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MEDICAL LEGAL

Perceived "War on Doctors" Nearing 100 years: PART II (1990s - 2011)

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PART I of this article described the ongoing war on drugs, doctors and patients in the United States which began about 100 years ago. Law enforcement efforts to prevent diversion and abuse of opioid analgesics are important and necessary, but they should not be so restrictive as to interfere with medical practice and patient care resulting in under-treatment of pain. A balanced approach is necessary to resolve these two co-occurring serious public health problems. This PART II article discusses the current 21st century pain management policies which are aimed at a balanced approach to prescribing opioids, and describes the latest administrative regulation confronting physicians - namely, the Food and Drug Administration (FDA) Risk Evaluation and Mitigation Strategy (REMS) for oipoid medications.

PAIN MANAGEMENT POLICIES

Pain management is governed by three types of interrelated policies:

1. **Law** – refers to rules of conduct with binding legal force adopted by a legislative or other government body.
2. **Regulation** - is issued by an agency of the executive branch of government pursuant to statutory authority and has legal force.
3. **Guideline** – has no binding legal force. It is issued by a government agency or a non-governmental organization to express the attitude about, or position on, a particular matter.

PRINCIPLE OF BALANCE[2]

The purpose of pain management laws, regulations and guidelines is essentially two-fold: Drug Control and Drug Availability. Drug refers to a legally approved medication.

1. **Drug control** by law enforcement is aimed at preventing diversion and abuse of prescription medications.
2. **Drug Availability** to patients, on the other hand, recognizes that many opioids and other controlled substances are necessary for pain relief and that governments must ensure their adequate availability for medical prescribing, dispensing and scientific purposes.

When ***both*** drug control and drug availability are appropriately recognized in public policy, and implemented in everyday pain management practice, this is referred to as the **principle of balance** or a **balanced approach.**

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Review of Pain management in the U.S. during the past 176 years reveals an imbalanced approach in favor of drug control and the war on drugs, doctors and patients. Compounding the problem is the fact that the availability of opioid prescription drugs to alleviate the pain and suffering of some patients neither have been *appropriately* recognized in public policy nor *implemented safely in everyday pain management practice*. The result has been under-treatment of pain, because physicians feared prosecution and utter devastation.

2011 PRESCRIPTION DRUG ABUSE PREVENTION PLAN[3]

In April 2011, in an attempt to achieve a more balanced approach, the Obama Administration unveiled a Prescription Drug Abuse Prevention Plan which expands upon the Administration's *National Drug Control Strategy*. The plan comprises four major action areas:

1. **EDUCATION**. Education of the public and healthcare providers about the dangers and safe use of prescription drug abuse;
2. **MONITORING**. Implement prescription drug monitoring programs (PDMPs) in every state, share data across states and have healthcare providers use them. PDMP is an extremely important component of the Prescription Drug Abuse Prevention Plan which targets "doctor shoppers" and "pill mills". It is aided by the implementation of the Electronic Health Records, thereby facilitating the sharing of information among states and prescribers.
3. **ENFORCEMENT**. Provide law enforcement agencies with support and the tools they need to expand their efforts to shut down "pill mills" and stop "doctor shoppers";
4. **DISPOSAL**. Development of consumer-friendly and environmentally-responsible prescription drug disposal programs to limit the diversion of drugs. Indeed, the Drug Enforcement Administration (DEA), in conjunction with state and local law enforcement agencies throughout the United States, conducted the first ever National Prescription Drug Take Back Day in September 2010, and the second in April 2011. The purpose of this National Take Back Day is to provide a venue for persons who wanted to dispose of unwanted and unused prescription drugs. This effort has been a huge success in removing several hundred tons of potentially dangerous prescription drugs, particularly controlled substances, from patients' medicine cabinets.

PAIN MANAGEMENT GUIDELINES

Around the latter part of the 20th Century and the beginning of the 21st Century, several studies by both individuals and groups began identifying regulatory impediments to pain management in state policies, leading to inadequate pain management. In response to the imbalanced approach to the pain problem, numerous pain management recommendations, guidelines and policies have been introduced during the past two decades including among others:

- Medical board guidelines or policy statements concerning pain management ;
- Federation of State Medical Board (FSMB) - Model Guidelines;
- Joint commission on accreditation of healthcare organizations;
- Agency for Health Care Policy and Research (AHCPR) Guidelines for Cancer pain management;
- American Academy of Orofacial Pain;
- American Academy of Pain Management (AAPM);
- American Chronic Pain Association;
- American Headache Society;
- American Pain Foundation;
- American Pain Society (APS);
- American Society of Addiction Medicine;
- American Society of Regional Anesthesia and Pain Medicine;
- International Association for the Study of Pain;
- The American Cancer Society;
- The Institute of Medicine;
- Te National Institutes of Health;
- The International Narcotics Control Board (1996); and
- The World Health Organization (WHO).

The WHO, the APS/AAPM and other organizations acknowledge that opioids are an essential treatment option in the management of patients with moderate to severe pain. They also acknowledge that opioids are associated with significant risks including misuse, abuse, addiction, and overdose.

The impact of the pain management guidelines has been profound. Terms used in pain management have been clarified, such as addiction, dependence, tolerance and pseudo-tolerance. Intractable Pain Statutes have been enacted, wherein a physician may prescribe or administer controlled substances to a patient in the course of the physician's treatment of that patient for a diagnosed medical condition causing intractable pain. And, no physician shall be subject to disciplinary action by the medical board for prescribing or administering controlled substances in the course of treating the person for intractable pain. Other state statutes and regulations have been revised to accommodate the new guidelines.

Pain management guidelines and the new statutes and regulations have delineated the physicians' duties and responsibilities when treating patients with chronic cancer and non-cancer pain. The FSMB Guidelines, which have been adopted by all state medical licensing boards, require physicians to obtain:

1. History/physical examination;
2. Treatment plan with objectives;
3. Informed consent of patient and a pain contract;
4. Periodic review and follow up, with outcome data documenting pain levels, level of function, and quality of life;
5. Consultation or referral;
6. Accurate and complete records; and
7. Compliance with controlled substances laws and regulations.

Pain Management Guidelines have also recommended that physicians who are involved in treating chronic pain should complete a certain number of hours of approved CME on pain management and end-of-life care, as a requisite for licensure. This required physician education in pain management has been enacted by statute in some states, for example California and Florida.

RISK EVALUATION AND MITIGATION STRATEGY (REMS)[5]

Law enforcement of opioids and specifically the control of prescription drug abuse have been of great concern to the U.S. beginning in the 19th century. The 100-year-war on drugs is ongoing and has no end in sight. In the early 21st century, prescription drug abuse is the Nation's fastest-growing drug problem. Law enforcement views "Pain Management" with opioids as a public health and public safety crisis because of its potential for diversion, abuse, morbidity, and mortality.

The FDA Amendments Act (FDAAA) of 2007[6] gave the FDA the authority to require Risk Evaluation and Mitigation Strategy (REMS) as part of the ongoing evolution of managing risk. REMS are FDA-mandated requirements to minimize the risks associated with certain medications. An important part of the REMS program is the requirement that drug manufacturers thoroughly ***educate*** Health Care providers (HCP) and the Public about their drugs.

1. The REMS program focuses on drugs or biologics that have a known or potential safety risk. REMS may be required by the manufacturer prior to approval of a drug or post-approval if new safety information becomes available or if it is determined that REMS is necessary to ensure that drug benefits outweigh risks.
2. REMS can be mandated for any medication or class of medication.
3. REMS may include medication guides and Patient Package Insert, communications to healthcare providers, information to patients, elements to assure safe use, and implementation systems to assure safe use.
4. The goal of the opioid REMS is to ensure balance between appropriate access to opioid therapy and risk mitigation.

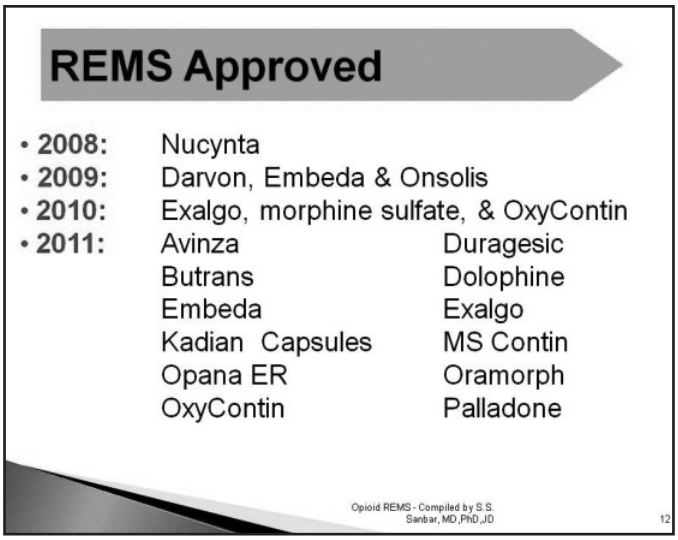
From the FDA side, the REMS programs are intended to formalize ways to minimize the opioid risks while maintaining access for patients who need opioid medication.

From the medical side, Good medical practice requires physicians to maintain the balance of benefits and risks of opioids by:

1. Screening all patients and monitoring them for signs of abuse and addiction;
2. Using an opioid agreement and keeping detailed prescribing records; and
3. Reminding patients/caregivers to take their medication only as prescribed and to protect their prescriptions against accidental use, theft, and misuse.

Certain opioid analgesics will be required to have REMS.[7]

- All extended-release oral opioid analgesics:
  1. Hydromorphone
  2. Morphine
  3. Oxycodone
- Methadone and Transdermal fentanyl



By the end of 2008 there was one approved opioid REMS for Nucynta (tapentadol) which is in a group of drugs called narcotic pain relievers. It is similar to morphine and is used to treat moderate to severe pain. Three REMS were approved in 2009 for DARVON, EMBEDA® (morphine sulfate and naltrexone hydrochloride), and Onsolis (Fentanyl Buccal, Transmucosal) bringing the total at the end of 2009 to four. By 2010, a total of seven drugs required REMS, and in early 2011, the number reached 12 **(See Figure)**.

The Opioids used for moderate-to-severe pain can be classified into various categories:

1. Long-acting opioids (LAOs) including extended-release opioids Longer onset and longer duration of analgesia
2. Short-acting opioids (SAOs) -
   a. Traditional short-acting opioids have an onset of 30–45 minutes and a shorter duration of analgesia
   b. Rapid-onset opioids (ROOs) have an onset of 15 minutes or less and a shorter duration of analgesia

The FDA discussion has centered on the long-acting opioids class-wide REMS. The REMS requirements for ROOs are under review. The FDA has not required class-wide REMS for other Short-acting opioids.[8]

There are five different components for a drug REMS:

1. **Medication Guide/PPI** (patient package insert) - Educational tools provided to each patient when the drug is prescribed / dispensed.
2. **Communication Plan** - such as letters to healthcare providers, communications to professional societies, professional education, etc.
3. **Elements to Assure Safe Use** (ETASU) - Special requirements or restrictions to optimize safe use of products.
4. I**mplementation System** - System to monitor, evaluate, and improve elements to assure safe use.
5. **Timetable for Assessment** - Minimum FDA requirement 18 months, 3 years, and 7 years after REMS approval. This element is the only compulsory element for all REMS programs.

An individual program does not have to include all five components. Of the five components, the two that are most relevant to prescribers are the Medication Guide/PPI, and Elements to Assure Safe Use (ETASU). ETASU may be required if the drug is associated with a serious adverse event and the medication guide, Patient Package Insert, or communication plan plus assessment are not sufficient to mitigate these risks. ETASU may require any of the following:

1. Training / certification of prescribers (Doctors, Physician Assistants, Nurse Practitioners);
2. Training / certification of pharmacists / pharmacies;
3. Restrictions on where the drug is dispensed;
4. Evidence of patient safe use conditions;
5. Patient monitoring;
6. Enrolment of patients in a registry.

COMMUNICATION

The American Society for Automation in Pharmacy (ASAP) has announced a new version of its widely used standard for prescription-monitoring programs (PMPs). This new Standard for Real-Time "Safety Adjudication" for REMS ETASU Programs based on the current American Society for Automation in Pharmacy (ASAP) Prescription Monitoring Program (PMP) transaction that is widely used today. The latest version follows the design and syntax of the 2005 ASAP standard, but it has been enhanced to allow for more precise reporting of controlled substances and other drugs required by state reporting programs. This new communication standard is designed to support the various Elements to Assure Safe Use (ETASU) requirements of a REMS program. It is designed to minimize software development time and time to market.

HOW TO LOOK UP ONLINE OPIOID REMS

OxyContin is used in this example.

- First, type in and search (Google or Bing) for "Oxycontin REMS", then login to obtain the Home page for Oxycontin REMS.
- There are two links on the Home Page:
  1. For Patients & Caregivers;
  2. For Healthcare Professionals.
- Click on "For Health Professionals" and you will find three links which you should open individually and read:
  1. Dear Healthcare Professional Letter;
  2. Healthcare Provider Training Guide;
  3. Education Confirmation Form.
- You will also find two other items:
  1. IMPORTANT SAFETY INFORMATION WARNING: IMPORTANCE OF PROPER PATIENT SELECTION AND POTENTIAL FOR ABUSE;and
  2. Please go to http://www.purduepharma.com/pressroom/news/OxycontinPI.pdf for Full Prescribing Information.

HEALTHCARE PROFESSIONAL LETTER

By clicking on the "Dear Healthcare Professional Letter" from the Manufacturer, the letter re-iterates the purpose of the REMS, the goals to EDUCATE both the physicians and patients about the benefits and risks of the drug, prescribing and dispensing information, misuse and abuse, patient counseling and the four contents included in the packet.

TRAINING PROGRAMS

There are two types training programs, one Online and the second by print. Physicians who prescribe opioids are required to "Complete Training Program" for each drug that they prescribe which has a REMS approved. In addition, the

physician is required to complete the "Education Confirmation Form", which comprises exam questions, and mail to the manufacturer.

HOW TO GET READY FOR REMS

1. Coordinate the office, clinic and pharmacy policies by reviewing your current standard operating procedures and staff roles to prepare for more interaction with staff, patients, and pharmacists and for potential new documentation requirements with REMS.
2. Ensure that you understand the federal and state regulations on prescribing opioids. Note that the drug REMS is in addition to, and not a replacement for, federal and state regulations.
3. Visit the National Association for State Controlled Substances Authority[9] to find links to access a state's profile. The profile contains information and additional links to the state's controlled substance regulatory functions.
4. Visit the DEA Website for controlled substance policies.[10]

PATIENT COMMUNICATION

Enhance Communication with patients. Explain that REMS are coming and that there may be new requirements with their opioid medications.

SIX STEPS TO ZERO[11]

The following are six recommendations that should be communicated to patients who are treated with controlled substances.

1. Never take a prescription painkiller unless it is prescribed to you.
   Everyone responds differently to pain medications. What is safe for one person may not be safe for another.
2. Do not take pain medicine with alcohol.
   Never mix the two; it is a dangerous combination that can be deadly. Alcohol increases the toxicity of pain medication.
3. Do not take more doses than prescribed.
   Even after the effects of pain medicine seem to have worn off, it is still depressing the respiratory system. The body must develop a tolerance to the respiratory depressant effects before the dose can be increased.
4. Use of other sedative or anti-anxiety medications can be dangerous.
   Combining pain medicines with other sedative drugs, such as valium, can increase the toxicity of the pain medication. Only take other medications, if directed by the prescribing doctor.
5. Avoid using prescription painkillers to facilitate sleep.
   Prescription pain medications can suppress respiration during sleep. Speak to your physician about safe methods to manage pain during sleep.
6. Lock up prescription painkillers.
   If consumed by children or other family members, or stolen and sold on the street, prescription pain medicine can kill.

SUMMARY

The ongoing 100-year-war on drugs, doctors and patients has no end in sight. Pain management stakeholders in the 21st century have been attempting to achieve a balanced approach to drug control and availability through guidelines, law and regulation. The FDA REMS program is the latest federal regulation. The FDA has proposed a class-wide REMS program for long-acting opioids. There is no class-wide REMS for short acting opioids as yet, including rapid onset opioids. In the foreseeable future, physicians will be required to learn not only the new opioid regulations and REMS, but also may be required to take special postgraduate continuing medical education to demonstrate competency in prescribing opioid medications, as a requisite for DEA licensing and in some states state medical licensing.

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