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NCCN Guidelines Panel: Kidney Cancer

On behalf of Eisai Inc., I respectfully request the *NCCN Kidney Cancer Panel* to review the enclosed data for Lenvima® (*lenvatinib*) capsules in combination with Afinitor®(*everolimus*) tablets for the treatment of non-clear cell renal cell carcinoma.

Specific Changes: Recommend Lenvatinib + everolimus as "other recommended regimens" for treatment of non-clear cell renal cell carcinoma (nccRCC) (changed from "useful under certain circumstances").

FDA Clearance: On May 13, 2016, the Food and Drug Administration (FDA) approved Lenvima (*lenvatinib*) capsules in combination with Afinitor (*everolimus*) tablets for the treatment of patients with advanced renal cell carcinoma following one prior antiangiogenic therapy. Please refer to the enclosed prescribing information for a complete list of FDA-approved indications for Lenvima and safety information.[1]

Rationale: A prospective, phase 2, single-arm, multicenter study evaluating the safety and efficacy of lenvatinib + everolimus demonstrated activity of the combination as first-line treatment in 31 patients with unresectable advanced or metastatic nccRCC. Patients who had histologically confirmed nccRCC and no prior chemotherapy for advanced disease were treated with lenvatinib + everolimus and achieved an overall objective response rate (ORR) of 25.8% (95% CI, 11.9-44.6) by both investigator assessment and independent imaging review (IIR). When stratified by histology, ORR was 15% (95% CI 3.2 – 37.9) in the papillary group, 44.4% (95% CI 13.7 – 78.8) in the chromophobe group, and 50% (95% CI 1.3 – 98.7) in those who were unclassified. Median progression-free survival (PFS) was 9.23 months (95% CI, 5.49 – not estimable [NE]) by investigator assessment and 5.62 months (95% CI, 3.48 – NE) by IIR. Median overall survival was 15.64 months (95% CI, 9.23 – NE). The safety profile observed in this study was similar to the established profile of the study-drug combination,[2] with no new safety signals. The most common treatment-emergent adverse events (≥10%) in the study were fatigue, diarrhea, decreased appetite, nausea, vomiting, stomatitis, and weight decrease.[3]

The following literature is submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.

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References

1. LENVIMA full prescribing information. Woodcliff Lake, NJ: Eisai Inc., February 2020.
2. Motzer RJ et al. Lenvatinib, everolimus, and the combination in patients with metastatic renal cell carcinoma: a randomised, phase 2, open-label, multicentre trial. *Lancet Oncol*. 2015;16:1473-1482.
3. Hutson TE, et al. A phase 2 study of lenvatinib plus everolimus in patients with advanced non-clear cell renal cell carcinoma. Poster presented at: American Society of Clinical Oncology Genitourinary Cancers Symposium; 2020; San Francisco, CA. Abstract available at: https://meetinglibrary.asco.org/record/183799/abstract

Sincerely,

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