

ARPO

Advocates for the Reform of Prescription Opioids

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January 22, 2012

Dr. Margaret A. Hamburg
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: New Drug Applications for Extended-Release Hydrocodone

Dear Commissioner Hamburg,

Advocates for the Reform of Prescription Opioids, Inc. (ARPO) is troubled by the recently revealed plans of several drug companies to submit new drug applications (NDAs) for pure, extended-release (ER) hydrocodone, and wishes to object strongly to FDA approval of such formulations.

For more than 10 years there has been a well-documented epidemic of addiction and death from prescription opioid drugs in the United States, with a six-fold increase in addiction treatment and a four-fold increase in deaths to around 15,000 annually (CDC 2012). This trend now qualifies as a national public health crisis, and has directly paralleled a dramatic increase in the prescribing of opioids, the majority of which are for chronic non-cancer pain (CNCP). This increase in prescribing has been fueled primarily by drug manufacturers' unsubstantiated claims of long-term efficacy and minimal risks, by inadequately trained physicians, and by pain advocacy groups, many of which are heavily subsidized by the drug industry and who have alleged (despite steadily increasing sales of opioids) that chronic pain is 'undertreated' with opioids and that the preponderance of addiction and death is attributable to misuse and abuse.

For its part, the FDA's actions have been largely ineffective at stemming the tide of increasing deaths and addictions. Federal drug policy appears to be unduly influenced by many myths:

- There is no objective evidence of ‘under-treatment’ of chronic pain with opioids in the U.S.; there is considerable evidence of uneducated, non-selective, inappropriate and/or unethical treatment of pain.
- There is no substantiation of under-availability or under-prescribing of prescription opioids; there is a significant oversupply and excessive over-prescribing of opioid drugs due to improper schedule classification, scientifically unsupported medical indications, and overly liberal and unethical prescribing practices, as evidenced by the four-fold increase in the sale of prescription opioids since 1999 and U.S. consumption of over 90% of such drugs world-wide (CDC 2012).
- There is no documentation that prescription opioid drug benefits outweigh risks in the treatment, particularly long-term, of CNCP; there is ample data documenting lack of effectiveness in controlling pain, and serious side effects such as dosage-related pain hypersensitivity, as well as increased addiction potential and respiratory depression due to the higher strengths of the ER formulations.
- There is little evidence that the opioid problem is primarily driven by willful abusers or illicit sources; there is recent evidence that as many as 35% of patients receiving legitimate prescription long-term opioid therapy may suffer from lifetime opioid use disorder based on proposed DSM-5 criteria (Boscarino et al. 2011).

ARPO also has a significant concern about the pure hydrocodone formulation. Hydrocodone, the active opioid ingredient of the well-known brands Vicodin, Norco and Lortab, was prescribed 123 million times in 2009 (about 53% of the immediate-release opioid market; Governale 2010), and Vicodin was recently rated as the third most dangerous prescription drug in America based on DAWN data on emergency room visits (Gray 2012). Hydrocodone has been implicated in the deaths of thousands of Americans each year (Florida Department of Law Enforcement 2006-2010). Combine these facts with the much higher hydrocodone dose in a pure ER formulation, and you have a recipe for disaster, similar to the tragedy that has happened with OxyContin. How could that be worth any small alleged benefit realized from the removal of acetaminophen?

Considering all of the above, ARPO believes it is clear that there is absolutely no medical “need” or pharmacologic justification for the proposed “pure” ER hydrocodone preparations, and that allegations to the contrary by the pharmaceutical industry and pain organizations are just another example of the marketing practices and patient care ‘myths’ which were the initial source as well as the ongoing accelerant of the prescription opioid scourge now afflicting our nation. ARPO and other similar groups striving to reverse the prescription opioid public health crisis have always supported effective and readily accessible treatment for pain, but we feel strongly that it must be predicated on certain principles: comprehensive and scientifically valid diagnosis and therapy; properly educated and ethical providers; medications that are regulated, marketed, prescribed, and used in an evidence-based manner; and viewing addiction as a disease, a medical not a moral issue which requires treatment not stigmatization.

In conclusion, in light of the ongoing opioid epidemic, the failure of government, industry and the medical community to stem the resulting tide of deaths and addictions, and a number of serious public health concerns, ARPO strongly opposes FDA approval of a new ER formulation of hydrocodone. Our government agencies, working with the medical profession, must fix what is wrong with the current opioid crisis before considering additional products that will offer more of the same risks as the current opioid formulations without any demonstrable benefits. Accordingly, FDA must send a strong signal to

the pharmaceutical industry that it will not entertain any NDAs for an ER formulation of pure hydrocodone.

Sincerely,



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cc: Senator Charles E. Schumer, NY

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The Honorable Kathleen Sebelius, Secretary of Health and Human Services
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The Honorable Michele M. Leonhart, Administrator
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Douglas Throckmorton, M.D., Deputy Director for Regulatory Programs
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