



Adelle Berezinsky, PharmD

Eisai Inc.

100 Tice Blvd

Woodcliff Lake, NJ 07677

Phone: 201-746-2353

Adelle_Berezinsky@eisai.com

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NCCN Guidelines Panel: Kidney Cancer

On behalf of Eisai Inc., I respectfully request the *NCCN Kidney Panel* to review and consider the enclosed data for Lenvima[™] (*lenvatinib*) capsules for the treatment of metastatic renal cell carcinoma (mRCC).

Specific Changes: Inclusion of lenvatinib as a treatment option for subsequent therapy in combination with everolimus for relapse or for surgically unresectable Stage IV disease with predominant clear cell histology.

FDA Clearance: The FDA has not approved lenvatinib for the treatment of mRCC. Please refer to the enclosed prescribing information for the FDA-approved indication and safety information.

Rationale: Results from a randomized, phase 2, open-label, multicenter, three-arm study (N=153) demonstrated the efficacy and safety of lenvatinib + everolimus in patients with mRCC with radiographic evidence of disease progression within 9 months of stopping prior therapy, with one prior disease progression on or after VEGF-targeted therapy. This trial met its primary outcome measure of progression-free survival (PFS) in which patients taking lenvatinib + everolimus experienced a statistically significant prolonged median PFS of 14.6 months compared with a median PFS of 5.5 months in patients taking everolimus alone (HR, 0.40; 95% CI 0.24-0.68; $p < 0.001$). An improvement in median overall survival (OS) was observed with lenvatinib + everolimus compared with everolimus alone (25.5 vs 17.5 months, $p = 0.062$); this reached significance ($p = 0.024$) in an updated analysis. The most common treatment-emergent adverse events (TEAEs) that occurred in the lenvatinib + everolimus arm were diarrhea (84%), fatigue/asthenia (59%), and decreased appetite (51%). In patients who received everolimus alone, the most common TEAEs (all grades) were stomatitis (42%), fatigue/asthenia (38%), and diarrhea (34%). Grade 3 or 4 events occurred more frequently in the lenvatinib + everolimus arm (71%) compared with the everolimus arm alone (50%). (Motzer 2015).

The above clinical trial conducted by Motzer et al. has been accepted for publication and is currently in press with *Lancet Oncology*. A copy of the full manuscript will be provided when published. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of this publication.



Eisai Inc. Medical Affairs

100 Tice Blvd Woodcliff Lake, NJ 07677

Phone: 888-274-2378 • Fax: 732-791-1399 • <http://www.eisai.com/us>

1. LENVIMA (lenvatinib) full prescribing information. Woodcliff Lake, NJ: Eisai Inc., 02/2015.
2. Motzer RJ, Hutson TE, Glen H, et al. Randomized phase 2 three-arm trial of lenvatinib, everolimus, and the combination in patients with metastatic renal cell carcinoma. *Lancet Oncology*. 2015; Accepted for publication.

Sincerely,

A handwritten signature in black ink, appearing to read "Adelle Berezinsky", with a stylized flourish at the end.

Adelle Berezinsky, PharmD
Senior Manager, Medical Information
Medical Affairs, Eisai Inc.