
Risk Evaluation and Mitigation Strategies (REMS): Fundamental Issues

Nathaniel Katz, MD, MS
Tufts Health Care Institute
Program on Opioid Risk Management
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What Problem are We Trying to Solve?

- Prescription opioid deaths: 8500/yr
 - Alcohol co-ingestion
 - Inappropriate patient selection, prescribing errors, misuse, abuse
- Addiction: 1.7 million in US
- Pediatric exposure: >1000/yr
- High rates of injection diseases among prescription opioid abusers
- \$12 billion annual US cost

Are we the only industry that
accepts imposing solutions without
ever defining the problem?

REMS vs. PLAS

- REMS could potentially mean ANY strategy to address prescription opioid risks
- In fact REMS has been used primarily to refer to a Performance-Linked Access System where access is linked to prescriber and patient training
- This is necessary but not sufficient to reduce prescription opioid risks

US Strategy to Reduce Prescription Opioid Risks

- **Universal mandatory training on safe opioid prescribing for clinicians**
- **Universal mandatory training on safe opioid use for patients**
- **Modernize Prescription Monitoring Programs and their use**
- **Mandatory insurance reimbursement for safe opioid prescribing practices**
- **Substance Abuse Treatment Hotline**
- **Targeted research on root causes of prescription opioid overdoses**
- **National media campaign modeled after smoking**
- **Update data collection systems on opioid misuse, abuse, and diversion**
- **Serialized tamper-resistant prescriptions in every state**
- **Mandatory random drug screening in schools with appropriate resourcing**
- **Pharmacy-based pharmaceutical disposal programs**
- **Incentivize development of abuse-deterrent opioid formulations**
- **Lockboxes for home medication storage**
- **Portable child-proof senior-friendly medication dispensers**
- **Microscopic barcoding of individual dosage units**

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FDA and REMS

- “Prescription opioids are at the center of a major public health crisis of addiction, misuse, abuse, overdose, and death
- The current strategies for intervening ...are inadequate
- The risks must be addressed
- New authorities under FDAAA
- We recognize the challenge
- We expect all companies ...to work with us to get this done expeditiously
- ***“If not, we cannot guarantee that these products remain on the market”***

Rappaport BA. *REMS for Opioid Analgesics: How Did We Get Here? Where are We Going?* FDA meeting of manufacturers of ER Opioids, FDA White Oak Campus, Silver Spring, MD. March 3, 2009.

What has failed?

- Treatment guidelines
- Voluntary education
- Self-policing by medical profession
- Risk management
- Surveillance
- Current research paradigm

“The definition of insanity is doing the same thing over and over again and expecting different results” – A. Einstein

The Legislation

505-1(f)(3) (The Elements)

- Training/certification of HCPs and dispensing organizations
- Dispensing under safe use conditions
- “Each patient must be subject to monitoring”
- “Patients must be enrolled in a registry”

505-1(f)(4) (Implementation System)

- **Must monitor and evaluate implementation of The Elements**
- Must work to improve implementation of such elements

Axelrad J. Title IX of FDAAA: REMS Authorities. FDA meeting of manufacturers of ER Opioids, FDA White Oak Campus, Silver Spring, MD. March 3, 2009.

Registries: Verification Methods

Product	Indication	Distribution Agent	Verification Method
Nplate	ITP	Distributor	Specialty pharmacy verifies provider and patient enrollment and notifies distributor to ship drug directly to provider
Promacta	ITP	Manufacturer	Pharmacy verifies provider and patient enrollment by calling a 1-800 number and processes order through their normal distributor or wholesaler., which forwards request to GSK. GSK verifies pharmacy enrollment and then ships to pharmacy
Letairis	PAH	Specialty	Specialty pharmacies receive and process prescriptions and send drug directly to patient
Tikoskyn	Atrial fib.	Manufacturer	The pharmacist verifies prescriber enrollment via IVRS or website, orders drug through wholesaler, which sends request to Pfizer. Pfizer verifies pharmacy status and ships to pharmacy (usually inpatient). Product is not actively marketed by Pfizer.
Entereg	GI recovery	Wholesaler	Hospital pharmacy orders product, via wholesaler. Wholesaler verifies enrollment of hospital pharmacy and ships to hospital .
Tysabri	MS	Specialty / Wholesaler	Infusion center orders product via a registered pharmacy or wholesaler., which verifies provider, patient, an infusion center enrollment before shipping to infusion center
Accutane	Acne	Retail	Pharmacist obtains authorization from iPledge and writes authorization number on prescription and dispenses to patient
Suboxone	Opioid dependence	Retail	Pharmacist verifies prescriber enrollment by looking at DEA number (specially modified with an X), logging onto website, or calling 1-800- ¹⁰ number and dispenses to patient

Successful REMS Requires:

- Root cause analysis of the problem
- Clear determination of exactly what we want prescribers to do
- Clear determination of exactly what we want patients to do
- Clear determination of exactly what we want pharmacists to do
- Efficient and effective method to shape behavior
- Efficient method to assess training status prior to dispensing
- A credible method for evaluating positive and negative impact of programs

Core Meeting Deliverables

- Proposal for core safe opioid prescribing practices
 - Principles for changing prescriber behavior
- Proposal for core safe opioid use practices among patients
 - Principles for changing patient behavior