דצמבר 2023

רופא/ה נכבד/ה,

רוקח/ת נכבד/ה,

הנדון: לנווימה 4 מ"ג, 10 מ"ג- Lenvima 4 mg, 10mg, Hard Capsule

חברת אסאיי ישראל בע"מ (Eisai Israel Ltd.) מבקשת להודיעכם כי העלון לרופא של התכשירים שלהלן התעדכן בנובמבר 2023.

Lenvima 4 mg
Lenvima 10mg

פרטי העדכון העיקריים מופיעים בהמשך (טקסט שנוסף מסומן באדום, טקסט שהושמט מסומן בטקסט ~~אדום עם קו חוצה~~).

ההתוויות המאושרות לתכשיר בישראל:

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 clear cell 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, in combination with pembrolizumab, is indicated for the treatment of adult patients with advanced or recurrent endometrial carcinoma who have disease progression on or following prior treatment with a platinum containing therapy and who are not candidates for curative surgery or radiation.
LENVIMA is indicated in combination with pembrolizumab for the first-line treatment of adult patients with advanced RCC.

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות ומצורפים לפרסום זה. כמו כן, ניתן לקבל העתקים מודפסים באמצעות פנייה לבעל הרישום: אסאיי ישראל בע"מ, ת.ד. 8049 כפר סבא, 4418001.

להלן העדכונים בעלון לרופא:

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5.1 Pharmacodynamic properties

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First-line treatment of patients with RCC (in combination with pembrolizumab)

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The primary efficacy outcome measure was progression free survival (PFS) based on RECIST 1.1 per IRC. Key secondary efficacy outcome measures included overall survival (OS) and objective response rate (ORR). ~~Median duration of treatment for lenvatinib plus pembrolizumab was 17.0 months.~~ Lenvatinib in combination with pembrolizumab demonstrated statistically significant improvements in PFS, OS and ORR compared with sunitinib at the prespecified interim analysis (final analysis for PFS). The median PFS for lenvatinib in combination with pembrolizumab was 23.9 months (95% CI: 20.8, 27.7) compared with 9.2 months (95% CI: 6.0, 11.0) for sunitinib, with HR 0.39 (95% CI: 0.32, 0.49; P value <0.0001). For OS, HR was 0.66 (95% CI: 0.49, 0.88; P value 0.0049) with the median OS follow-up time of 26.5 months and the median duration of treatment for lenvatinib plus pembrolizumab of 17.0 months. The ORR for lenvatinib in combination with pembrolizumab was 71% (95% CI: 66, 76) vs 36% (95% CI: 31, 41) P value <0.0001 for sunitinib. Efficacy results for PFS, OS and ORR at the protocol-specified final analysis (median follow-up time of 49.4 months) are summarised in Table 9, Figure 1 , ~~at a median OS follow-up time of 26.5 months~~ and Figure 2. PFS results were consistent across pre-specified subgroups, MSKCC prognostic groups and PD-L1 tumour expression status. Efficacy results by MSKCC prognostic group are summarised in the following table.

The final OS analysis was not adjusted to account for subsequent therapies, with 195/357 (54.6%) patients in the sunitinib arm and 56/355 (15.8%) patients in the lenvatinib plus pembrolizumab arm receiving subsequent anti-PD-1/PD-L1 therapy.

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Table 9 Efficacy Results in Renal Cell Carcinoma Per IRC in CLEAR		
	Lenvatinib 20 mg with Pembrolizumab 200mg N=355	**Sunitinib 50mg N=357**
Progression-Free Survival (PFS)*		
Number of events, n (%)	207 (58%)	214 (60%)
Median PFS in months (95% CI)[a]	23.9 (20.8, 27.7)	9.2 (6.0, 11.0)
Hazard Ratio (95% CI)[b, c]	0.47 (0.38, 0.57)	
p-Value[c]	<0.0001	
Overall Survival (OS)		
Number of deaths, n (%)	149 (42%)	159 (45%)
Median OS in months (95% CI)	53.7 (48.7, NE)	54.3 (40.9, NE)
Hazard Ratio (95% CI)[b, c]	0.79 (0.63, 0.99)	
p-Value[c]	0.0424	
Objective Response Rate (Confirmed)		
Objective response rate, n (%)	253 (71.3%)	131 (36.7%)
(95% CI)	(66.6, 76.0)	(31.7, 41.7)
Number of complete responses (CR), n (%)	65 (18.3%)	17 (4.8%)
Number of partial responses (PR), n (%)	188 (53.0%)	114 (32%)
p-Value[d]	<0.0001	
Duration of Response[a]		
Median in months (range)	26.7 (1. 64+, 55.92+)	14.7 (1. 64+, 54.08+)

Tumour assessments were based on RECIST 1.1; only confirmed responses are included for ORR.
Data cutoff date = (DCO) = 31 July 2022
CI = confidence interval; NE= Not estimable; NR= Not reached

* The primary analysis of PFS included censoring for new anti-cancer treatment. Results for PFS with and without censoring for new anti-cancer treatment were consistent.

a Quartiles are estimated by Kaplan-Meier method.

b Hazard ratio is based on a Cox Proportional Hazards Model including treatment group as a factor; Efron method is used for ties.

c Stratified by geographic region (Region 1: Western Europe and North America, Region 2: Rest of the World) and MSKCC prognostic groups (favourable, intermediate and poor risk) in IxRS. Nominal two-sided p-value based on stratified log-rank test.

d Nominal two-sided p-value based on the stratified Cochran-Mantel-Haenszel (CMH) test. At the earlier pre-specified final analysis of ORR (median follow-up time of 17.3 months), statistically significant superiority was achieved for ORR comparing lenvatinib plus pembrolizumab with sunitinib, (odds ratio: 3.84 (95% CI: 2.81, 5.26), p-value <0.0001).

~~The primary OS analysis was not adjusted to account for subsequent therapies.~~

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The CLEAR study was not powered to evaluate efficacy of individual subgroups. Table 6 summarises the efficacy measures by MSKCC prognostic group based on ~~pre-specified primary analysis and the updated~~ the final OS analysis at a median follow-up of 49.4 months.

Table 10 Efficacy Results in CLEAR by MSKCC Prognostic Group

	Lenvatinib + Pembrolizumab (N=355)		**Sunitinib (N=357)**		**Lenvatinib + Pembrolizumab vs. Sunitinib**
	Number of	**Number of**	**Number of**	**Number of**	

	Patients	Events	Patients	Events	
Progression-Free Survival (PFS) by IRC[a]					**PFS HR (95% CI)**
Favourable	96	56	97	65	0.46 (0.32, 0.67)
Intermediate	227	129	228	130	0.51 (0.40, 0.65)
Poor	32	22	32	19	0.18 (0.08, 0.42)
Overall Survival (OS)[a]					**OS HR (95% CI)**
Favourable[b]	96	27	97	31	0.89 (0.53, 1.50)
Intermediate	227	104	228	108	0.81 (0.62, 1.06)
Poor	32	18	32	20	0.59 (0.31, 1.12)

[a] Median follow up 49.4 months (DCO - 31 July 2022)

בברכה,
אלינה ורמן, רוקחת ממונה
אסאיי ישראל בע"מ