



Physicians for Responsible Opioid Prescribing
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Scott Gottlieb, MD
Commissioner of Food and Drugs,
U.S. Food and Drug Administration
10923 New Hampshire Avenue
Silver Spring, MD 20993

RE: Docket No. FDA-2017-D-2497

Dear Dr. Gottlieb,

Physicians for Responsible Opioid Prescribing (PROP) is pleased that FDA intends to revise the Blueprint for Prescriber Education for Extended-Release and Long-Acting (ER/LA) Opioids Risk Evaluation and Mitigation Strategies (REMS). When the original Blueprint curriculum was released as a draft in 2011, PROP urged FDA to make changes (see attached). Our 2011 letter was signed by some of the nation's leading experts in the fields of Pain, Addiction, Public Health, Primary Care and Internal Medicine. Unfortunately, FDA disregarded our requested changes.

PROP has serious concerns about the revised Blueprint curriculum. We believe that serious flaws in the original Blueprint remain unaddressed. Furthermore, the Blueprint curriculum contradicts key recommendations found in the 2016 Centers for Disease Control and Prevention *Guideline for Prescribing Opioids for Chronic Pain*, which recommended "nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain" and the more recent Department of Veterans Affairs (VA) and Department of Defense (DoD) *Clinical Practice Guideline for Opioid Therapy for Chronic Pain* which recommended "against initiation of long-term opioid therapy for chronic pain." We believe the REMS curriculum should be based on the CDC guideline and the VA/DOD guideline.

Specific example of inconsistencies between the Blueprint and the CDC and VA/DOD guidelines include the following:

- 1) The CDC and VA/DOD guideline warn against prescribing high doses of opioids and specifically recommend against doses greater than 90mg morphine equivalents. The Blueprint omits this critical topic.
- 2) The CDC and VA/DOD guideline highlight the lack of evidence supporting long-term use of opioids for chronic pain. The Blueprint omits this critical topic.
- 3) The VA/DOD guideline rejected the recommendation for opioid rotation as a strategy for managing tolerance, and the CDC guideline notes that the practice is not supported by evidence. The Blueprint encourages opioid rotation.

- 4) The VA/DOD guideline describes the practice of prescribing immediate release (IR) opioids to patients on ER/LA opioids for “breakthrough pain” as controversial and the CDC guideline notes that the practice is not supported by evidence. The Blueprint calls for teaching this practice.
- 5) The CDC guideline states that when opioids are prescribed for acute pain “three days or less will often be sufficient; more than seven days will rarely be needed.” The Blueprint omits this critical prevention recommendation.

Since the purpose of the Blueprint is to teach more cautious prescribing the focus should be first and foremost on when to use opioids for acute and chronic pain, and secondly, on how to use opioids as safely as possible. The Blueprint does not need to teach how to make a pain diagnosis, or what alternatives there are to opioids, both of which should be considered beyond the scope of REMS.

We believe the Blueprint should be revised to include the following educational messages for prescribers:

- 1) Opioids are rarely needed for chronic pain. Given the poor safety profile for long-term opioid therapy, indications should be restricted to those where evidence suggests that benefit predictably exceeds risk. There are many common pain conditions, particularly chronic pain conditions where a central component is dominant, for which no such evidence exists, and for which alternatives to opioids have demonstrated superior long-term efficacy, in addition to greater safety. This includes fibromyalgia, pelvic pain syndromes, irritable bowel disease, chronic non-structural back pain, other non-specific musculoskeletal disorders and headache. Recent evidence-based guidelines for these conditions emphasize avoiding opioids.
- 2) ER/LA versus IR opioids. Evidence increasingly suggests that when opioids are required A) intermittent IR opioid therapy at low doses is often sufficient, B) tolerance, dependence and dose escalation are more likely to arise with continuous (round-the-clock) opioid therapy than with intermittent therapy. Tolerance and dependence reduce efficacy and increase risk. Many clinicians are under the false impression that physiological dependence is benign and that opioids can be easily tapered. REMS education should help correct this serious misunderstanding. It is well established that daily long-term use and higher dose therapy are associated with greater risk, including greater risk for addiction and death.
- 3) Evidence suggest that children and adolescents are at greater risk of developing future misuse and addiction when exposed to addictive drugs, even when the exposure is brief and for acute pain, such as after dental extraction. Young people have a greater range of options for treating pain without the need to resort to opioids.
- 4) While close monitoring of patients using opioids is essential, due to inherent risks of overdose, physiological dependence and prescription opioid use disorder, there is no evidence that recommended monitoring practices, including risk screening, treatment agreements, urine drug screening and regular follow-up visits, are effective in reducing risks of overdose or prescription opioid use disorder. There is evidence that reducing opioid prescribing and lowering opioid doses can reduce risks of prescription opioid use disorder and opioid overdose.

In summary, we believe a prescriber education effort to improve outcomes for patients with pain will be ineffective unless past misinformation on risks and benefits are explicitly and forcefully corrected.

Prescribers are in need of education that will allow them to properly weigh risks versus benefits before prescribing opioids. An educational effort that fails to do this and instead continues to equate treatment of pain with a prescription for opioids is likely to worsen rather than improve the opioid crisis.

Until opioids are prescribed more cautiously it will not be possible to bring the opioid addiction epidemic under control. In 2011, FDA disregarded concerns of experts about its REMS Blueprint and an opportunity to promote more cautious prescribing was lost. Over the past 6 years, opioid overprescribing has led to many lost lives and many new cases of addiction. We hope FDA gets it right this time.

Sincerely,

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