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ACMT Position Statement:

Mifepristone and Misoprostol are Not “Controlled Dangerous Substances”

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The position of the American College of Medical Toxicology (ACMT), endorsed by the American Academy of Clinical Toxicology (AACT), is as follows:

Introduction

In May 2024, the Governor of Louisiana signed into state law an act that classified mifepristone and misoprostol, as Schedule IV “controlled dangerous substances”.¹ Under this law, these medications are classified in a similar manner to medications at risk for addiction, misuse, and diversion, such as benzodiazepines and certain opioid analgesics. As such, possession or distribution of mifepristone and misoprostol without a prescription is now considered a felony, with significant legal implications, including monetary fines up to \$15,000 and up to 10 years in prison.² While the law in Louisiana is the first of its kind, other states may consider similar laws. Although these drugs will be classified as controlled dangerous substances, they do not meet the definition or intent of what a controlled substance is, and categorizing them as such can lead to harm.

Controlled Dangerous Substance Definition

According to the Controlled Substances Act (CSA), substances are regulated and placed into a specific schedule based on the compound’s medical indications and potential for dependence and abuse. Controlled substances are placed in one of five schedules based on certain criteria (Table).³

Table: Factors used to determine schedule (CSA)

- Actual or relative potential for abuse
- Scientific evidence of its pharmacologic effect

- Current knowledge regarding the substance
- History and pattern of abuse of the substance
- Scope, duration, and significance of abuse
- Risk to public health
- Psychic or physiologic dependence liability
- If the substance is an immediate precursor to another controlled substance

Five schedules are used to classify controlled substances. Schedule I substances, such as heroin, have no accepted medical use with significant abuse liability. The remaining schedules include substances that have recognized medical indications, but various degrees of misuse or addiction liability. Specifically, Schedule IV medications (which include benzodiazepines and certain opioid analgesics) have some potential for abuse or dependence, but less so than Schedules II and III.⁴ While the Supreme Court has allowed for both federal and state regulation of controlled substances, state laws rarely depart to such an extent from federal guidance and scientific evidence.

Mifepristone and Misoprostol

Mifepristone and misoprostol are the most common medications used for medication abortion in the U.S. and worldwide.⁵ They are also used for management of early pregnancy loss and other indications.⁶ Misoprostol (a prostaglandin analogue) is indicated for prevention of peptic ulcer disease, although more commonly is used to induce labor and for postpartum hemorrhage.^{7,8} Mifepristone (a progesterone antagonist) is indicated for management of hyperglycemia in certain patients with Cushing's syndrome.⁸ Both medications have been approved by the Food and Drug Administration (FDA) for decades and are safe and effective for their intended use. Neither medication has misuse or addiction potential (and there are no reports in the medical literature of this), and neither is classified as controlled dangerous substances by the DEA or similar agency outside of the U.S.^{7,9} In fact, mifepristone has been investigated for the treatment of alcohol use disorder.¹⁰ When compared to the criteria for classification as a controlled dangerous substance, it is obvious neither medication meets the definition.

Unintended Consequences

Scheduling of medications as controlled dangerous substances should have a scientific basis and the unnecessary scheduling of these two medications may lead to harm. Illegal possession of mifepristone or misoprostol does not occur under the same circumstances as other Schedule IV substances, yet the penalties are as severe. For example, an individual found in possession of a benzodiazepine or opioid may be misusing the drug for its euphoric effects, whereas this is not the case with either

misoprostol or mifepristone. The significant legal repercussions of possessing mifepristone or misoprostol could lead individuals to use more toxic or less effective medications as alternatives. They may also prevent individuals who experience complications of using these medications regardless of indication, to delay or avoid seeking emergency care.¹¹

Controlled substances also require special storage, ordering, and documentation procedures, which can increase pharmacy workload and may impact patient care. Because controlled dangerous substances need to be stored in a different manner than non controlled medications, it may impact the medications availability in postpartum hemorrhage carts and kits. This could lead to delays in critical medication administration in the setting of postpartum hemorrhage and could lead to adverse outcomes.

In summary, scheduling mifepristone and misoprostol as controlled dangerous substances is not consistent with decades of scientific evidence regarding the safety and misuse and addiction potential of these medications, and may lead to harm. Additionally, it sets a dangerous precedence of politicizing pharmaceutical regulation.

Disclaimer

While individual practices may differ, this is the position of the American College of Medical Toxicology at the time written, after a review of the issue and pertinent literature.

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