PDL NEW DRUG REVIEW

Proprietary Name: Lenvima®
Common Name: lenvatinib
PDL Category: Antineoplastics- Kinase Inhibitors

Comparable Products	Preferred Drug List Status
NexAVAR	Non-Recommended

Summary

Indications and Usage: Treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC)

Per data from animal reproduction studies and its mechanism of action, Lenvima® can cause fetal harm if given to a pregnant woman. Females of reproductive potential should be educated to use effective contraception during treatment and for at least 2 weeks after the completion of treatment. The safety and efficacy of use in children have not been established.

Dosage Forms: Capsules: 4mg, 10mg

Recommended Dosage: 24mg once daily; continue until disease progression or until unacceptable toxicity occurs. Dose modifications, withholding of dose, or treatment discontinuations may be required in the following conditions: hypertension, cardiac dysfunction or hemorrhage, arterial thrombotic event, renal failure and impairment or hepatoxicity, proteinuria, GI perforation or fistula formation, QT prolongation, reversible posterior leukoencephalopathy syndrome (RPLS), or other persistent/intolerable grade 2 or 3 adverse reactions. Please refer to the prescribing information for additional and specific recommendations.

Dose adjustments are not required for those with mild or moderate renal or hepatic impairment; however, the dose should be reduced to 14mg daily in those with severe renal or severe hepatic impairment. It is recommended to monitor for liver function before starting therapy, every 2 weeks for 2 months and then monthly thereafter.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Lenvima® 24mg) minus reported % incidence for placebo for all grades of adverse events. Please note that an incidence of 0% means the incidence was the same or that the active drug was less than placebo.* The most frequently reported adverse events included hypertension (57%), hypotension (2%), diarrhea (50%), nausea (22%), stomatitis (33%), vomiting (21%), abdominal pain (20%), constipation (14%), oral pain (23%), dry mouth (9%), dyspepsia (9%), fatigue (32%), peripheral edema (13%), arthralgia/myalgia (34%), weight decreased (36%), decreased appetite (36%), dehydration (7%), headache (27%), dysgeusia (15%), dizziness (6%), proteinuria (31%), palmar-plantar erythrodysesthesia (31%), rash (18%), alopecia (7%), hyperkeratosis (5%), dysphonia (26%), cough (6%), epistaxis (11%), insomnia (9%), dental/oral infections (9%), urinary tract infections (6%), and electrocardiogram QT prolonged (7%).

Laboratory abnormalities included: creatinine increased (3%), ALT increased (4%), AST increased (5%), hypocalcemia (7%), hypokalemia (5%), lipase increased (3%), and platelet count decreased (2%).

Contraindications: None

Manufacturer: Eisai

Analysis: Lenvatinib, the active ingredient of Lenvima®, is a kinase inhibitor. Specifically, it is a receptor tyrosine kinase (RTK) inhibitor that inhibits kinase activities of vascular endothelial growth factor (VEGF) receptors. In addition, lenvatinib inhibits other RTKs associated in pathogenic angiogenesis, tumor growth, and cancer progression.

A multicenter, double-blind, placebo-controlled study assessed the safety of lenvatinib as compared to placebo in adults with locally recurrent or metastatic radioactive iodine-refractory differentiated thyroid cancer. The primary efficacy outcome was progression-free survival (PFS) using Response Evaluation Criteria in Solid Tumors (RECIST). Statistically significant prolongation in PFS was seen with Lenvima® vs placebo.

The table below, which was completely adapted from the prescribing information, illustrates the results.

Endpoint	Lenvima® (N=261)	Placebo (N=131)
Progression-free Survival (PFS)		
Number of Events (%)	107 (41%)	113 (86%)
Progressive disease	93 (36%)	109 (83%)
Death	14 (5%)	4 (3%)
Median PFS in months	18.3	3.6
Hazard ratio & p-value	0.21; p<0.001	
Objective Response Rate (ORR)		
ORR	65%	2%
Complete Response	2%	0%
Partial Response	63%	2%
p-value	p<0.001	
Overall Survival (OS)		
Number of deaths (%)	71 (27%)	47 (36%)
Median OS in months	Not estimable	Not estimable
Hazard ratio & p-value	0.73; p=0.10	

Place in Therapy: Lenvima® is a multi-targeted kinase inhibitor (MKI) indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC). One noted reference source suggests that "For patients with metastatic unresponsive DTC (tumors >1 to 2 cm and growing by at least 20 percent/year) or symptomatic metastatic disease, who are unable to participate in clinical trials, we recommend an oral MKI, rather than a cytotoxic agent. Among the MKIs, we prefer lenvatinib."

It is recommended that Lenvima® be added to the Recommended Drug List as a non-recommended drug as it is not intended as a first line treatment option.

PDL Placement: ☐ **Recommended**
☒ **Non-Recommended**

References

[1] Lenvima [package insert]. Woodcliff Lake, NJ: Eisai Inc; 2015.

[2] UpToDate desktop. Differentiated thyroid cancer refractory to standard treatment: chemotherapy. Accessed June 2015.