State Medical Board of Ohio

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April 9, 2014

Michael Botticelli, Acting Director
Office of National Drug Control Policy
The White House
1600 Pennsylvania Avenue NW
Washington, DC 20500

Dear Acting Director Botticelli:

This is to express The State Medical Board of Ohio's concerns regarding Zohydro ER®, an extended release product containing the schedule II narcotic drug hydrocodone bitartrate, which was introduced to the market in March, 2014 without tamper-resistant features. The information we have reviewed suggests that distribution of this product *in its present formulation* will impose on the citizens of Ohio serious risks of addiction and overdose which will outweigh its value as a tool in the physician's armamentarium for the treatment of pain.

As the state agency responsible for the licensure of physicians and physician assistants in Ohio, the State Medical Board has long been committed to promoting the appropriate treatment of pain and lessening the extraordinary damage that results from the substandard prescribing and misuse of narcotics. The Board has great familiarity not only with the efficacy, adverse reactions, and dangers associated with the use of strong opioid pain medications, but also with the beliefs and behaviors of both physicians and patients regarding the various opioid products, including products containing hydrocodone.

Hydrocodone is the most frequently prescribed narcotic pain reliever in Ohio, and indeed in the United States. Despite its widespread use, indeed possibly in part because of its widespread use, both patients and drug abusers often believe that hydrocodone presents less of a danger to users than do any of the other available opioid agonists. Unfortunately, investigations, disciplinary actions, and discussions with physicians have revealed that prescribers, too, frequently view hydrocodone as less of a danger than other opioid agonists, such as morphine, hydromorphone, oxycodone, and oxymorphone. While this is certainly attributable in part to the drug's previous unavailability in a high-dose, single-entity product, we believe it is also based on long-held erroneous beliefs about the drug itself. Many physicians simply view hydrocodone as being a weaker, and therefore less dangerous drug than the other available opioid agonists.

Prior to the introduction of Zohydro ER®, physicians and patients in the United States had essentially no experience with high dose hydrocodone products. It is very likely that many drug abusers, legitimate patients, and even physicians, will underestimate the potential of this new drug to produce addiction and cause fatal overdoses. In addition, it is our understanding from review of the literature

that the extended release properties of Zohydro ER® can be defeated by unintentional means, such as breaking the capsules or consuming alcohol with the capsules, thus presenting additional risks for legitimate patients.

Based on our years of experience with other long acting/extended release narcotic pain medications, both in tamper resistant and non-tamper resistant formulations, we are certain that many people will consume excessive doses of Zohydro ER®; that many of those people will become addicted; and that many addicts and abusers will die. Weighing these high expected costs against the limited expected benefit that a new extended release strong pain medication will provide for patients suffering serious pain, The State Medical Board of Ohio strongly encourages the Office of National Drug Control Policy to work with FDA, DEA, and other interested federal agencies to restrict the availability of Zohydro ER® until the manufacturer develops an effective, tamper resistant formulation. If the drug cannot be at least temporarily removed from the market, we believe that FDA should require a risk evaluation and mitigation strategy (REMS) apart from the current REMS applicable to other long acting/extended release opioid pain medications, which might limit distribution of the drug to selected pharmacies and set minimum training standards for prescribers.

Sincerely,

Krishnamurthi Ramprasad, M.D.
President

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF NATIONAL DRUG CONTROL POLICY
Washington, D.C. 20503

May 13, 2014

Krishnamurthi Ramprasad, M.D.
President
State Medical Board of Ohio
30 East Broad Street, 3rd Floor
Columbus, OH 43215

Dear Dr. Ramprasad:

Thank you for your April 9, 2014, letter regarding the Food and Drug Administration's (FDA) recent approval of Zohydro ER (hydrocodone bitartrate). The Office of National Drug Control Policy (ONDCP) shares your concern about the potential for abuse of Zohydro and other prescription opioid analgesics, and the dangers they pose.

According to the Centers for Disease Control and Prevention (CDC), of the more than 38,300 overdose deaths in 2010, opioid pain relievers were involved in over 16,600, while heroin was involved in approximately 3,000. In 2012, approximately 2.1 million Americans met the diagnostic criteria for abuse or dependence on prescription pain relievers, while heroin accounted for approximately 470,000 people with past year abuse or dependence.

Since 2009, the Obama Administration has deployed a comprehensive and evidence-based strategy to address the threat posed by opioid drugs. Within 30 days of his confirmation, then-ONDCP Director Kerlikowske declared combatting prescription drug abuse a top drug control priority for the Administration. Since then, the Administration has coordinated a Government-wide response to the prescription drug abuse epidemic, significantly bolstered support for medication-assisted opioid treatment and overdose prevention, and pursued action against criminal organizations trafficking in opioid drugs. President Obama's inaugural *National Drug Control Strategy*, released in May 2010, labeled opioid overdose a "growing national crisis" and laid out specific actions and goals for reducing the abuse of prescription opioids and heroin.

As you are aware, the FDA's Center for Drug Evaluation and Research (CDER) approval process ensures that drugs work correctly and balances the risk of harm associated with misuse versus the benefits to patients in legitimate need. The FDA then continues to monitor performance and use of the drug, and can take appropriate actions under its enforcement and regulatory capacity.

The FDA tailored and has proactively modified its risk evaluation and mitigation strategy (REMS) for extended release/long-acting (ER/LA) opioid analgesics. Originally approved in July 2012, and modified in April 2013, the REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS. In April 2014, the FDA modified REMS to include revisions to the ER/LA Opioid Analgesics REMS Blueprint, ER/LA analgesic Website, and Dear Prescriber Letter which conform to new safety labeling changes instituted in 2013.

In September 2013, FDA notified drug companies and sponsors about mandatory safety labeling changes to ER/LA opioid analgesics. These labeling changes will more effectively communicate to prescribers the serious risks associated with the drug and clearly describe the patients whom the drug should be prescribed in light of the serious risks. Drug companies and sponsors will also be required to conduct additional studies and clinical trials to assess the known serious risks of misuse, abuse, addiction, increased sensitivity to pain (hyperalgesia), overdose, and death associated with long-term use of ER/LA opioids.

Zohydro ER is the first drug to be approved with the new labeling, and the manufacturer of Zohydro is being required to conduct the post-market studies for long-term use beyond 12 weeks. Additionally, Zohydro ER is a Schedule II drug which means that it can only be dispensed through a physician's written prescription and no refills are allowed. Schedule II controlled substances also require stringent recordkeeping, reporting and physical security.

According to the FDA, there are currently no available hydrocodone products on the level of Zohydro ER with meaningful abuse-deterrent properties. The Obama Administration supports a transition to abuse-deterrent opioids as quickly, and safely as possible, and the manufacturer of Zohydro has publicly stated that it is working to create an abuse-deterrent formulation. In the interim, ONDCP will continue to work closely with our federal partners and state & local stakeholders to educate and train prescribers and the general public on the known serious risks of opioids; increase monitoring and information-sharing via Prescription Drug Monitoring Programs (PDMPs); promote prevention and treatment efforts; and expand access to lifesaving naloxone, which reverses opioid-related overdose.

We wish to commend the Ohio State Medical Board, Ohio Legislature and all Ohio officials and agencies who are working tirelessly to stem the opioid crises. Disseminating educational materials, offering prescriber trainings, spearheading initiatives such as Project DAWN, and equipping first responders with naloxone are imperative to preventing prescription drug abuse and your actions are saving lives.

Thank you for your dedication to the people of Ohio. Please let me know how I can be of further assistance in the future.

Sincerely,

Michael P. Botticelli
Acting Director