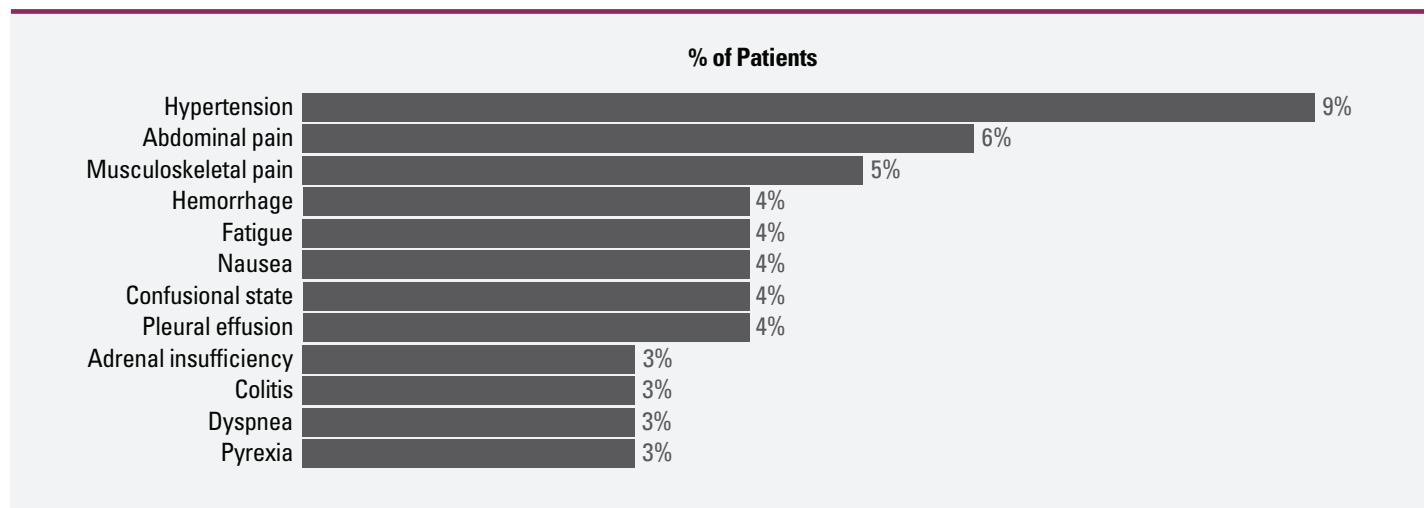
The safety of LENVIMA in combination with pembrolizumab was evaluated in Study 111, a single-arm, multicenter, open-label trial in 94 patients with endometrial carcinoma whose tumors had progressed following at least one line of systemic therapy and were not MSI-H or dMMR.

Fatal adverse events occurred in 3% of patients receiving LENVIMA + pembrolizumab, including:

- Gastrointestinal perforation
- RPLS with intraventricular hemorrhage
- Intracranial hemorrhage

Serious adverse events occurred in 52% of patients (n=94) receiving LENVIMA + pembrolizumab

The most common serious adverse events (≥3%) in patients treated with LENVIMA + pembrolizumab



LENVIMA was permanently discontinued for adverse events in 21% of patients.

- The most common adverse events (>2%) resulting in discontinuation of LENVIMA were:
 - Gastrointestinal perforation or fistula (2%)
 - Muscular weakness (2%)
 - Pancreatitis (2%)

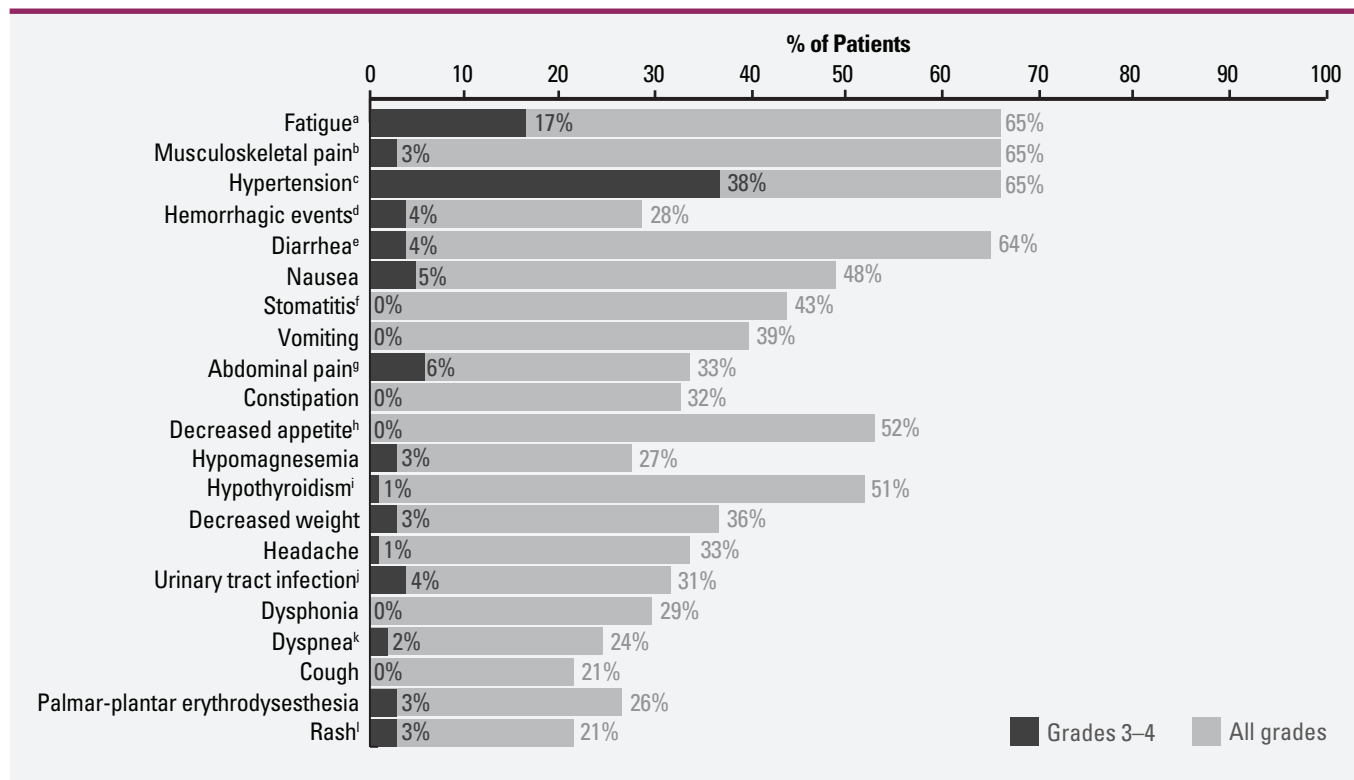
Adverse events led to the dose reduction or interruption of LENVIMA in 88% of patients.

Most common adverse events (≥5%) resulting in dose reduction or interruption of LENVIMA

Adverse Events	LENVIMA (20 mg) (%)
Fatigue	32
Hypertension	26
Diarrhea	18
Nausea	13
Palmar-plantar erythrodysesthesia	13
Vomiting	13
Decreased appetite	12
Musculoskeletal pain	11
Stomatitis	9
Abdominal pain	7
Hemorrhages	7
Renal impairment	6
Decreased weight	6
Rash	5
Headache	5
Increased lipase	5
Proteinuria	5

Adverse events in Study 111 (continued)⁴

Adverse events that occurred in $\geq 20\%$ of patients (n=94) receiving LENVIMA + pembrolizumab



^aIncludes asthenia, fatigue, and malaise.

^bIncludes arthralgia, arthritis, back pain, breast pain, musculoskeletal chest pain, musculoskeletal pain, musculoskeletal stiffness, myalgia, neck pain, non-cardiac chest pain, pain in extremity.

^cIncludes essential hypertension, hypertension, and hypertensive encephalopathy.

^dIncludes catheter site bruise, contusion, epistaxis, gastrointestinal hemorrhage, hematemesis, hematuria, hemorrhage intracranial, injection site hemorrhage, intraventricular hemorrhage, large intestinal hemorrhage, metrorrhagia, mouth hemorrhage, uterine hemorrhage, and vaginal hemorrhage.

^eIncludes diarrhea, gastroenteritis, gastrointestinal viral infection, and viral diarrhea.

^fIncludes glossitis, mouth ulceration, oral discomfort, oral mucosal blistering, oropharyngeal pain, and stomatitis.

^gIncludes abdominal discomfort, abdominal pain, lower abdominal pain, and upper abdominal pain.

^hIncludes decreased appetite and early satiety.

ⁱIncludes increased blood thyroid stimulating hormone and hypothyroidism.

^jIncludes cystitis and urinary tract infection.

^kIncludes dyspnea and exertional dyspnea.

^lIncludes rash, rash generalized, rash macular, and rash maculo-papular.

Choose **LENVIMA + pembrolizumab** for patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.¹

LENVIMA + pembrolizumab overview

Efficacy in advanced endometrial carcinoma that is not MSI-H or dMMR (n=94)

Primary Endpoints

- **38.3% objective response rate** (95% CI, 29%–49%).^{a,1}
 - **10.6% complete response; 27.7% partial response.**
- **Median duration of response (DOR) had not been reached at time of analysis.**^{a,1,2,3}
 - **The DOR ranged from 1.2+ to 33.1+ months among the 36 responding patients.**
 - **76% had a response of 6 months or longer.**^b
 - **Median follow-up time of 18.7 months.**

Safety⁴

- **The most common adverse reactions (≥20%) observed in LENVIMA + pembrolizumab-treated patients were:** fatigue (65%), musculoskeletal pain (65%), hypertension (65%), hemorrhagic events (28%), diarrhea (64%), nausea (48%), stomatitis (43%), vomiting (39%), abdominal pain (33%), constipation (32%), decreased appetite (52%), hypomagnesemia (27%), hypothyroidism (51%), decreased weight (36%), headache (33%), urinary tract infection (31%), dysphonia (29%), dyspnea (24%), cough (21%), palmar-plantar erythrodysesthesia (26%), and rash (21%).

Dose Adjustment¹

- **Manage adverse events to LENVIMA + pembrolizumab by** interrupting one or both or dose reduce **LENVIMA**, as appropriate. No dose reductions of pembrolizumab are recommended.

^aOverall response and DOR were assessed by independent radiologic review committee (IRC) on RECIST 1.1.

^bBased on Kaplan-Meier estimates.

CI = confidence interval; dMMR = mismatch repair deficient; DOR = duration of response;

ECOG PS = Eastern Cooperative Oncology Group performance status; MMR = mismatch repair; MSI-H = microsatellite instability-high;

RECIST 1.1 = Response Evaluation Criteria In Solid Tumors v1.1; RPLS = reversible posterior leukoencephalopathy syndrome.

References: 1. Lenvima [package insert]. Thailand; approved 30 Dec 2020. 2. Makker V, Taylor MH, Aghajanian C, et al. Lenvatinib plus pembrolizumab in patients with advanced endometrial cancer. J Clin Oncol. 2020; 38:1–13. doi:10.1200/JCO.19.02627. 3. Makker V, Taylor MH, Aghajanian C, et al. Supplementary appendix to: Lenvatinib and pembrolizumab in patients with advanced endometrial cancer. 4. Lenvima [package insert]. U.S.; revised 12/2020.

Abbreviated Prescribing Information

Composition: 4 mg hard capsules: Each hard capsule contains lenvatinib mesilate equivalent to 4 mg lenvatinib. 10 mg hard capsules: Each hard capsule contains lenvatinib mesilate equivalent to 10 mg lenvatinib. **Pharmacology:** Lenvatinib is a receptor tyrosine kinase (RTK) inhibitor that selectively inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4), in addition to other proangiogenic and oncogenic pathway-related RTKs including fibroblast growth factor (FGF) receptors FGFR1, 2, 3 and 4, the platelet derived growth factor (PDGF) receptor PDGFR α , KIT, and RET. **Indication:** LENVIMA[®] is indicated for the treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/ Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI). LENVIMA[®] is indicated in combination with everolimus for the treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF)-targeted therapy. LENVIMA is indicated as monotherapy for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC) who have received no prior systemic therapy. LENVIMA[®] is indicated in combination with pembrolizumab for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation. **Dose and Administration:** Differentiated Thyroid Cancer (DTC) - The recommended daily dose of lenvatinib is 24 mg taken once daily. Renal Cell Carcinoma (RCC) - The recommended daily dose of lenvatinib is 18 mg once daily in combination with 5 mg of everolimus once daily. HCC - The recommended daily dose of lenvatinib is 8 mg (two 4 mg capsules) once daily for patients with a body weight of < 60 kg and 12 mg (three 4 mg capsules) once daily for patients with a body weight of \geq 60 kg. Dose adjustments are based only on toxicities observed and not on body weight changes during treatment. The daily dose is to be modified, as needed, according to the dose/toxicity management plan. Endometrial Carcinoma - The recommended dosage of lenvatinib is 20 mg orally once daily in combination with pembrolizumab 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks until unacceptable toxicity or disease progression. **Warnings and precautions:** Hypertension, Proteinuria, Hepatotoxicity, Renal failure and impairment, Diarrhoea, Cardiac dysfunction, Posterior reversible encephalopathy syndrome (PRES) / Reversible posterior leukoencephalopathy syndrome (RPLS), Arterial thromboembolisms, Women of childbearing potential, Haemorrhage, Gastrointestinal perforation and fistula formation, Non-Gastrointestinal fistula, QT interval prolongation, Impairment of thyroid stimulating hormone suppression. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients, listed. Breast-feeding. **Drug interaction:** No significant drug-drug interaction is expected between lenvatinib and other CYP3A4/P-gp substrates. Women using oral hormonal contraceptives should add a barrier method. **Adverse reactions:** The most frequently reported adverse reactions in the DTC and RCC patient populations (occurring in \geq 30% of patients) are diarrhoea (80.6%), hypertension (70.1%)*, fatigue (59.7%), decreased appetite (53.7%), decreased weight (52.6%)*, vomiting (48.4%), nausea (45.2%), proteinuria (38.9%)*, stomatitis (36.9%)*, headache (35.8%)*, dysphonia (35.6%)*, palmar-plantar erythrodysesthesia syndrome (PPE) (34.1%)*, peripheral oedema (33.9%), and hypercholesterolemia (30.6%); the asterisked frequencies are from the DTC patient population. The most frequently reported adverse reactions in HCC (occurring in \geq 30% of patients) are hypertension (44.0%), diarrhoea (38.1%), decreased appetite (34.9%), fatigue (30.6%), and decreased weight (30.4%). **Storage:** Do not store above 30°C. Store in the original blister in order to protect from moisture. **Container:** Polyamide/ Aluminium/PVC/Aluminium blisters containing 10 capsules. Each carton contains 20 capsules.

โปรดอ่านรายละเอียดเพิ่มเติมในเอกสารกำกับยาและเอกสารอ้างอิง

Further information is available on request

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แพทย์ควรติดตามผลการรักษา

เลขทะเบียนตำรับยาที่ 1C 22/59 (N), 1C 23/59 (N)

ใบอนุญาตโฆษณาเลขที่ มส. 718/2564



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