Res. A-04-18

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TITLE: Removing REMS Categorization on Mifepristone

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WHEREAS, the Food and Drug Administration (FDA) uses the Risk Evaluation and Mitigation Strategies (REMS) classification to impose restrictions on only the most dangerous drugs with known or suspected serious complications or contraindications;[1] [2] and

WHEREAS, although the current FDA label for mifepristone was modified in 2016 to reflect more evidenced-based dosing and gestational limits,[3] [4] the label still includes a REMS classification requiring three provisions to "assure safe use,"[5] including that 1) mifepristone be dispensed in a healthcare setting under supervision from 2) a provider who is registered and has signed a provider agreement with the pharmaceutical distributor, and 3) the patient sign an FDA-approved Patient Agreement Form; and

WHEREAS, the American Academy of Family Physicians (AAFP) "supports a woman's access to reproductive health services and opposes non-evidence-based restrictions on medical care and the provision of such services;"[6] and

WHEREAS, the REMS restrictions on mifepristone are not based on scientific evidence[7] [8] [9] [10] [11] and cause significant barriers to accessing abortion care,[12] (such as landlords whose leases don't allow abortions to be done on site, managers who won't allow stocking of mifepristone, and colleagues who object to provision); and

WHEREAS, there are 16 years of data proving an outstanding safety record of mifepristone,[7-11] including a 0.05 percent risk of major complications;[11] and

WHEREAS, other drugs with higher complication rates, such as acetaminophen, aspirin, loratadine, and sildenafil, do not have REMS restrictions;[13] [14] [15] [16] and

WHEREAS, the REMS classification contributes to delays in care,[7, 17] thereby increasing second-trimester and surgical abortions, both of which have increased complication rates; and

WHEREAS, the REMS classification creates a barrier to safe and effective off-label uses of mifepristone, such as for anti-corticoid treatment of Cushing's disease, term labor induction, and miscarriage management;[18] now, therefore be it

RESOLVED, that the California Academy of Family Physicians (CAFP) endorse the principle that the REMS classification on mifepristone is not based on scientific evidence and limits access to abortion care; and be it further

RESOLVED, that the CAFP engage in advocacy and lobbying efforts to overturn the REMS classification on mifepristone; and be it further

RESOLVED, that the CAFP submit a resolution to the 2018 AAFP Congress of Delegates calling on the AAFP also to endorse the principle that the REMS classification on mifepristone is not based on scientific evidence and limits access to abortion care; and be it further

RESOLVED, that the CAFP submit a resolution to the 2018 AAFP Congress of Delegates calling on the AAFP to engage in advocacy and lobbying efforts to overturn the REMS classification on mifepristone.

Speaker's Note: CAFP currently is party to an Americans for Civil Liberties Union lawsuit against the Food and Drug Administration seeking to overturn the REMS classification on mifepristone.

Fiscal Note: Depending on the extent of advocacy/lobbying effort beyond staff time currently required to oversee legal matters, expenses and additional staff time could range between $20,000-$50,000.

Removing REMS Categorization on Mifepristone

1) PROBLEM STATEMENT: What specific practice problem does this resolution seek to solve, or, if this resolution pertains to a proposed new CAFP policy or change of policy, what issue does it seek to address?
This resolution aims to remove the Risk Evaluation and Mitigation Strategies (REMS) categorization on mifepristone to increase access and availability of medication abortions.

2) PROBLEM UNIVERSE: Approximately how many CAFP members or members' patients are affected by this problem or proposed policy?
As one in three women is known to have an abortion at some point in their lives, all CAFP patients would most likely have a family member, spouse, mother, or friend who would have received an abortion their lifetime. As CAFP physicians would either be caring for these individual women or their families, access and safety of abortion care would affect all member physicians.

3) WHAT SPECIFIC SOLUTION ARE YOU PROPOSING TO RESOLVE THE PROBLEM OR POLICY, i.e., what action do you wish CAFP to take?
Please see RESOLVED statements. We would like the CAFP to recognize that the REMS classification on mifepristone is not based on scientific evidence and limits access to abortion care, and to further engage in advocacy and lobbying efforts to overturn this REMS classification. We would like the CAFP to support these resolutions on a national scale through the AAFP by forwarding or submitting similar resolutions.

4) WHAT EVIDENCE EXISTS TO: 1) INDICATE THAT A PROBLEM EXISTS; OR 2) THAT THERE IS NEED FOR A NEW OR REVISED POLICY?
Please see endnotes.

5) PLEASE PROVIDE CITATIONS to support the existence of the problem and your proposed solution.
Please see endnotes.

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[1] https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm184128.pdf
[2] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM521504.pdf
[3] https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf
[4] Greene MF, Drazen JM. A new label for mifepristone. *N Engl J Med*. 2016;374(23):2281-2282.
[5] Approved Risk Evaluation and Mitigation Strategies (REMS): Mifeprex (mifepristone). Silver Spring, MD: Food and Drug Administration, March 29, 2016.
https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=IndvRemsDetails.page&REMS=35
[6] Reproductive Health Services. Leawood, KS: American Academy of Family Physicians, 2014.
http://www.aafp.org/about/policies/all/reproductivehealth-services.html
[7] Mifeprex REMS Study Group. Sixteen years of overregulation: time to unburden Mifeprex. *N Engl J Med.* 2017;376(8):760-794.
[8] Hausknecht R. Mifepristone and misoprostol for early medical abortion: 18 months experience in the United States. *Contraception*. 2003;67(6):463-465.

[9] Upadhyay UD, Desai S, Zlidar V, et al. Incidence of emergency department visits and complications after abortion. *Obstet Gynecol*. 2015;125(1):175-183.
[10] Zane S, Creanga AA, Berg CJ, Pazol K, et al. Abortion-related mortality in the United States, 1998–2010. *Obstet Gynecol*. 2015;126(2):258–265
[11] Weitz TA, Taylor D, Desai S et al. Safety of aspiration abortion performed by nurse practitioners, certified nurse midwives, and physician assistants under a California legal waiver, *Am J Public Health.* 2013;103(3):454–461.
[12] Sheldon WR, Winikoff B. Mifepristone label laws and trends in use: recent experiences in four US states. *Contraception.* 2015;92(3):182-185
[13] Ostapowicz G, Fontana R, Schiodt F, et al. Results of a prospective study of acute liver failure at 17 tertiary care centers in the United States. *Ann Intern Med*. 2002;137(12):947-954.
[14] McNeil Consumer & Specialty Pharmaceuticals. Aspirin and other OTC NSAIDs: background information for Nonprescription Drugs Advisory Committee Meeting. September 20, 2002.
[15] US Food and Drug Administration. Executive summary on risk issues draft presented at joint meeting of the Nonprescription Drugs Advisory Committee and the Pulmonary Allergy Drugs Advisory Committee. May 11, 2001.
[16] Lowe G, Costabile RA. 10-year analysis of adverse event reports to the Food and Drug Administration for phosphodiesterase type-5 inhibitors. *J Sex Med*. 2012;9(1):265-270.
[17] Grossman DA, Grindlay K, Buchacker T, Potter JE, Schmertmann CP. Changes in service delivery patterns after introduction of telemedicine provision of medical abortion in Iowa. *Am J Public Health* 2013;103(1):73-78.
[18] Dzuba IG, Grossman D, Schreiber CA. Off-label indications for mifepristone in gynecology and obstetrics. *Contraception*. 2015:92(3):203-205