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Prescribing Intervention – Exploring a Strategy for Implementation

Comments from the American Academy of Pain Medicine

Docket No. FDA-2017-N-6502

The American Academy of Pain Medicine (AAPM) is extremely appreciative of this major effort on the part of the Food and Drug Administration (FDA) to address the opioid crisis in America, and we recognize that this is a particular challenge given the limitations of the enabling legislation under which FDA operates.

However, we are concerned that these limitations diminish the ability of FDA to be effective in this effort. Because FDA can only regulate the manufacturers/purveyors of drugs and not the prescribers, the interventions are indirect and depend heavily on those who bear some responsibility for the epidemic they are now asked to solve. We lack confidence that businesses dependent on opioid prescribing are the optimal agents to correct overprescribing. That concern is present throughout our discussion of this issue and will not be reiterated in our comments on each of the eight questions provided to us.

1. If a REMS were to specify threshold drug amounts for opioid analgesic prescriptions above which prescribers would be required to provide additional documentation of medical necessity, what should the amounts be and how should they be determined for various clinical indications?

Response:
Different types of pain must be addressed separately. Multiple guidelines, state legislatures, and medical boards have made opioid dosing recommendations concerning acute and chronic non-cancer pain. They have acknowledged that there is no inflection point at which dosing abruptly becomes more hazardous, and that all such recommendations are of necessity arbitrary.

The concern of the Academy is that any rule be predicated on the fact that patient variability is marked. People differ in opioid metabolism, opioid receptors, and psychological strengths and vulnerabilities. Diseases differ in their opioid responsiveness and expected duration. Therefore, a prominent feature of any rule must be ease of allowing for exceptions, which should never be more difficult than documentation of diagnosis or reason for exception on the prescription. In no case should conformity be

attained through erecting burdensome barriers which disincentivize the treating of patients with pain. Preauthorization requirements are a classic example of this.

The Academy is also concerned that use of arbitrary dose thresholds may lead to stigmatization of high dose patients or inappropriate scrutiny of prescribers. For example, specialists in Pain Medicine predominantly see patients who have failed usual treatments and therefore may require more aggressive treatment than regulations based on average patient need would allow.

a. Although acute pain can result from situations ranging from dental extraction to major traumas, the Academy believes that a 7-day supply of opioids is sufficient for a large majority of patients, so long as exceptions are provided for.

b. The evidence supporting opioid treatment of chronic non-cancer pain is meager, and that supporting appropriate long-term dosing is nonexistent. Doses in the range of 80-120 MME (daily oral morphine milligram equivalents) have been widely recommended as appropriate, based primarily on concerns of hazards. The Academy would support a dose of 100 as reasonable, so long as higher dosing is available to those who have shown clear benefit from the treatment. Documentation that the patient has demonstrated reduced pain and increased function should suffice to demonstrate benefit.

Any restriction on maximum daily opioid dosing must be accompanied by education on the need and technique for compassionate tapering of patients who present taking higher doses and on the inappropriateness of sudden discontinuation.

2.

a. If such measures were required, how should prescribers be made aware of them?

Response:
The Academy lacks expertise in this question; however, numerous methods are currently available, including letters to DEA registrants and calls from pharmacists.

b. Within the Agency's statutory REMS authority, how should the Agency require sponsors to ensure compliance with them?

Response:
Prescriptions for doses or durations that exceed the threshold could be denied at the pharmacy unless a) the prescription documented the reason for an exception or b) the physician described such circumstance by phone annually or c) the patient can present a pain contract or agreement dated within 12 months documenting current dosing.

c. How should the Agency require sponsors to assess their effect in reducing misuse, abuse, and new addictions?

Response:
It is not advisable to delegate this task to sponsors.

3. [Should the Agency] consider requiring sponsors to create a system that utilizes a nationwide prescription history database to facilitate safe use of opioid analgesics?

Response:
With regard to PDMP implementation and requiring sponsors to develop a national database or PDMP, AAPM is optimistic regarding the current development of state PDMPs, despite some limitations that could be addressed with greater funding and standardization.

PDMPs have demonstrated benefits for providers including improved ability for a physician to more easily and accurately monitor scheduled prescription refills, identify patterns of abuse so prevention, intervention and treatment can occur, combat "doctor shopping," and help providers avoid potential drug-drug interactions. And while data shows that use of PDMPs, as measured by the number of annual queries has greatly increased, greater use, modernization, innovation and improved access is still needed, in some states more than others.

For example, in the state of Washington, there were 4.2 million queries by medical prescribers, their delegates, and pharmacists in 2016 (seven times more than in 2012). The Washington State PDMP has been part of the solution to decrease diversion, over-prescribing and prescription opioid-related overdose deaths. The state is expanding its program by integration with an Emergency Departments alert system, establishing overdose notifications to prescribers, and periodic individual provider reports around their prescribing practices.

Other state PDMPs can meet similar challenges, but they need more support in getting more prescribers registered and querying their systems more frequently.

With regard to limitations, the existing state PDMP map is a patchwork, lacking consistency in schedules reported, access permissions, inter-state data sharing, and ease of access within EHRs. Use varies dramatically. For example, there were over 24 million annual queries in Ohio compared to less than a quarter of a million in North Carolina. Typically, providers can access data from some, but not all neighboring states. There have been recent successes of *PMP Interconnect* which now includes 43 states sharing data.

In the best-case scenario, standardization of existing state-based PDMPs should be the focus prior to considering or undertaking development of a national database or PDMP.

Standardization should include:
1) Mandatory checks in certain clinical situations (i.e. new starts, conversion to chronic use, aberrant behaviors), but in other situations the decision should remain in the hands of the physicians who are most familiar with patient risk factors
2) More seamless EHR integration and ease of PDMP registration (possibly through state licensing renewal processes)
3) Inter-state access and interoperability
4) Ability for providers to more easily delegate access to their office personnel

Finally, funding is an obvious critical need to improve state PDMPs. NASPER was reauthorized as part of CARA legislation in 2016 and was funded indirectly through the 21st Century CURES Bill. It remains unclear how much money was allocated directly to PDMPs. AAPM recommends new funding for PDMPs based on individual state agency needs, not those of local law enforcement. Funding could come

through specific NASPER appropriation or through block grants mixed with other treatment programs or initiatives.

4. If this approach were adopted, how should the Agency require sponsors to assess the impact of such requirements?

Response:
We do not find a reason to delegate this task to sponsors, and we note that numerous agencies already collect data on admissions for addiction, ED visits for overdose, drug-induced poisoning, and other metrics which are likely to detect changes subsequent to implementation of a national PDMP.

5. Consistent with its statutory authority, should FDA require sponsors to take additional measures to ensure that health care providers, their patients, and patient caregivers and family members are educated on safe storage and disposal and the risks of misuse, abuse, and addiction associated with opioid analgesics (e.g., a public health campaign targeted at these groups)?

Response:
Sponsors may have historically minimized the risks of opioids, especially tolerance and addiction, while exaggerating the benefit. It seems imprudent to entrust them with education.

They could be required to provide education regarding storage and disposal.

However, the Academy supports the need for an aggressive public education campaign concerning the risks and likely benefits of opioids. Such a campaign was effective in reducing tobacco use and thereby saved many lives. It is a reasonable way to counteract the unrealistic expectations which citizens have been encouraged to have regarding the ability of opioids to combat the “epidemic of chronic pain.”

A larger issue is that pain is also of epidemic proportions, involves many complex conditions, and requires a large number of therapeutic options for optimal management. The need for education into the nature of pain and its management is at least as great as the need to teach about opioids, which are often ineffective and almost always insufficient. The universal response to cautions about opioids is, “If not opioids, then what?” Opioid sponsors are ill-equipped to answer this.

6. Should the Agency consider additional measures intended to improve the safety of patient storage and handling of opioid analgesics?

Response:
We believe that every pharmacy that sells controlled substances should have some means (for example, a locked box bolted to the floor with a slot on top) to provide for convenient disposal and that should be available whenever the store is open.

7. How might use of unit-of-use packaging play a role in encouraging appropriate prescribing of opioid analgesics?

Response:
The Academy lacks expertise in this question and offers no opinion.

8. Should the Agency require sponsors to create a mechanism by which patients could return unused pills, and if so, to whom?

Response:
See answer to #6.

In addition, other technology should be encouraged, e.g. Walgreen's system for rendering medications inert or unusable and which is to be available at no cost.

AAPM appreciates this opportunity to contribute to this issue of major importance to the nation, treatment providers, and especially to those in pain.

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About AAPM

The American Academy of Pain Medicine is the premier medical association for pain physicians and their treatment teams with some 2,000 members. Now in its 34th year of service, the Academy's mission is to optimize the health of patients in pain and eliminate pain as a major public health problem by advancing the practice and specialty of pain medicine through education, training, advocacy and research. Information is available on the Academy's website at www.painmed.org.

Submitted by AAPM on March 16, 2018