## Priority Review to Lenvatinib for Thyroid Cancer Indication

The Food and Drug Administration has granted priority review designation to lenvatinib mesylate (lenvatinib) for the treatment of patients with progressive, radioactive iodine-refractory differentiated thyroid cancer.

The drug, marketed by Eisai, Inc., is an oral multiple receptor tyrosine kinase inhibitor with a unique binding mode that selectively inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors, in addition to other proangiogenic and oncogenic pathway-related tyrosine kinases thought to be involved in tumor proliferation.

The FDA's priority review designation shortens the time to complete a drug's review and aims to deliver a decision on marketing approval designation for drugs that may offer major advances in treatment or provide a treatment where no adequate therapy exists within six months under the Prescription Drug User Fee Act (PDUFA).

Approval for lenvatinib will be based on data from the SELECT (Study of [E7080] Lenvatinib in Differentiated Cancer of the Thyroid) trial. That multicenter, randomized, double-blind, placebo-controlled Phase III study compared progression-free survival of patients with radioactive iodine-refractory differentiated thyroid cancer and radiographic evidence of disease progression within the prior 12 months, treated with once-daily, oral lenvatinib versus placebo. The study included 392 patients.

## OPIOIDS & CANCER PAIN

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oids because they fear they may become addicted." And, she noted, "There has been a concerted effort to restrict the use of opioids in this country," to the extent that some pharmacies will not even fill opioid prescriptions.

She described the case of a post-polio patient in Oregon diagnosed with stage IV lymphoma, whose physician had told her that the state would no longer allow him to prescribe opioid pain-relieving medication at her current level. With her chronic pain persisting, the patient went to a pain specialist, but this health professional told her she would "just have to live with the pain." All this time, while seeking relief, the patient was without medication and began to spend many days in bed.

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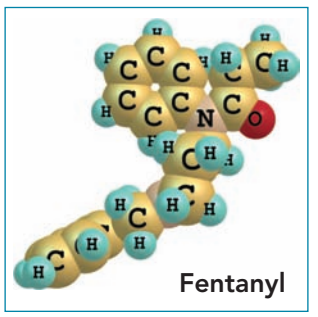
### 'Moral Imperative'

"The treatment of pain is a moral imperative," Christopher emphasized. "Health professionals have an obligation to relieve chronic pain."

The fears of physicians and other health professionals about using opioid therapy do contribute to barriers in relieving chronic pain, said David J. Tauben, MD, Clinical Associate Professor in the Department of Medicine, Chief of the Division of Pain Medicine, and Medical Director of the Center for Pain Relief at the University of Washington. "I'm not an 'opiophobe' or an 'opiophile.' I just want to be doing the right thing for patients."



Fentanyl

In an interview, he said, "Ignorance can be more powerful than good medical decision-making." Barriers to relieving chronic pain with opioids can include uninformed medical directors at clinics and physicians afraid of being singled out for prescribing opioids. He also stressed that physicians who treat patients in chronic pain need to ask their patients about post-traumatic stress, since PTSD can amplify chronic pain.

### More Research

All the speakers at the workshop emphasized the need for more research to better define the role of opioids in treatment of chronic pain. "Even for cancer pain, evidence for long-term efficacy of opioids is weak," said Russell K. Portenoy, MD, Chief Medical Officer of the Metropolitan Jewish Health System (MJHS) Hospice and Palliative Care, Director of the MJHS Institute for Innovation in Palliative Care, and Professor of Neurology at Albert Einstein College of Medicine.

He noted that although randomized controlled clinical trials on opioids have often yielded poor or conflicting data, even with a weak science base for palliative care, long-term opioid therapy is considered best practice for patients with active cancer. "We have to look at why the research hasn't been giving us answers," he said in an interview.

"A physician like me would like to see a really heavy emphasis on health professional education on opioid use." He added that he would also like to see better patient selection in opioid prescribing, especially opioid-abuse risk selection.

"Everyone has accepted the need for more regulation of opioids," he said, and along with this regulation, physicians need to do a better job of documentation and monitoring of their patients on opioid pain-relieving medicines.

> "What I would like not to see is to pit one epidemic against the other; we have to fight both epidemics at the same time. We must reduce prescription opioid abuse, but people in pain must be helped."

## Recommendations

The draft panel report on opioids for chronic pain makes the following recommendations:

1. Federal and non-federal agencies should sponsor research to identify which types of pain, specific diseases and patients are most likely to benefit from opioids;
2. Federal and non-federal agencies should sponsor research to identify which types of pain, specific diseases, and patients are most likely to incur harm from opioids;
3. Federal and non-federal agencies should sponsor the development and evaluation of multidisciplinary pain interventions, including cost-benefit analyses and identifying barriers to dissemination;
4. Federal and non-federal agencies should sponsor research to develop and validate research measurement tools for identification of patient risk and outcomes (including benefit and harm) related to long-term opioid use that can be adapted for clinical settings;
5. Electronic health record vendors and health systems should incorporate decision support for pain management and facilitate export of clinical data to be combined with data from other health systems for analysis to better identify patients who respond to or have harm from opioid use;
6. Researchers on the effectiveness and harm of opioids should consider alternative designs (e.g., "N of 1" trials, qualitative studies, implementation science, secondary analysis, Phase I and II design) in addition to randomized clinical trials;
7. Federal and non-federal agencies should sponsor research on risk identification and mitigation strategies prior to widespread integration of opioid use for chronic pain into clinical care;
8. Federal and non-federal agencies and health care systems should sponsor research and quality improvement efforts to facilitate evidence-based decision-making at every step of the clinical decision process;
9. In the absence of definitive evidence, clinicians and health care systems should follow current guidelines by professional societies about which patients and which types of pain should be treated with opioids and about how best to monitor patients and mitigate risk for harm; and
10. NIH or other federal agencies should sponsor conferences to promote harmonization of guidelines of professional organizations to facilitate their implementation more consistently in clinical care.