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The Physician's Perspective:
Abuse-Deterrent Opioid Formulations

DECEMBER 2014

ABUSE-DETERRENT OPIOID FORMULATIONS: PROMISING TECHNOLOGY, UNIQUE CHALLENGES

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Prescription pain medications such as opioids offer important treatment options for people with severe pain, often providing relief and allowing some to resume their daily activities. Unfortunately, these drugs can be misused, abused, or diverted to others for illicit use—problems that have become pervasive across the country. Each year approximately 4.5 million Americans use prescription pain medications for nonmedical purposes,[1] contributing to more than 16,000 deaths annually.[2]

Comprehensive approaches must combat the misuse and abuse of prescription pain medications while maintaining access for patients who need them. As one component of this overall strategy, new drug formulations offer promising deterrents against certain types of abuse. Designed to make pills more difficult to crush or melt, abuse-deterrent formulations can impede the intense high that abusers and addicts seek through manipulating the medication.

In response to the prescription drug abuse crisis in the US, the Office of National Drug Control Policy has set as one of its objectives the development of abuse-deterrent formulations of opioid medications and other drugs with abuse potential.[3] These abuse-deterrent formulations are a welcome advance. But they pose challenging questions about who should receive them, who should pay for them, and whether pharmacists may substitute the traditional formulations. This policy brief provides an overview of recent regulatory guidelines on abuse-deterrent opioid formulations and considers the pressing issues raised by their availability.

FOOD AND DRUG ADMINISTRATION (FDA) GUIDANCE ON OPIOID FORMULATIONS DESIGNED TO REDUCE ABUSE

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The FDA considers abuse-deterrent opioid formulations a priority and has issued a guidance policy for manufacturers seeking to develop such medications.[4] In that policy, the FDA recognizes that abuse-deterrent opioid formulations represent one aspect of a desperately needed, comprehensive program to address prescription opioid misuse, abuse, and diversion.

The FDA guidance document describes the major methods of misusing or abusing opioids and indicates that abuse-deterrent formulations should target one or more of these routes. Table 1.1 categorizes abuse-deterrent formulation designs.

The FDA guidance also sets out the types of studies that demonstrate abuse-deterrent properties, how the studies will be evaluated, and the labeling claims that may be approved based on the studies' results. If the appropriate studies are conducted, products designed with abuse-deterrent properties may be eligible for one of four levels of label claims, as listed in Table 1.2.

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TABLE 1.1

CATEGORIZATION OF ABUSE-DETERRENT FORMULATION STRATEGIES PER FDA GUIDANCE

PHYSICAL/ CHEMICAL BARRIERS	• Physical barriers can prevent chewing or crushing. • Chemical barriers can render the drug useless when exposed to certain liquids.
AGONIST/ANTAGONIST COMBINATIONS	• An antagonist is a chemical that interferes with or reduces the actions of another chemical. Antagonists can be added to the pill along with the opioid medication (the agonist) to defeat the euphoria associated with abuse. • An antagonist may be chemically "hidden" in the pill so that it is released only if the pill is crushed.
AVERSION	• Substances can be combined in the pill to produce an unpleasant effect if the pill is crushed.
DELIVERY SYSTEM	• Drugs can be formulated for delivery in ways that resist abuse, such as sustained-release formulations that are given intramuscularly or as subcutaneous implants.
PRODRUG	• The medication in the pill can be included in a form that is inactive until it is transformed into its active form in the stomach or intestines.

Adapted from US Department of Health and Human Services, 2013[4]

THE PROMISE AND CHALLENGES OF OPIOIDS WITH ABUSE-DETERRENT PROPERTIES

Most agree that abuse-deterrent opioids mark a valuable step in the right direction. Physicians recognize that these formulations may have significant potential for certain patients, such as those who have struggled with addiction or substance abuse in the past, those who live with others who are current or recovering addicts, and those who live with teens or young adults who may seek opioids for recreational use.

Along with their promise for some patient groups, however, these formulations raise several important issues related to prescribing, reimbursement, and generic substitution.

TABLE 1.2

TIERS OF LABEL CLAIMS THAT DESCRIBE PRODUCTS' ABUSE-DETERRENT PROPERTIES

TIER 1	Physical or chemical barriers to abuse
TIER 2	Expected to reduce or block effect of the opioid if it is manipulated
TIER 3	Expected to reduce abuse
TIER 4	Demonstrated reduction for abuse

Adapted from US Department of Health and Human Services, 2013[4]

Prescribing

Who determines which patients need opioid medications with abuse-deterrent properties? Should the physician and patient decide whether to prescribe an abuse-deterrent formulation of an opioid? A thorough assessment of the risk for misuse, abuse, or diversion includes considering both the patient and the people around the patient. To assist the physician, the FDA has mandated a Risk Evaluation and Mitigation Strategy (REMS) that requires manufacturers to offer educational materials for safe use and information on how to recognize misuse, abuse, and diversion.[5]

Reimbursement

New formulations must undergo extensive clinical trials to determine safety and efficacy. This means that opioids with abuse-deterrent properties are much more expensive than generics without abuse-deterrent properties. It seems reasonable that a patient who demonstrates minimal risk for misuse, abuse, or deterrence should not be forced to pay for abuse-deterrent opioid formulations. Alternatively, therapy formulation cost parity should apply to patients with legitimate medical need so they will not be punished with

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higher expenses for opting to use abuse-deterrent formulations. For abuse-deterrent products to be widely adopted, insurers and pharmacy benefits managers must provide affordable coverage. Over the next year, it is anticipated that several states will consider legislation related to this issue.

Pharmacy Substitution Policies

The availability of abuse-deterrent opioid formulations also raises the issue of pharmacy substitution policies. Clearly, if a physician prescribes an abuse-deterrent opioid formulation, the pharmacist, insurance company, or pharmacy benefit manager should not be allowed to substitute a generic without abuse-deterrent properties.

Pharmacists should be allowed, however, to substitute the same medication in an abuse-deterrent preparation without physician approval, but only if there is no increased cost to the patient. However, if the pharmacist recommends a substitution from an abuse-deterrent to a generic without abuse deterrence, the physician must approve. These policies acknowledge the pharmacist's importance but prioritize the patient-physician relationship in determining which treatment is best for which patient. Physicians are uniquely qualified to make these decisions based on their training and their knowledge of the patient, his or her medical history, and comorbidities.

CONCLUSIONS

Opioids with abuse-deterrent properties represent an important component of a desperately needed, overarching strategy to address prescription opioid misuse, abuse, and diversion. For certain patient groups, these formulations offer significant potential to curb abuse.

The availability of these new formulations raises questions about who should receive them, who should pay for them, and whether a pharmacist may substitute a generic. These issues must be addressed to ensure that patients who use these medications are not subjected to extra charges or medication substitution without the knowledge or consent of their physician. What is best for the patient and the physician-patient relationship must take priority as regulators and legislatures consider policies pertaining to abuse-deterrent medications.

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