Hello again! While awaiting some comments and feedback from my PharmD colleagues, I thought perhaps I’d add my two cents on the FDA PROP (physicians for responsible opioid prescribing) letter. In doing so, I’m going to assume that the FDA takes their requests seriously enough as to actually Implement all or part of the PROP letter suggestions.

From the very beginning of their letter to the end, I have more questions than answers. Here’s how I see it…

“PROP (physicians for responsible opioid prescribing)”

Are there any law-abiding physicians out there that are particularly in favor of “irresponsible” prescribing?

“The undersigned clinicians, researchers and health officials from fields that include Pain, Addiction, Primary Care, Internal Medicine, Anesthesiology, Psychiatry, Neurology, Emergency Medicine, Toxicology, Rheumatology, and Public Health submit this petition…”

Would such a document be accepted for publication in a peer reviewed journal from a group that has a potential for publication bias? As Dr. Passik points out, 10 of the 37 signatories (27%) are from the State of Washington, obviously the mecca of pain management by which all other states should be measured against.

“These overly broad indications imply a determination by FDA that they are safe and effective for long-term use.”

According the Merriam-Webster Dictionary, the definition of “imply” is to “involve or indicate by inference, association, or necessary consequence rather than by direct statement”. Why doesn’t somebody that wrote the FDA letter simply ask the FDA to clarify what they mean? And, why are we singling out opioids? To use the same logic, does the FDA “imply” that NSAIDS “are safe and effective for long-term use?” Do they imply any of the following “are safe and effective for long-term use”, all of which can be found on Drug Watch. [Accutane® (Isotretinoin); Actos® (Pioglitazone); DePuy® (ASR Hip Implant); Zimmer® NexGen Knee; Yaz® & Yasmin® (ethinyl estradiol, drospirenone); Avandia® (Rosiglitazone); Prozac® (Fluoxetine)]

I will give you this; the use of opioids far exceeds any of the individual drugs listed immediately above, but certainly they do not exceed NSAID use. I’m pretty confident that all of the signatories on the FDA letter realize the ubiquity of NSAID-induced GI bleeds, kidney dysfunction and adverse cardiac events. Is there a group called PRNP (physicians for responsible NSAID prescribing)?

“Unfortunately, many clinicians are under the false impression that chronic opioid therapy (COT) is an Evidence-based treatment for chronic non-cancer pain (CNCP)…” “These misperceptions lead to over-prescribing and high dose prescribing.”

What if we substituted “opioid therapy (COT)” in the sentence above with any of the following? “NSAID therapy”, “antidepressant therapy in the absence of psychotherapy”, “interventional spinal procedures”, or multiple surgical interventions”. Personally, I think all of these would fit quite nicely into the equation as long as the second sentence is adjusted. For example, “Unfortunately, many clinicians are under the false impression that multiple surgical interventions are evidence-based treatment for chronic non-cancer pain (CNCP). Furthermore, some anesthesiologists, neurologists, and physiatrists routinely employ interventional procedures containing FDA approved drugs almost all of which are used off-label. The evidence to support such interventions is lacking and the cost for these surgeries to the healthcare system is millions of dollars per year. “These misperceptions lead to millions of unnecessary medical expenses. Research suggests that of the 500,000-plus disk surgeries performed annually, as many as 90
percent are unnecessary and ineffective.” While mainstream media focuses on the millions of dollars spent on prescription pain-relievers, articles are sorely lacking on the cost of routine back procedures such as Anterior cervical fusion at $44,000; Cervical fusion at $19,850; Decompression back surgery at $24,000; Lumbar laminectomy at $18,000; and Lumbar spinal fusion at $34,500. In fact, according to Dr. David Spodick, professor of medicine at the University of Massachusetts, "Surgery is the sacred cow of our health-care system and surgeons are the sacred cowboys who milk it."

“By implementing the label changes proposed in this petition, FDA has an opportunity to reduce harm caused to chronic pain patients as well as societal harm caused by diversion of prescribed opioids.”

Where is the proof that this can or will happen? Many of the signatories on the FDA letter are renowned researchers that should know better than to make such a statement without legitimate outcomes data.

“The Federal Food, Drug and Cosmetic Act established that a drug intended to treat a condition must be proven safe and effective for use as labeled. The current label on opioid analgesics does not comply with this law.”

Does the current label for the following comply with this law, specifically “proven safe”? warfarin, ibuprofen, digoxin, metoclopramide, any number of cytotoxic chemotherapy regimens, etc.

SPECIFIC ACTIONS REQUESTED FOR CHANGES TO OPIOID ANALGESIC LABELS:

“Strike the term “moderate” from the indication for non-cancer pain.”

What do we do for an 84 year old man with SEVERE low back pain and whole body DJD that has a head injury, CAD, PUD, a Crs of 1.6, and cannot tolerate or doesn’t respond to anticonvulsants? Surely we can’t use NSAIDs because potential end organ disease or worse yet, DEATH, and acetaminophen won’t be effective. The patient complains of severe pain, level 10/10. Do we tell the patient that opioids aren’t approved by the FDA? No you say…use the drug off label; well really, what’s the point then?

“Add a maximum daily dose, equivalent to 100 milligrams of morphine for non-cancer pain.”

Really? Whose equivalency chart will you use? According to a recent presentation by Dr. Kathryn Shaw (presented at Eastern States Pharmacy Residents Conference, Hershey PA, 2012), a review of 6 online opioid conversion calculators (all of which were based off peer-reviewed opioid conversion tables) yielded a difference in opioid conversion from (-50%) to (+242%), and that excluded 2 of the calculators because their percent deviation was even more egregious. Talk about risk of harm!!!

STATEMENTS OF SCIENTIFIC BASIS FOR PETITION:

“Long-term safety and effectiveness of managing CNCP with opioids has not been established.”

I beg to differ. Few drugs have been available for centuries like opioids. I personally have patients that have been on opioids for 30-40 years. Not a single one has had opioid-induced liver disease (excluding those on combination opioids containing APAP), kidney dysfunction, or has become crippled from multiple surgeries.
“Recent surveys of CNCP patients receiving COT have shown that many continue to experience significant chronic pain and dysfunction.”

I agree. How is this different from interventional procedures or surgery?

“Recent surveys using DSM criteria found high rates of addiction in CNCP patients receiving COT.”

True enough. Maybe we need to teach prescribers about risk assessment and careful monitoring, including how to interpret the urine screens they order and the potential usefulness of serum analysis. How many patients have severe depression or suicide risk per DSM criteria because they are non-functional without opioids?

“A large sample of medical and pharmacy claims records found that two-thirds of patients who took opioids on a daily basis for 90 days were still taking opioids five years later.”

That’s wonderful. Why does it matter; maybe they worked? What percentage of patients remain on statin therapy 90 days after they start them, assuming their LFT’s are normal? Geeze folks, didn’t you know that chronic pain is a chronic disease like hypercholesterolemia?

Patients with mental health and substance abuse co-morbidities are more likely to receive COT than patients who lack these risk factors, a phenomenon referred to as adverse selection.

Which came first; the chicken or the egg?

“Three large observational studies published in 2010 and 2011 found dose-related overdose risk in CNCP patients on COT. COT at high doses is associated with increased risk of overdose death 18, emergency room visits 19 and fractures in the elderly.”

Really, how about this? In a NEJM published study of patients 80 years or older, “…researchers reported that 65.7 percent of hospitalizations were due to unintentional overdoses and four drug classes were the culprit of 67 percent of these hospitalizations: warfarin (33.3 percent), insulins (13.9 percent), oral antiplatelet agents (13.3 percent) and oral hypoglycemic agents (10.7 percent).” Hey what do you know; opioids aren’t listed!

I’m not opposed to making prescribed opioids safer, and I don’t profess that they aren’t dangerous if not prescribed for the correct patient with risk stratification and ongoing monitoring. The PROP petition was perhaps an attempt to make a step in a positive direction. But it is misguided to say the least. I believe that treating all scheduled opioids as schedule II might be beneficial to monitor prescriptions. Also, perhaps significant headway would be made in mitigating diversion if all prescribers and all pharmacists had direct real time access to an online data base, which would need to include all DoD and VA facilities. This at least could help to prevent multiple prescribers and pharmacies from writing and dispensing opioids nationwide.

Keep the comments coming!