A Dark Cloud Over U.S. Drug Approval

Mifepristone Case Will Create Chaos in the U.S. Drug Approval Process, Threaten Investment in Innovation, and Take Safe and Effective Life-Saving Drugs Off the Market

PROTECT
OUR CARE

December 2023

Introduction

In 2020, medication abortion accounted for 54 percent of all abortions in the United States. Mifepristone, the drug primarily used for medication abortion, has been safely used since it was approved by the Food and Drug Administration (FDA) in 2000, and the agency has since amended its regulations to increase access to the drug based on robust data demonstrating its safety.

On August 16, 2023, the Fifth Circuit Court of Appeals, in Alliance for Hippocratic Medicine v. FDA brought by anti-abortion advocates, upheld part of a decision by a Texas district court that would severely limit access to mifepristone. The ruling will be most detrimental for women of color, people living in rural areas, and low-income people who face the steepest barriers to accessing care.

While this decision will not take effect until the Supreme Court weighs in, if the Supreme Court upholds the decision, it would severely curtail use of mifepristone, prohibiting its use after seven weeks of pregnancy (before many people even know they're pregnant), banning its prescription via telehealth or through the mail, and possibly require providers to prescribe a less-safe higher dosage, which was the pre-2016 standard of care. If the Supreme Court upholds the 5th Circuit's ruling or requires the withdrawal of mifepristone, the outcome would end abortion access for millions more women in America and throw our drug approval system into chaos by setting a precedent for courts to intervene in our drug approval system for ideological reasons. This outcome would invite additional challenges to the legality of a range of medical innovations based on political or religious objections.

This report details the therapeutic areas at risk of being challenged and pulled from the market if the Supreme Court sets the precedent of allowing courts to overrule the FDA's drug approval decisions.

Therapeutic Areas at Risk

Following the ruling, the Department of Health and Human Services (HHS) Secretary Xavier Becerra stated that the decision "undermines our nation's entire system of drug approval by overriding the scientific, evidence-based decision-making of the FDA." If the ruling is upheld by the Supreme Court, it creates a dangerous precedent to challenge the safety and efficacy of any FDA-approved product. In this report, we describe therapeutic areas that would be at risk of judicial challenge if the ruling is upheld and related implications:

> ***"Today's decision undermines our nation's entire system of drug approval by overriding the scientific, evidence-based decision-making of the FDA."***
>
> - Xavier Becerra, HHS Secretary

Other Abortion Medications

While mifepristone is the primary drug used for medication abortion, opponents could use this ruling to challenge the approval of other prescription drugs related to abortion. Mifepristone is typically prescribed in conjunction with misoprostol for medication abortion, but misoprostol can also be prescribed by itself to carry out an abortion. Research has also confirmed that the misoprostol-only protocol is as safe as the two-medication protocol, and is recommended by professional societies when mifepristone is not available. Anti-abortion activists may also seek to eliminate the use of misoprostol-only abortions, which would effectively eliminate all available medication abortion options.

Contraception

In addition to medication abortion, opponents could use this ruling to challenge the approval of prescription drugs for contraception. For example, Norgestrel, branded as Opill, was approved by

the FDA in July 2023 as the first daily progestin-only oral contraception pill (POP) for use in the U.S. without a prescription. Norgestrel was initially approved for prescription use in 1973 and in 2022 its manufacturer, HRA Pharma, applied to switch the product for use in the nonprescription, over-the-counter, setting to increase access to contraceptive options. The FDA states that POPs have been approved and marketed in the U.S. for close to 50 years and have a well-established clinical profile of safety and efficacy.

In 2022, the National Catholic Bioethics Center urged the FDA to not approve Opill for non-prescription use. The group asserts that making such a product available without a prescription "can only cause avoidable harm, violating the Hippocratic tradition embraced by the FDA." The National Catholic Bioethics Center also states that the "failure rate of the minipill is higher than that of other hormonal contraceptive methods and will result in many unintended pregnancies, leading to potentially more abortions."

Vaccines Opposed By Anti-Vaxxers

While many vaccines have been safely used for decades and are viewed as one of the most important public health tools, the rise of the anti-vaxxer movement threatens to roll back the progress vaccines have made in preventing disease and premature death. If this ruling is upheld, it would set a precedent that would embolden anti-vaxxers to challenge the approval of vaccines, including the following which are commonly opposed by anti-vaxxers:

- COVID-19 Vaccines: The FDA has authorized several COVID-19 vaccines, of which the Moderna and Pfizer vaccines were developed using fetal cell lines. The CDC details that as of March 2023, 672 million doses of COVID-19 vaccine have been administered and have been proven to be safe and effective. The CDC has also collected extensive data on the effectiveness of the vaccines in preventing COVID-19 infection, as well as COVID-related hospitalizations, emergency department visits, and death.
- M-M-R®II, which vaccinates against measles, mumps, and rubella, received FDA approval in 1978, and was recommended for use in individuals 12 months of age and older. The CDC states that one dose of MMR II is 93% effective against measles, 78% effective against mumps, and 97% effective against rubella, and two doses are 97% effective against measles and 88% effective against mumps.
- Varivax, which vaccinates against varicella (chickenpox), was approved by the FDA in 1995 and was subsequently recommended by the Centers for Disease Control and Prevention (CDC)

Advisory Committee on Immunization Practices (ACIP) for pediatric use. Since its approval, Varivax is estimated to have prevented 91 million chickenpox cases, 238,000 hospitalizations, and 2,000 deaths. In 2019, Merck, published a 22-year review of post-marketing safety data, finding that adverse events comprised 0.8 reported per one million doses administered.

The rising anti-vaxxer movement has impacted public views of vaccines and vaccination rates. A 2022 survey found that 71 percent of adults think children should receive the MMR vaccine to attend school, down from 82 percent in 2019. Additionally, 28 percent of adults feel that parents should be able to decide to not vaccinate their school-age children, even if it creates health risks for others, up from 16 percent in 2019. These views have led to measles and chickenpox outbreaks and the vaccination rate for children dipped for the first time in 12 years.

Vaccines and Drugs Developed with Fetal Cell Lines

The following vaccines and drugs were developed by growing the viruses or testing the products in the WI-38, MRC-5, HEK-293, or RA273 fetal cell lines, which were created from aborted fetal tissue. As stated above, while many states already allow religious exemptions for vaccination requirements, opponents may go a step further and call for the approval of such products to be withdrawn, given their linkage to abortions, despite the FDA confirming their safety and efficacy. Below we describe the public health importance and safety of each of these vaccines and drugs.

- Several of the COVID-19 vaccines, M-M-R®II, and Varivax were developed using fetal cell lines. The public health importance of each vaccine is detailed above.
- Havrix and Vaqta, which vaccinate against Hepatitis A, were approved by the FDA in 1995 and 1996 respectively, and are also part of the ACIP-recommended vaccines. Following the approval of the vaccines, the rate of Hepatitis A declined by 95 percent between 1996 and 2011. The

CDC also details that 85 percent of children received their first dose and 76 percent of children received their second dose in 2017. Regarding safety, among the approximately 50 million doses distributed since 1995, only 6,136 adverse events, such as site reaction rash, fever, and headache, have been reported. A separate study of Vaqta administered to a large group of California patients found no health problems linked to vaccination.

- Enbrel is a widely used drug that is indicated to treat several autoimmune diseases including Rheumatoid Arthritis, Polyarticular Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, and Plaque Psoriasis. It is estimated that 1.3 million people in the United States have RA.
- Procrit was approved by the FDA for the treatment of anemia associated with chronic renal failure. The American Kidney Fund estimates that approximately 807,000 Americans are living with kidney failure. Regarding safety, adverse events, such as nausea, vomiting, headache, and injection site pain, were found in less than 5 percent of individuals treated with Procrit.
- Pulmozyme is an FDA-approved therapy for the management of Cystic Fibrosis (CF) patients to improve pulmonary function. Approximately, 40,000 individuals in the United States have CF and Pulmozyme was the first approved product specifically developed for CF patients.
- Cell and Gene Therapies (CGTs): The following CGTs were developed using the HEK-294 fetal cell line. While these products are typically indicated for small patient populations, CGTs present the opportunity to prevent, treat, or cure a number of inherited disorders, cancers, and infections.
    - Nuwiq is a recombinant anti-hemophilic factor for the treatment of Hemophilia A (FDA approval).
    - Luxturna is a gene therapy for mutation-associated retinal dystrophy (FDA approval).
    - Yescarta is chimeric antigen receptor T-cell (CAR-T) therapy for non-Hodgkin lymphoma (FDA approval).
    - Kymriah is a CAR-T cell therapy for the treatment of relapsed or refractory follicular lymphoma after two or more lines of therapy (FDA approval).
    - Zolgesma is a gene therapy for spinal muscular atrophy (FDA approval).
    - Breyanzi is a CAR-T cell therapy for the treatment of large B-cell lymphoma (LBCL) (FDA approval).
    - Abecma is a CAR-T cell therapy for the treatment of relapsed or refractory multiple myeloma after four or more prior lines of therapy (FDA approval).

Gender-Affirming Care

In recent years, the rights of transgender people, including their access to health care and gender-affirming care, have been systematically targeted by well-funded organizations with social agendas opposing gender-affirming care. In gender-affirming care, puberty blockers and hormonal therapies are prescribed to delay the changes of puberty in transgender youth who have started puberty. Puberty blockers were initially approved by the FDA in 1993, to treat early puberty, and have been found to have well-established safety profiles.

Many national medical societies have issued statements on the medical necessity of gender-affirming care. The Endocrine Society issued Clinical Practice Guidelines that support the use of puberty blockers for adolescents at the first sign of puberty. Additionally, the American Academy of Pediatrics issued a policy statement that asserts that children who identify as transgender and receive puberty blockers generally report improved psychological functioning.

In September 2023, a group that includes Detrans Help, Foundation Against Intolerance and Racism in Medicine, Gender Dysphoria Alliance, Gender Exploratory Therapy Alliance, Genspect, International Partners for Ethical Care, Our Duty USA, and Rethink Identity Medicine Ethics submitted an FDA citizen's petition requesting the agency assess the potential harm caused by the off-label use of a class of puberty blockers known as GnRH agonists in children. The group asserts that despite the widespread use of these drugs among children with gender dysphoria, the use has never been evaluated for safety and effectiveness by the FDA. The petition further states that there is no demonstrated benefit of the drug, despite numerous medical societies endorsing the use of puberty blockers for gender-affirming care.

HIV Treatments

Pre-exposure prophylaxis (PrEP) treatments reduce an individual's chances of contracting HIV, and when taken as prescribed, are highly effective for preventing HIV. PrEP was first approved in 2012, and the CDC estimates that approximately 360,000 individuals were prescribed PrEP in 2021 and new HIV infections have decreased by 12 percent between 2017 and 2021. The U.S. Preventive Services Task Force (USPSTF) has also recommended that clinicians prescribe PrEP to adolescents and adults at increased risk of HIV and found that the benefits of such treatments outweigh the potential risks.

Despite the benefits, such products have been subject to challenges. In 2012, when Truvada was approved, Michael Weinstein, former President of the AIDS Healthcare Foundation, called the product a "public health disaster in the making" and a "party drug." The group also filed an FDA citizen's petition against Truvada's approval. In a further effort to reduce access to PrEP, Braidwood Management is challenging the U.S. Preventive Services Task Force recommendation that would require private health insurance plans to cover PrEP without cost sharing, claiming the coverage requirement violates the Religious Freedom Restoration Act.

Impact on Future Access and Innovation

While this report details currently approved products that may be at risk if the Supreme Court upholds lower courts' decisions in Alliance for Hippocratic Medicine v. Becerra, this ruling has the potential to undermine any approved product or the approval of future products that may be deemed controversial among certain groups. An adverse decision in this case is a direct threat to pharmaceutical innovation and would deter investment in cures and treatments that may be interpreted as controversial. If upheld, the decision allows courts with little to no experience in the safety and efficacy of medicine to decide what products may be available in the U.S. Many of these concerns are outlined in further detail in the Amicus Curiae Brief submitted on behalf of numerous patient advocacy groups, medical experts, and pharmaceutical manufacturers to the Fifth Circuit Court of Appeals in support of overturning the Northern District of Texas court's decision. Their main arguments include the following:

- Allowing courts to decide the validity of FDA approvals could result in sudden loss of access to needed drugs which could jeopardize patient health;
- Uncertainty about the reliability of drug approvals would discourage research and development into new therapies; and
- Future suits against FDA approval would create uncertainty among patients, providers, and drug developers.

Below we describe future treatments that may be at risk due to this ruling:

- **Mifepristone's Other Potential Indications** – If mifepristone's approval is invalidated, it could impact the discovery of other important uses for the drug. Mifepristone is currently approved to treat Cushing's Disease and is being investigated in clinical trials to treat breast cancer, brain cancer, prostate cancer, alcoholism, post-traumatic stress disorder, and depression.

- **Embryonic Stem Cell Research** – While no products have been successfully developed using embryonic stem cell research, there are many ongoing trials attempting to translate such research to treatments and cures for diseases such as Parkinson's Disease, epilepsy, and diabetes. Embryonic stem cells are also being explored to treat infertility. The Supreme Court has previously rejected a request to ban U.S.-funded research on human embryonic stem cells, but if future treatments are eventually successfully developed, their approval could be challenged by opponents.
- **Psychedelic Drugs and Medical Cannabis** – In June, the FDA issued guidance that encourages drug companies to investigate use of psychedelic drugs, such as psilocybin and lysergic acid diethylamide (LSD), for potential treatment of medical conditions, including psychiatric or substance use disorders. Additionally, in August the Department of Health and Human Services (HHS) requested that the Drug Enforcement Agency (DEA) reschedule marijuana from Schedule I to Schedule III. If the DEA does reschedule marijuana, research and development of cannabis-based products will become more feasible, potentially leading to new treatments. Opponents may argue that there is no medical use for "recreational drugs" or that such drugs are not safe for medicinal use.

Conclusion

If the Supreme Court decides to overturn FDA's 2016 and 2021 decisions on the prescribing of mifepristone, not only would it impact access to the widely-used, safe, and effective drug,it has the potential to undermine the approval of any prescription drug caught in the crosshairs of culture wars. In following this precedent, the public could lose access to other abortion and contraception products, common vaccines, vital treatments for gender-affirming care and HIV prevention, and innovative cell and gene therapies. The ruling also threatens investment into future treatments with the potential to treat or cure diseases like Parkinson's, cancer, and diabetes. Bottomline, judicial interference in the legitimacy of FDA-approved drugs jeopardizes access to a multitude of prescription drugs and threatens public health.

Authors

The report was authored by Impact Health Policy Partners, the only mission-driven, public-interest government relations firm focused on health and well-being. Impact Health Policy Partners is committed to improving health for all by partnering with visionary organizations to advance well-being and expand access to more equitable, cost-effective, quality care.