



*Integrative pain management for optimal patient care*

**American Academy of Pain Management  
Statement on Extended-Release Hydrocodone (Zohydro™ ER)  
April 8, 2014**

In October, 2013, the US Food and Drug Administration (FDA) approved Zohydro™ ER, the first single-agent extended release hydrocodone product to enter the US market. This approval came despite an FDA advisory committee vote recommending non-approval, based on the fact that Zohydro™ ER does not incorporate features that would qualify it as an abuse-deterrent formulation (ADF) under proposed FDA regulations. No concerns were expressed about Zohydro™ ER's efficacy in reducing pain, as demonstrated in the FDA-required clinical trials. Rather, the advisory committee's concerns centered around the likelihood that Zohydro™ ER, as every other opioid analgesic on the market, would be abused (both by swallowing intact dosage units and by crushing the capsules to produce a powder that can be inhaled or prepared for injection), resulting in unintended overdose deaths.

In the months since FDA's approval decision, many individuals and groups representing a variety of constituencies have urged FDA to reverse its decision. These entities have sought legislative and regulatory vehicles that would either ban Zohydro™ ER from the market or make its use so cumbersome for prescribers, dispensers, and people with pain, that it would effectively be banned. To date, the pinnacle of these efforts was an executive order from Massachusetts governor Deval Patrick, directing members of his administration to ban the prescribing and dispensing of Zohydro™ ER in Massachusetts by declaring it a Schedule I controlled substance under the state's Controlled Substances Act. Some states have implemented regulatory efforts to restrict Zohydro™ ER prescribing (such as Vermont), while still other states (such as Ohio and Kentucky) and the US Congress have legislation pending to ban the medication in those jurisdictions.

As an organization representing healthcare providers engaged in the management of pain, the American Academy of Pain Management (the Academy) is concerned about prescription drug abuse and related overdose deaths and is engaged in substantial efforts to address this public health crisis in ways that do not adversely affect individuals affected by an even larger public health crisis—that of uncontrolled chronic pain. The Academy appreciates the concerns of advocates calling for Zohydro™ ER's removal from the marketplace, but believes that Zohydro™ ER represents a valuable tool for many people with pain, and that much of the hysteria over its abuse potential overlooks a number of key facts and risk mitigation strategies that should render it as safe as any other opioid analgesic on the market.

Zohydro™ ER has a place in the pain management armamentarium

Until the approval of Zohydro™ ER, the only pain medications containing hydrocodone available in the US market were combination products, in which hydrocodone was combined with non-opioid analgesics, typically acetaminophen, ibuprofen, or aspirin. These combination products have represented the single most-prescribed medication type in the United States, with roughly 130 million

975 Morning Star Dr., Suite A, Sonoma, CA 95370

T: 209-533-9744 F: 209-533-9750 E: [aapm@aapainmanage.org](mailto:aapm@aapainmanage.org) W: [www.aapainmanage.org](http://www.aapainmanage.org)

prescriptions per year. These medications are commonly used to treat acute pain and breakthrough pain in people taking extended release and long-acting opioid analgesics, but also appear to be used by many people as their primary means of managing chronic pain. When used in this manner, these products expose users to significant risk of liver toxicity (when acetaminophen is the non-opioid component) or ulcers, excessive bleeding, kidney damage, high blood pressure, and cardiac disease (when ibuprofen or aspirin is the non-opioid component). Thus, for those individuals who need an opioid analgesic for treatment of chronic pain, an extended-release single-agent hydrocodone medication (like Zohydro™ ER) can literally be a life-saver. Additionally, using immediate release hydrocodone to treat continuous chronic pain requires taking the medication every 3 to 4 hours, as that is the duration of its analgesic effects.

It is well-known that individuals respond differently to different opioid analgesics, in terms of both the primary analgesic effect and the array of side effects experienced. That is why having a variety of opioids available is important. The Academy recognizes that a product like Zohydro™ ER offers benefits to some people with chronic pain that are not offered by other opioid analgesics. Some of these patients may not benefit at all, or as much, from the use of other opioids because of their idiosyncratic responses. For some individuals, hydrocodone is the best choice among opioid analgesics, and the Academy believes medications like Zohydro™ ER should be available for those individuals.

#### Zohydro™ ER likely will be abused

We recognize the likelihood that Zohydro™ ER will be misused, abused, and/or diverted by individuals whose motives are other than the intended use of the product. In this sense, it is no different than any other opioid analgesic, immediate release or extended release, on the market. It also is no different from any benzodiazepine, any stimulant, or any barbiturate on the market, and it is no different from alcohol and nicotine in this regard. Substance use disorders and the criminal activity that often supports them are tragic, causing untold suffering, disability, and death. The Academy has been active in promoting efforts to reduce the improper use of opioid analgesics and other controlled substances, and will continue doing so.

Zohydro™ ER, as a non-ADF opioid analgesic, doubtless will be misused by individuals who crush it, and by those who swallow intact dosage units when they are not under medical supervision in the service of treating pain. This is unfortunate and entirely foreseeable, but only somewhat preventable, even with the one ADF controlled release opioid analgesic currently on the market. The Academy also recognizes that the ratio of people using Zohydro™ ER appropriately to those misusing it is likely to be approximately 9:1. Given this, is it right to deny access to the nine because of the behavior of the one? Clearly, it is an ethical conundrum involving the principles of beneficence, non-maleficence, and justice—in other words, a problem that is roughly as complicated as the two public health crises of chronic pain and prescription drug abuse.

Many of the voices advocating for a Zohydro™ ER ban have trumpeted the news that the highest dosage strength of Zohydro™ ER contains 50 mg of hydrocodone, as much as ten dosage units of the most commonly-prescribed hydrocodone-containing combination opioid products. The implication is that misusing one Zohydro™ ER capsule, either by swallowing it or by crushing it and consuming it by another route, is ten times as likely to cause an overdose death. In isolation, this might be true, but it ignores three relevant facts: 1) this amount is only in the highest dose of Zohydro™ ER, which is far less

likely to be prescribed than the lower doses, which contain from 10 to 40 mg of hydrocodone; 2) if swallowed intact, the drug is released over the course of 12 hours, not immediately; and 3) three other extended release opioids currently on the market, containing morphine, oxycodone, and oxymorphone, all have three dosage forms that contain more opioid on an equianalgesic basis. Further, there are a number of immediate release opioid analgesics with doses comparable to the lesser strengths of Zohydro™ ER, and when they are taken as an intact dosage unit, they release all of their drug over the course of no more than four hours. Why, then, is Zohydro™ ER so much more concerning than other opioid analgesics on the market?

### Where do we go from here?

The Academy believes that banning Zohydro™ ER is not the right solution. Doing so would unfairly penalize the vast majority of individuals for whom it would be prescribed, in the service of protecting those relative few who would choose to use it inappropriately. Instead, the Academy calls on experienced and well-educated clinicians to exercise their best judgment in using this medication to treat pain.

The Academy strongly encourages clinicians considering the use of Zohydro™ ER to ensure that their skills in assessing patients' medical conditions and risk of misusing their medication are optimally developed, and that they use these skills with all of their patients for whom opioid analgesics are indicated. This comprehensive risk assessment should include other people in the patient's social milieu, who might seek the medication for improper and/or illegal purposes. Clinicians are further urged to follow all patients using opioid analgesics very closely, using the full array of monitoring tools and information sources available (e.g., prescription drug monitoring programs, urine/saliva/serum drug testing, family informants, etc.) to do their utmost to ensure that patients are using these powerful and potentially dangerous medications safely and effectively. Finally, clinicians are reminded that these methods should be used with any opioid prescription—not just with Zohydro™ ER—because all opioid analgesics expose people who use them to the same risks. This is not a problem that is inherent to a single medication, but instead, a class-wide concern. (In fact, many states maintain preferred drug lists for their Medicaid and state employee health insurance plans that recommend the use of an even more dangerous opioid analgesic—methadone. It is ironic that some of these states are among those most vociferously advocating for a Zohydro™ ER ban.)

The Academy also reminds clinicians that many, if not most, people with chronic pain find that non-pharmacological methods of managing pain are as beneficial, if not more beneficial, in controlling pain when compared to medications, and that combinations of these methods likely will produce better outcomes with a lower required dose of opioid analgesics. Clinicians are encouraged to educate themselves about these other methods of pain control, and to use them to the greatest extent possible. The Academy also encourages insurers to provide adequate reimbursement for non-pharmacological treatment services, and calls on the educational institutions that train healthcare providers to teach their students about this comprehensive integrative approach to pain management.

Finally, the Academy encourages clinicians to educate each patient using opioid analgesics to:

- Use their medications only as directed;
- Refrain from sharing their medications with anyone else, for any reason;
- Store their medications securely; and

- Dispose of unused/unneeded/expired medications safely and appropriately

### A final word

The Academy remains committed to helping develop and implement solutions to these two public health crises, solutions that consider two groups of people with different needs, and which seek to maximize the benefits and minimize the risks for both. Policymakers need to seek solutions that recognize that both of these problems are extraordinarily complex and unlikely to be solved by simple interventions. Further, it must be recognized that this is not a “zero-sum game,” in which solutions ameliorating one problem can only worsen the other; instead, identification and implementation of solutions that address both problems simultaneously must be priorities, followed by solutions that selectively target one problem or the other.

The Academy firmly believes that an integrative approach to health care in general, and to pain care in particular, provides a model that will enable us all to reach the goal of restoring wellness to those who are suffering, whether that suffering is rooted in substance abuse, in chronic pain, or in both simultaneously. These are problems of the “whole” person, not just of biological systems, and until we address them in a manner that recognizes this fact, we are doomed to remain mired in the tragic circumstances that characterize our current reality.