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NCCN Guidelines Panel: Antiemesis Panel

On behalf of Eisai, Inc., I respectfully request the *NCCN Antiemesis Panel* to review the enclosed data for the emetic potential of Lenvima® (*lenvatinib*) monotherapy \leq 12mg

Specific Changes:

Add lenvatinib \leq 12mg/day to the minimal to low emetic risk group for oral anticancer agents

FDA Clearance¹:

Lenvatinib is a kinase inhibitor that is FDA-indicated:

- For the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (RAI-R DTC)
- In combination with everolimus, for the treatment of patients with advanced renal cell carcinoma (aRCC) following one prior antiangiogenic therapy
- For the first-line treatment of patients with unresectable hepatocellular carcinoma (uHCC)
- In combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma (aEC) 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 accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial

Rationale^{1,2}:

Lenvatinib has four FDA-approved indications and the dosage for lenvatinib is indication-specific. The lenvatinib dosage for RAI-R DTC is 24mg once daily, for aRCC is 18mg once daily in combination with everolimus, and for aEC is 20mg once daily in combination with pembrolizumab. In patients with uHCC, lenvatinib is dosed at 12mg (if baseline actual body weight \geq 60kg) or 8 mg (if baseline actual body weight $<$ 60) orally once daily. The lenvatinib dose for uHCC is much lower than that of RAI-R DTC, aRCC, and aEC indications.

The minimal to low emetic potential group for oral anticancer agents is emesis $<$ 30% per NCCN.

The REFLECT study was a phase 3, global, randomized, open-label trial that showed non-inferiority of lenvatinib versus sorafenib in terms of median overall survival. It was the first successful trial vs sorafenib in the first line setting in unresectable HCC. In REFLECT, 16% (77/476) of the patients on lenvatinib 8mg/12mg experienced any grade vomiting and 1% (6/476) of the patients experienced grade \geq 3 vomiting. In REFLECT, 20% (93/476) of the patients experienced any grade nausea and 1% (4/476) of the patients experienced grade \geq 3 nausea.

The following document/articles are 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.

References

1. LENVIMA full prescribing information. Woodcliff Lake, NJ: Eisai Inc., 2020
2. Kudo M, Finn RS, Qin S, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. The Lancet. Published online: February 9, 2018. DOI: [https://doi.org/10.1016/S0140-6736\(18\)30207-1](https://doi.org/10.1016/S0140-6736(18)30207-1)

Sincerely,

A handwritten signature in cursive script, appearing to read "Cathy Cao", with a horizontal line extending to the right.

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