Lifting the restrictions on mifepristone during COVID-19: A step in the right direction

The FDA's Elements to Assure Safe Use restrictions mandate in-person distribution of mifepristone at health care facilities. This in-person signature process places women at unnecessary risk during the COVID-19 pandemic.

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Mifepristone is a safe, effective, and well-tolerated medication for managing miscarriage and for medical abortion when combined with misoprostol.[1,2] Since the US Food and Drug Administration (FDA) approved its use in 2000, more than 4 million women have used this medication.[3] The combination of mifepristone with misoprostol was used for 39% of all US abortions in 2017.[4] Approximately 10% of all clinically recognized pregnancies end in miscarriages, and many are safely managed with either misoprostol alone or with the combination of mifepristone and misoprostol.[5]

The issue

The prescription and distribution of mifepristone is highly regulated by the FDA via requirements outlined in the Risk Evaluation and Mitigation Strategies (REMS) drug safety program. The FDA may determine a REMS is necessary for a specific drug to ensure the benefits of a drug outweigh the potential risks. A REMS may include an informative package insert for patients, follow-up communication to prescribers—including letters, safety protocols or recommended laboratory tests, or Elements to Assure Safe Use (ETASU). ETASU are types of REMS that are placed on medications that have significant potential for serious adverse effects, and without such restrictions FDA approval would be rescinded.

Are mifepristone requirements fairly applied?

The 3 ETASU restrictions on the distribution of mifepristone are in-person dispensation, prescriber certification, and patient signatures on special forms.[6] The in-person dispensing requirement is applied to only 16 other medications (one of which is Mifeprex, the brand version of mifepristone), and Mifeprex/mifepristone are the only ones deemed safe for self-administration—meaning that patients receive the drug from a clinic but then may take it at a site of their choosing. The prescriber certification requirement places expectations on providers to account for distribution of doses and keep records of serial numbers (in effect, having clinicians act as both physician and pharmacist, as most medications are distributed and recorded in pharmacies). The patient form was recommended for elimination in 2016 due to its duplicative information and burden on patients—a recommendation that was then overruled by the FDA commissioner.[7]

These 3 requirements placed on mifepristone specifically target dosages for use related to abortions and miscarriages. Mifepristone is used to treat other medical conditions, with much higher doses, without the same restrictions—in fact, the FDA has allowed much higher doses of mifepristone to be mailed directly to a patient when prescribed for different disorders. The American College of Obstetricians and Gynecologists (ACOG) has long opposed the burdensome REMS requirements on mifepristone for reproductive health indications.[8]

Arguments regarding the safety of mifepristone must be understood in the context of how the medication is taken, and the unique difference with other medications that must be administered by physicians or in health care facilities. Mifepristone is self-administered, and the desired

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effect—evacuation of uterine contents—typically occurs after a patient takes the accompanying medication misoprostol, which is some 24 to 72 hours later. This timeframe makes it highly unlikely that any patient would be in the presence of their provider at the time of medication effect, thus an in-person dispensing requirement has no medical bearing on the outcome of the health of the patient.

REMS changes during the COVID-19 pandemic

The coronavirus disease 2019 (COVID-19) pandemic has necessarily changed the structure of REMS and ETASU requirements for many medications, with changes made in order to mitigate viral transmission through the limitation of unnecessary visits to clinics or hospitals. The FDA announced in March of 2020 that it would not enforce pre-prescription requirements, such as laboratory or magnetic resonance imaging results, for many medications (including those more toxic then mifepristone), and that it would lift the requirement for in-person dispensation of several medications.[9] Also in March 2020 the Department of Health and Human Services Secretary (HHS) and the Drug Enforcement Agency (DEA) activated a "telemedicine exception" to allow physicians to use telemedicine to satisfy mandatory requirements for prescribing controlled substances, including opioids.[10]

Despite repeated pleas from organizations, individuals, and physician groups, the FDA continued to enforce the REMS/ETASU for mifepristone as the pandemic decimated communities. Importantly, the pandemic has not had an equal effect on all communities, and the disparities highlighted in outcomes as related to COVID-19 are also reflected in disparities to access to reproductive choices.[11] By enforcing REMS/ETASU for mifepristone during a global pandemic, the FDA has placed additional burden on women and people who menstruate. As offices and clinics have closed, and as many jobs have evaporated, additional barriers have emerged, such as lack of childcare, fewer transportation options, and decreased clinic appointments.

As the pandemic continues to affect communities in the United States, ACOG has issued guidance recommending assessment for eligibility for medical abortion remotely, and has encouraged the use of telemedicine and other remote interactions for its members and patients to limit transmission of the virus.

The lawsuit

On May 27, 2020, the American Civil Liberties Union (ACLU) (on behalf of ACOG, the Council of University Chairs of Obstetrics and Gynecology, New York State Academy of Family Physicians, SisterSong, and Honor MacNaughton, MD) filed a civil action against the FDA and HHS challenging the requirement for in-person dispensing of mifepristone and associated ETASU requirements during the COVID-19 pandemic. The plaintiffs sought this injunction based on the claim that these restrictions during the pandemic infringe on the constitutional rights to patients' privacy and liberty and to equal protection of the law as protected by the Due Process Clause of the Fifth Amendment. Additionally, the ACLU and other organizations said these unnecessary restrictions place patients, providers, and staff at unnecessary risk of viral exposure amidst a global pandemic.

The verdict

On July 13, 2020, a federal court granted the preliminary injunction to suspend FDA's enforcement of the in-person requirements of mifepristone for abortion during the COVID-19 pandemic. The court denied the motion for suspension of in-person restrictions as applied to miscarriage management. The preliminary injunction applies nationwide without geographic limitation. It will remain in effect until the end of the litigation or for 30 days following the expiration of the public health emergency.

What the outcome means

This injunction is a step in the right direction for patients and providers to allow for autonomy and clinical practice guided by clinician expertise. However, this ruling remains narrow. Patients must be counseled about mifepristone via telemedicine and sign a Patient Agreement Form, which must be returned electronically or by mail. Patients must receive a copy of the mifepristone medication guide, and dispensing of mifepristone must still be conducted by or under the supervision of a certified provider. The medication may not be dispensed by retail pharmacies, thus requiring providers to arrange for mailing of prescriptions to patients. Given state-based legal statutes regarding mailing of medications, this injunction may not lead to an immediate increase in access to care. In addition, patients seeking management for miscarriage must go to clinic to have mifepristone dispensed and thus risk exposure to viral transmission.

What now?

The regulation of mifepristone—in spite of excellent safety and specifically for the narrow purpose of administration in the setting of

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abortion and miscarriage care—is by definition a discriminatory practice against patients and providers. As clinicians, we are duty-bound to speak out against injustices to our practices and our patients. At a local level, we can work to implement safe practices in the setting of this injunction and continue to work on a national level to ensure this injunction becomes permanent and with more broad scope to eliminate all of the REMS requirements for mifepristone.

Action items

- Act locally! Are you an abortion provider? Contact your local ACLU or lawyer in your area for assistance navigating the legal landscape to prescribe after this injunction.
- Act statewide! Press candidates in your state to stand up for science and data. Support legislative acts and bills that address combating discriminatory regulations.
- Act nationally! The President is responsible for appointing the Commissioner of the FDA and the Secretary of Health and Human Services (with Senate advice and consent). Who we elect matters. Seek out opportunities to become involved in increasing access to and awareness of voter registration and Election Day, and speak out against voter suppression. Make sure you are always registered to vote and check your area to review new recommendations amidst the pandemic. ●