IN THE UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF MISSOURI SOUTHEASTERN DIVISION

THE STATE OF MISSOURI, *et al.*,	§	
	§	
Intervenor Plaintiffs,	§	
	§	Case No. 4:25-cv-01580-CMS
v.	§	
	§	
U.S. FOOD AND DRUG ADMINISTRATION, *et al.*,	§	
	§	
Defendants.	§	

MOTION FOR LEAVE TO SUPPLEMENT THE AMENDED COMPLAINT

Pursuant to Federal Rule of Civil Procedure 15(d), the State of Missouri, the State of Kansas, and the State of Iowa ("Plaintiffs") respectfully move the Court for leave to file their First Supplemental Complaint "setting out . . . event[s] that happened after the date of the [original] pleading . . . ." Fed R. Civ. P. 15(d). Plaintiffs respectfully request that the attached proposed Supplemental Complaint be accepted and docketed as filed, and Defendants be ordered to "plead to the supplemental pleading within a specified time." *Id.* The grounds for this motion are set forth in the attached memorandum in support.

MEMORANDUM IN SUPPORT OF THE PLAINTIFFS' MOTION FOR LEAVE TO SUPPLEMENT THE AMENDED COMPLAINT

INTRODUCTION

In 2019, the U.S. Food and Drug Administration ("FDA") approved GenBioPro Inc.'s ("GenBioPro") amended new drug application ("ANDA") for a generic form of mifepristone ("2019 ANDA Approval"). Am. Compl. ¶ 164, ECF No. 217; Ex. 30. This was the FDA's first approval of a generic version of mifepristone. Am. Compl. ¶ 164, ECF No. 217. The FDA's approval subjected GenBioPro's generic drug to the same labeling and REMS requirements as its reference drug, Mifeprex which is produced by Danco Laboratories, LLC ("Danco"). *Id.*; Ex. 30. At the same time, the FDA approved a single, shared risk evaluation and mitigation strategy ("REMS") for all mifepristone products ("Mifepristone REMS Program"). *Id.* ¶ 165; Ex. 31. Along with other actions by Defendants, these approvals form the basis of this lawsuit.

Six years after the 2019 ANDA Approval and eight months after Plaintiffs filed their Amended Complaint, the FDA approved Evita Solutions, LLC's ("Evita") ANDA for its generic version of Mifeprex ("2025 ANDA Approval").[1] Like GenBioPro's generic drug, Evita's generic mifepristone is subject to the same labeling and REMS requirements as Mifeprex, which Plaintiffs challenge as being unlawful and arbitrary and capricious.[2] In addition, Evita's generic mifepristone is chemically identical to Danco's Mifeprex and GenBioPro's generic mifepristone, meaning it poses the same

[1] 2025 FDA ANDA Approval Letter to Evita Solutions, LLC p. 1 (September 30, 2025), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2025/216616s000ltr.pdf ("2025 FDA ANDA Approval Letter").
[2] *See id.*

health risks to pregnant woman that the FDA ignored when first approving the chemical abortion drug.

The 2025 ANDA Approval, in short, represents a continuance of the underlying case brought by Plaintiffs—one that must be addressed if Plaintiffs are to obtain complete and speedy relief from the FDA's illegal actions. For these reasons, as well as for the sake of judicial economy, Plaintiffs respectfully request leave to supplement their Amended Complaint to update their claims to reflect the FDA's approval of a second generic mifepristone.

BACKGROUND

This lawsuit originated in 2022, when several doctors and four medical associations ("Original Plaintiffs") filed a complaint against the FDA; Robert M. Califf, M.D., in his official capacity as Commissioner of Food and Drugs, U.S. Food and Drug Administration; Janet Woodcock, M.D., in her official capacity as Principal Deputy Commissioner, U.S. Food and Drug Administration; Patrizia Cavazzoni, M.D., in her official capacity as Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration; the U.S. Department of Health and Human Services; and Xavier Becerra, in his official capacity as Secretary, U.S. Department of Health and Human Services ("Original Defendants")[3] in the Northern District of Texas. ECF No. 1. In their complaint, the Original Plaintiffs challenged the FDA's 2000 approval of name-brand mifepristone, its 2019 approval of generic mifepristone,

[3] This list of defendants reflects the list of parties at the initiation of this lawsuit. Since that time, the office of Principal Deputy Director of the FDA has been dropped and pursuant to Federal Rule of Civil Procedure 25(d), the current occupants of the official positions have been substituted for those no longer in office.

and its subsequent 2016 and 2021 loosening of federal regulations pertaining to mifepristone. *Id.*

In February 2023, the court granted Danco leave to intervene. ECF No. 33. GenBioPro was granted leave to intervene in February 2025 (together with Danco and the Original Defendants "Defendants"). Plaintiffs, meanwhile, intervened in this lawsuit in 2024 and filed their initial complaint that same month. ECF Nos. 175, 176. In January 2025—after the Supreme Court decided *FDA v. Alliance for Hippocratic Medicine*, 602 U.S. 367 (2024) and the original plaintiffs voluntarily dismissed from the lawsuit, ECF No. 203—Plaintiffs filed an amended complaint ("Amended Complaint"), ECF No. 217. The Amended Complaint brought Administrative Procedure Act ("APA") challenges against the FDA's decisions in 2016, 2021, and 2023 to loosen federal regulations of mifepristone related to labeling and REMS; its 2019 issuance of the Mifepristone REMS Program; and its 2019 ANDA Approval. *Id.* Defendants have not filed an answer in response to the Amended Complaint and discovery has not commenced in relation to the Amended Complaint.

On September 30, 2025, the Northern District of Texas court issued an order transferring this case to the Eastern District of Missouri. ECF No. 273. The case was officially transferred to this Court on October 23, 2025 and assigned a judge the same day. ECF No. 274. Neither the Court nor the Parties have taken any since. Plaintiffs now move to supplement their Amended Complaint in order to incorporate events that occurred after Plaintiffs filed the Amended Complaint and are directly

related to the existing controversy and necessary to achieve orderly, fair, and complete relief.

LEGAL STANDARD

Under Rule 15(d), "the court may, on just terms, permit a party to serve a supplemental pleading setting out any transaction, occurrence, or event that happened after the date of the pleading to be supplemented." Fed. R. Civ. P. 15(d). Rule 15(d) "is designed to cover matters subsequently occurring but pertaining to the original cause." *Weeks v. Birch*, No. 1:17-CV-00022 AGF, 2020 WL 33089, at *2 (E.D. Mo. Jan. 2, 2020) (quoting *Schreier v. Drealan Kvilhaug Hoefker & Co. P.A.*, 018-CV-02310-DSDKMM, 2019 WL 1923111, at *1 (D. Minn. Apr. 30, 2019) (citing *U.S. v. Vorachek*, 563 F.2d 884, 886 (8th Cir. 1977))).

Rule 15(d) "gives the trial court, in the exercise of its sound discretion, the right to determine whether or not leave should be granted to file a supplemental pleading," *Minn. Min. & Mfg. Co. v. Superior Insulating Tape Co.*, 284 F.2d 478, 481 (8th Cir. 1960), and "is intended to give district courts broad discretion in allowing supplemental pleadings." *In re Bankamerica Corp. Sec. Litig.*, No. 4:99-MD-1264 CEJ, 2010 WL 4622530, at *1 (E.D. Mo. Nov. 5, 2010) (quoting Fed. R. Civ. P 15, 1963 Amendment notes).

"Supplemental complaints stating claims against new parties are acceptable, so long as the claims are a continuation of the underlying case and the supplemental complaint is necessary 'to achieve an orderly and fair administration of justice.'" *Id.* (quoting *Griffin v. Cnty. Sch. Bd. Of Prince Edward Co.*, 377 U.S. 218, 226 (1964)). "However, when claims are separate and distinct from the underlying case, the claims

'are more appropriately brought in a separate suit.'" *Id.* (quoting *Paige v. Harper*, No. 4:99-MD-1264 CEJ, 2010 WL 4622530 (E.D. Mo. Nov. 5, 2010).

While the Eighth Circuit has not articulated a standard that applies "to the Court's exercise of discretion concerning a motion for leave to file a supplemental pleading under Rule 15(d)," this Court has consistently applied the same liberal principles that apply to amended pleadings under Rule 15(a). *Riggs v. City of Owensville*, No. 4:10-CV-793 CAS, 2011 WL 1576723, at *2 (E.D. Mo. Apr. 26, 2011); *see, e.g.*, *Weeks v. Birch*, No. 1:17-CV-00022 AGF, 2020 WL 33089, at *2 (E.D. Mo. Jan. 2, 2020); *Raineri Const., LLC v. Taylor*, No. 4:12-CV-2297 CEJ, 2013 WL 6050772, at *2 (E.D. Mo. Nov. 15, 2013).

Accordingly, courts are encouraged to grant a motion for leave to supplement under Rule 15(d), "when doing so will promote the economic and speedy disposition of the entire controversy between the parties, will not cause undue delay or trial inconvenience, and will not prejudice the rights of any of the other parties to the action." *Harris v. Adams*, No. 4:17-CV-00842 PLC, 2021 WL 5823885, at *6 (E.D. Mo. Dec. 8, 2021) (quoting *U.S. ex rel. Gadbois v. PharMerica Corp.*, 809 F.3d 1, 4 (1st Cir. 2015). "[A]bsent any suggestion of bad faith or dilatory motive," *Weeks*, 2020 WL 33089, at *3, "[f]actors to be considered include the futility of the supplementation, prejudice to the opposing party, unreasonable delay in the request to supplement, and whether the supplementation would 'unduly delay resolution of the case.'" *Harris*, 2021 WL 5823885, at *6 (quoting *PharMerica Corp.*, 809 F.3d at 7). Plaintiffs' motion for leave satisfies the above standard.

ARGUMENT

This Court should grant the Plaintiffs' motion to supplement their Amended Complaint because the supplemental complaint is directly related to the existing controversy and supplementation is necessary to ensure complete relief. Moreover, granting Plaintiffs' motion to supplement will not cause undue delay nor will it prejudice the parties but instead will help promote judicial economy by allowing Plaintiffs' APA claims against the 2019 ANDA Approval and the 2025 ANDA Approval be heard simultaneously.

As a preliminary matter, Rule 15(d) is the proper mechanism for adding a cause of action necessary to afford Plaintiffs complete relief based on events that occurred after the underlying pleading. Plaintiffs' filed their Amended Complaint in January 2025. ECF No. 217. Over eight months later, on September 30, 2025, the FDA approved Evita's ANDA. *See* 2025 FDA ANDA Approval Letter. This event provides the basis for Plaintiffs' supplemental complaint. Thus the events giving rise to the supplement "happened after the date of the pleading to be supplemented" and Rule 15(d) is appropriate. Fed. R. Civ. P. 15(d); *see United States ex rel. Kenny v. Stoltz*, 327 F.3d 671, 674 n.4 (8th Cir. 2003) ("[S]upplemental pleadings, not amended pleadings, are intended to cover matters occurring after the original complaint is filed.").

Plaintiffs' motion should be granted because their supplemental complaint "is merely a continuation" of the Amended Complaint. *See Gen. Bronze Corp. v. Cupples Prods. Corp.,* 9 F.R.D. 269, 270 (E.D. Mo. 1949). Plaintiffs' supplemental complaint does not present a cause of action "separate and distinct" from the controversy. *In re*

Bankamerica Corp. Sec. Litig., 2010 WL 4622530, at *1. Rather, the supplement "justif[ies] further relief with respect to the same subject matter as the controversy referred to in the complaint." *Gen. Bronze Corp.*, 9 F.R.D. at 270–71 (E.D. Mo. 1949). The underlying Amended Complaint alleges violations of the APA by the Defendants related to the FDA's decisions regarding Mifeprex and generic mifepristone. ECF No. 217. In the Amended Complaint, Plaintiffs' assert two causes of action against the FDA's 2019 ANDA Approval. *Id.* at ¶¶ 763–767, 783–88. Building on this foundation, Plaintiffs' supplemental complaint contains two causes of action challenging the FDA's 2025 ANDA Approval on the *same legal grounds* that it challenges the FDA's 2019 ANDA Approval. *See id.* The causes of action and prayer for relief in Plaintiffs' supplemental complaint mirrors claims already alleged in the Amended Complaint and therefore does not present distinct new causes of action.

Supplementation is further appropriate because it "promote[s] the economic and speedy disposition of the entire controversy between the parties." *Harris*, 2021 WL 5823885 at *6. Generic drugs are inextricably linked to their reference drug. *See* Am. Compl. ¶ 88, ECF No. 217. And under the 2019 Mifepristone REMS Program, generic and brand drugs are subject to the same labeling requirements. *Id.* at ¶¶ 20, 165. Thus, Evita's generic drug is subject to the same labeling and REMS requirements as Danco's Mifeprex and BioGenPro's generic mifepristone. *See* 2025 FDA ANDA Approval Letter. These labeling requirements and REMS scheme are at the core of the controversy. *See* Am. Compl. ¶¶ 757–88, ECF No. 217. Moreover, the parties are already litigating the FDA's 2019 ANDA Approval which is nearly

identical to its 2025 FDA ANDA Approval. *Compare* Ex. 30, Am. Compl., ECF 217, and 2025 ANDA Approval Letter. Without supplementation, Plaintiffs will be required to seek complete relief by bringing these claims in a separate case and manage a separate trial, ultimately duplicating efforts. Thus, Plaintiffs should be allowed to supplement their complaint to "achieve an orderly and fair administration of justice," *In re Bankamerica Corp. Sec. Litig.*, 2010 WL 4622530, at *1 (quoting *Griffin*, 377 U.S. at 226 (1964)).

Further, the balance of the remaining factors weighs in favor of granting the Plaintiffs' motion. First, supplementation is not futile. Typically, courts review whether an amendment is futile based on whether it is meritorious and "would withstand a motion to dismiss under Rule 12(b)(6)." *Prowell v. OM Fin. Life Ins. Co.*, No. 4:09-CV-529 CAS, 2009 WL 1833463 (E.D. Mo. June 23, 2009). As discussed above, the courts apply similar standards to supplemental pleadings. The claims alleged in the supplemental complaint are part of a justiciable controversy between the parties. The claims rest on the same legal basis as claims already properly plead in the Amended Complaint. *See* Am. Compl. ¶¶ 763–767, 783–88, ECF No. 217. Plaintiffs are not "attempt[ing] to gain an advisory opinion." *Furminator, Inc. v. Ontel Prods. Corp.*, 246 F.R.D. 579, 596 (E.D. Mo. 2007).

Second, Plaintiffs do not seek to supplement their Amended Complaint out of "bad faith" or "dilatory motive," nor have they filed this motion with "undue delay." *Weeks*, 2020 WL 33089 at *3. Instead, Plaintiffs have filed this supplement in direct response to the FDA's decision to double down on its failure to protect women from

an unsafe abortion drug. As explained above, the FDA has only approved two generic forms of mifepristone. Plaintiffs challenged the approval of the first generic variant in their Amended Complaint. The supplement addresses the second. Moreover, Plaintiffs have acted with due diligence. This motion comes less than a month after this case was transferred and before any substantive steps were taken on the Amended Complaint. *See Daughters of Charity Nat'l v. Am. Int'l Grp., Inc.*, No. 4:04-CV-754 CAS, 2005 WL 8176860, at *1 (E.D. Mo. May 31, 2005) (finding no undue delay, bad faith, dilatory motive, or prejudice where plaintiffs brought a claim prior to the discovery completion deadline and in advance of trial

Third, Defendants are not prejudiced by the timing of this motion. *See Equal Emp. Opportunity Comm'n v. Convergys Customer Mgmt. Grp., Inc.*, No. 4:04-CV-846 CAS, 2005 WL 8176815, at *1 (E.D. Mo. Oct. 5, 2005) ("Delay in seeking to amend, alone, is a [sic] insufficient justification to deny leave. Prejudice to the nonmovant must also be shown."). Plaintiffs are pursuing a nearly identical claim in this litigation against the FDA's 2019 ANDA Approval. Defendants could have foreseen that Plaintiffs would seek to bring a claim for their nearly identical 2025 ANDA Approval. *Cf. Equal Emp. Opportunity Comm'n v. Convergys Customer Mgmt. Grp., Inc.*, No. 4:04-CV-846 CAS, 2005 WL 8176815 at *2 (E.D. Mo. Oct. 5, 2005) (finding no bad faith, dilatory motive, undue delay or prejudice even where the court determined the plaintiff should have filed an amendment sooner, but the amendment "was not a surprise that would prejudice" the defendants).

Finally, supplementation does not prejudice any of the Defendants because Plaintiffs' supplemental complaint "does not posit a new theory of recovery." *Weeks*, 2020 WL 33089 at *3. Instead, the causes of action against the FDA and prayer for relief mirror those already included in the Amended Complaint. Granting this motion would not require the FDA to brief new legal claims or factual defenses. Additionally, the supplemental complaint adds no new claims against GenBioPro or Danco and will not inhibit their ability to fully litigate their positions or even necessitate additional briefing on their part. Defendants will not be able to meet their burden of demonstrating prejudice.

Supplementation of the Plaintiffs' Amended Complaint will advance judicial economy for the benefit of the parties and the Court. Specifically, it will streamline the adjudication of the controversy and ensure order in litigating this controversy. Thus, this Court should utilize its broad discretion to grant Plaintiffs' motion to supplement their Amended Complaint.

CONCLUSION

For the reasons set forth above, Plaintiffs respectfully ask this Court for leave to file the attached supplemental complaint under Rule 15(d).

Date: November 19, 2025

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on November 19, 2025, a true and accurate copy of the foregoing was electronically filed by using the Court's CM/ECF system to be served on all counsel of record entered in the case.

/s/ *Louis J. Capozzi, III*

IN THE UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF MISSOURI SOUTHEASTERN DIVISION

THE STATE OF MISSOURI, *et al.*,	)	
	)	
Intervenor Plaintiffs,	)	
	)	Case No. 4:25-cv-01580-CMS
v.	)	
	)	
U.S. FOOD AND DRUG ADMINISTRATION, *et al.*,	)	
	)	
	)	
Defendants.	)	

[PROPOSED] SUPPLEMENTAL COMPLAINT

INTRODUCTION

1. Plaintiffs State of Missouri, State of Kansas, and State of Idaho filed the operative Amended Complaint in this action on January 16, 2025. Am. Compl., ECF No. 217.

2. Plaintiffs' Amended Complaint named as defendants the U.S. Food and Drug Administration; Robert M. Califf, M.D., in his official capacity as Commissioner of Food and Drugs, U.S. Food and Drug Administration;[1] Patrizia Cavazzoni, M.D., in her official capacity as Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration;[2] U.S. Department of Health and Human Services;

[1] Pursuant to Federal Rule of Civil Procedure 25(d)(1), Martin A. Makary, M.D. has been substituted for Robert M. Califf in his official capacity as Commissioner of Food and Drugs.

[2] Pursuant to Federal Rule of Civil Procedure 25(d)(1), Richard Pazdur, M.D., has been substituted for Patrizia Cavazzoni in his official capacity as Director, Center for Drug Evaluation and Research.

and Xavier Becerra, in his official capacity as Secretary, U.S. Department of Health and Human Services[3] (Defendants). Plaintiffs' Amended Complaint pleaded four counts against Defendants for disregarding federal statutes and FDA regulations when approving unsafe and high-risk chemical abortion drugs for over-the-counter use. *Id.*

3. Pursuant to Federal Rule of Civil Procedure 15(d), Plaintiffs file this Supplemental Complaint for the purpose of setting forth events "that happened after the date of the pleading to be supplemented." Specifically, Plaintiffs wish to address the recent decision of Defendant U.S Food and Drug Administration (FDA) to grant Evita Solutions, LLC's (Evita) amended new drug application (ANDA) for a generic form of Mifeprex, Mifepristone Tablets, 200mg, despite mounting evidence that the drug poses serious, even life-threating harm to pregnant women.

4. Mifepristone is a high-risk drug that the FDA continues to green-light despite its devastating effects on pregnant women and girls. Studies of the real-world use of mifepristone concluded that significant morbidity and mortality have occurred following the use of mifepristone as an abortifacient.[4] And, as the FDA reports on its label, roughly one in 25 women who take abortion drugs will end up in the emergency

[3] Pursuant to Federal Rule of Civil Procedure 25(d)(1), Robert F. Kennedy, Jr. has been substituted for Xavier Becerra in his official capacity as Secretary, U.S. Department of Health and Human Services.

[4] Ex. 4, Am. Compl., ECF No. 217, Harrison Compl. Decl. ¶ 16; *see also* Am. Compl. ¶ 64, ECF No. 217.

room.[5] Many women who end up in the emergency room after taking abortion drugs suffer severe injuries. *See* Am. Compl. ¶ 66, ECF No. 217.

5. In spite of these realities, the FDA cut corners when it removed safeguards from this dangerous drug.

6. In 2016, the FDA engaged in a large-scale rollback of the safety precautions it put in place when it approved mifepristone in 2000 (2016 Major Changes). Through these changes, the FDA haphazardly stripped away vital safety precautions, which it characterized as "interrelated,"[6] without conducting a single study evaluating the impact of a simultaneous rollback. Instead, the FDA relied only on studies that evaluated one or some of the changes, and many such studies included additional safeguards not required under the 2016 Major Changes. *See* Am. Compl. ¶¶ 141–43, ECF No. 217. Sticking its head in the sand, the FDA eliminated non-fatal reporting requirements for abortion providers based on data collected under the originally approved safety standards,[7] leaving no way to fully evaluate the effects of the newly deregulated regime.

7. The 2016 Major Changes failed to satisfy the rigorous scientific standards of the Federal Food, Drug, and Cosmetic Act (FDCA).

8. In 2019, the FDA continued to ignore growing evidence of danger to

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[5] Ex. A, FDA-Approved Label for Mifepristone (Mifeprex) (March 2023), https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/020687Orig1s026lbl.pdf (Mifeprex March 2023 Label).

[6] Ex. 2, Am. Compl., ECF No. 217, FDA, Center for Drug Evaluation and Research, Summary Review of Application Number: 020687Orig1s020, at 6 (Mar. 29, 2016) (2016 Summary Review).

[7] Ex. 2, Am. Compl., ECF No. 217, 2016 Summary Review, *supra* note 6, at 6.

pregnant women and girls and approved the first generic version of mifepristone ("2019 ANDA Approval"), produced by GenBioPro, Inc. ("GenBioPro").[8] This approval increased the supply and availability of mifepristone, lowered the cost of the drug, and increased the use of chemical abortions.[9] As a result of the 2019 ANDA Approval, "the number of women experiencing medical complications after taking mifepristone has risen." *All. For Hippocratic Med. v. U.S. Food & Drug Admin.*, 78 F.4th 210, 241 (5th Cir. 2023).

9. In conjunction with this approval, the FDA adopted a single, shared system risk evaluation and mitigation strategy (REMS) for all mifepristone products used for "the medical termination of intrauterine pregnancy" through 70 days (known as the "Mifepristone REMS Program").[10] Thus creating a uniform REMS for brand and generic mifepristone.

10. The 2016 Major Changes left intact the REMS requirement that abortion providers dispense mifepristone only in certain healthcare settings, specifically clinics, medical offices, and hospitals.[11] In 2021, under the Biden-Harris administration, the FDA issued a non-enforcement decision on this in-person

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[8] Ex. 30, Am. Compl., ECF No. 217, 2019 FDA ANDA Approval Letter to GenBioPro, Inc. (Apr. 11, 2019), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/091178Orig1s000ltr.pdf.

[9] Ex. 108, Am. Compl., ECF No. 217, Solanky Affidavit; *see also* Am. Compl. ¶¶ 753–55, ECF No. 217.

[10] Ex. 30, Am. Compl., ECF No. 217, 2019 FDA Supplemental Approval Letter to Danco Laboratories, LLC (Apr. 11, 2019), Supplement Approval, https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/020687Orig1s022ltr.pdf.

[11] *See* Ex. 34, Am. Compl., ECF No. 217, 2021 FDA Letter to AAPLOG and Am. Coll. of Pediatricians denying in part and granting in part 2016 Citizen Petition, Docket No. FDA-2019-P-1534, 25 (Dec. 16, 2021) (2021 FDA Response).

dispensing protection. This decision subverted statutes expressly disallowing such conduct. 18 U.S.C. § 1461.

11. Doubling-down on its failure to consider the increasing evidence of the serious harms mifepristone causes pregnant women and girls, the Biden-Harris FDA announced it would gut the in-person dispensing protection from the Mifepristone REMS Program in December of 2021. The FDA also added a requirement allowing permitted pharmacies to become certified to dispense mifepristone.[12] The FDA made these decisions without any evidence that removing the in-person dispensing protection was safe for women's health. *See* Am. Compl. ¶¶ 181–198, ECF No. 217. Moreover, this relaxation effectively "allowed mifepristone to be prescribed remotely and sent via mail," *All. for Hippocratic Med. v. U.S. Food & Drug Admin.*, 78 F.4th 210, 226 (5th Cir. 2023), rev'd, 602 U.S. 367, 226 (2024), in violation of longstanding federal law prohibiting mailing abortion drugs, 18 U.S.C. § 1461.

12. In 2023, the FDA formalized the removal of in-person dispensing protections and expanded the REMS program to allow retail pharmacies to dispense mifepristone (the 2021/2023 Removal of the In-Person Dispensing Protection),[13] in blatant disregard for federal law, 18 U.S.C. § 1461.

13. The FDA's actions attempt to create a 50-state mail-order abortion drug

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[12] Ex. 33, Am. Compl., ECF No. 217, 2021 FDA Center for Drug Evaluation & Research Director Patrizia Cavazzoni Letter to Dr. Graham Chelius (Dec. 16, 2021).
[13] Ex. 3, Am. Compl., ECF No. 271, FDA, Center for Drug Evaluation and Research, Mifepristone Summary Review, dated Jan. 3, 2023 at 21 (FDA 2023 Summary Review).

economy, undermining state abortion laws in Plaintiff states.[14] It also enabled providers to dispense abortion drugs to residents of Plaintiff States later in pregnancy without follow-up care—causing women to seek emergency services in Plaintiff States for treatment of resulting complications. *See* Am. Compl. ¶¶ 258–78, ECF No. 217.

14. On September 30, 2025, the FDA continued its pattern of ignoring the dangerous effects of mifepristone on pregnant women and girls and, relying on the 2016 Major Changes, approved a second generic version of the drug. This approval marks the FDA's most recent violation in a long string of unlawful decisions.

15. This generic drug, produced by Evita Solutions LLC (Evita) is subject to the same REMS and labelling as the brand drug, Mifeprex which is produced by Danco Laboratories, LLC (Danco). The generic drug is chemically identical to Danco's Mifeprex and GenBioPro, Inc.'s generic mifepristone. Consequently, this generic drug produces the same side effects, the same consequences, and the same devastating impact on women and girls nationwide.

16. In this Supplemental Complaint, Plaintiffs plead additional facts and claims related to the FDA's misguided and unlawful approval of Evita's generic version of mifepristone against the Defendants.

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[14] The Missouri statute, Mo. Rev. Stat. § 118.021.1, requiring in-person administration of mifepristone for the purpose of an abortion is currently the subject of ongoing litigation, but remains in effect. *See Comprehensive Health of Planned Parenthood Great Plains v. State*, 2416-CV31931 (Mo. Cir. Jackson Cnty.). The same goes for Idaho's statute. Idaho Code § 18-622' *see St. Luke's Health System, Ltd.* v. *Labrador*, 1:25-cv-15 (D. Idaho). The Kansas statute, K.S.A. 65-4a10, was struck down by the Kansas Supreme Court in 2024. *See Hodes & Nauser, MDs, P.A. v. Stanek*, 318 Kan. 995 (S. Ct. Kan. 2024).

JURISDICTION OVER SUPPLEMENTAL CLAIM

17. The grounds for this Court's subject matter jurisdiction over the claim pleaded below are the same as the grounds set forth in the Amended Complaint. *See* Am. Compl.¶¶ 27–33, ECF No. 217.

18. Venue properly lies in this Court pursuant to 28 U.S.C. § 1391 because at least one party resides in the district. *See* Order Transferring to Another District 26, ECF No. 273. Venue is also proper because a substantial part of the facts, events or omissions giving rise to the claims occurred in this district.

19. Defendants are United States officers or agencies sued in their official capacities.

20. Therefore, this Court has personal jurisdiction over Defendants for purposes of this action because their immunity has been abrogated by 5 U.S.C. § 702, and they have "submit[ted]" to such jurisdiction "through contact with and" regulatory "activity directed at" Plaintiff States and their respective medical providers and health plans. *J. McIntyre Mach., Ltd. V. Nicastro*, 564 U.S. 873, 881 (2011).

SUPPLEMENTAL FACTUAL ALLEGATIONS

21. A generic drug manufacturer may submit an ANDA to introduce into commerce and to distribute a generic version of an approved drug. 21 U.S.C. § 355(j); *see also id.* at ¶ 87.

22. In the ANDA, the generic drug manufacturer must show, among other things, that (a) the conditions of use prescribed, recommended, or suggested in the

labeling proposed for the new drug have been previously approved for a drug listed and (b) the drug product is chemically identical to the approved drug. This allows the generic drug manufacturer to rely on the FDA's finding of safety and effectiveness for the reference drug. The route of administration, dosage form, and strength for the generic must also be identical to the approved drug. 21 U.S.C. § 355(j); 21 C.F.R. § 314.94; *see also* Am. Compl. ¶ 88, ECF No. 217.

23. On September 30, 2025, eight months after Plaintiffs filed their Amended Complaint, the FDA approved Evita's ANDA for its generic version of Danco's Mifeprex, "Mifepristone Tablets, 200 mg" (2025 ANDA Approval).[15] The FDA "concluded that adequate information has been presented to demonstrate that the drug meets the requirements for approval under the FD&C Act."[16] The FDA determined Evita's Mifepristone Tablets, 200 mg "to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Mifeprex (mifepristone) Tablets, 200 mg, of Danco Laboratories, LLC."[17]

24. Evita and GenBioPro sell the only generic mifepristone and misoprostol.

25. Evita's generic drug is subject to the same labeling and REMS requirements as Danco's Mifeprex and GenBioPro's generic mifepristone. In 2019, the FDA approved a single, shared REMS Program for brand and generic mifepristone. The program ensures that *all* mifepristone products for "the medical

[15] Ex. B, 2025 FDA ANDA Approval Letter to Evita Solutions, LLC p. 1 (September 30, 2025), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2025/216616s000ltr.pdf.
[16] *Id.*
[17] *Id.*

termination of intrauterine pregnancy" through 70 days follow a single REMS program to manage the risks associated with the drugs.[18] All mifepristone products are also subject to the same labeling requirements.[19]

26. The labeling and REMS requirements governing mifepristone products are not based on rigorous review of health and safety risks the drug pose. To approve Evita's generic drug, the FDA relied on only the unlawful and untested 2016 Major Changes labeling and the unlawful 2021/2023 Removal of the In-Person Dispensing Protection. In addition, despite the agency's elimination of non-fatal reporting requirements in 2016, the FDA did not require any additional investigations or studies that evaluated the drug's safety nor any specific assessments on the impact of the drug on the health of pregnant women and girls.

27. Evita's generic mifepristone tablets are chemically identical to Danco's Mifeprex and GenBioPro's generic mifepristone. Accordingly, Evita's generic mifepristone brings with it the same side effects, risks, and harms to pregnant women and girls as Mifeprex and GenBioPro. Just as the FDA's unlawful 2019 ANDA Approval led to an increase in the number of women obtaining chemical abortions, the FDA's 2025 ANDA Approval will increase accessibility to chemical abortions.[20]

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[18] Ex. 30, Am. Compl., ECF No. 217, 2019 FDA Supplemental Approval Letter to Danco Laboratories, LLC (Apr. 11, 2019), Supplement Approval, *supra* note 10.

[19] In 2000, the FDA stated that "[L]abeling is now part of a total risk management program," and "the professional labeling, Medication Guide, Patient Agreement, and Prescriber's Agreement will together constitute the approved product labeling to ensure any future generic drug manufacturers will have the same risk management program." Ex. 18, Am. Compl., ECF No. 217, 2000 FDA Approval Memo. to Population Council re: NDA 20-687 Mifeprex (mifepristone) at 2 (Sept. 28, 2000).

[20] *See* Ex. 108, Am. Compl., ECF No. 217, Solanky Affidavit.

The supply of mifepristone will increase, the cost will decrease, and the number of chemical abortions will rise in Plaintiff States and across the nation.[21]

28. Plaintiffs experience harm from the use of chemical abortions. Am. Compl. ¶¶ 525–756, ECF No. 217. Accordingly, the FDA's approval of another generic drug with the same chemical composition as Danco's Mifeprex and GenBioPro's generic mifepristone, aggravates and worsens Plaintiffs' harms as it increases the accessibility of this dangerous drug to the detriment of pregnant women and children.

SUPPLEMENTAL CLAIMS FOR RELIEF

SIXTH CLAIM

2025 ANDA APPROVAL

***ULTRA VIRES;* ADMINISTRATIVE PROCEDURE ACT (5 U.S.C. § 706)**

IN EXCESS OF STATUTORY JURISDICTION, AUTHORITY, OR LIMITATIONS, OR SHORT OF STATUTORY RIGHT; ARBITRARY, CAPRICIOUS, AN ABUSE OF DISCRETION, OR OTHERWISE NOT IN ACCORDANCE WITH LAW

29. Plaintiffs re-allege and incorporate paragraphs 1–28 above and all paragraphs in the Amended Complaint as if fully set forth in this paragraph.

30. The FDA lacked legal authority when issuing the 2025 ANDA Approval.

31. The FDA's actions seek to enable the violation of state laws restricting abortion, as described in the Amended Complaint. But a federal agency cannot disregard applicable state law or seek to enable and encourage what state law

[21] Evita has expressed that it believes abortion should be "accessible to all"—"regardless of their . . . age, . . . income, or where they live." Evita Solutions, *Making generic mifepristone available and accessible today*, perma.cc/BW83-MUE4.

expressly prohibits, so the FDA lacked legal authority and acted arbitrarily and capriciously when issuing the 2025 ANDA Approval.

32. Therefore, the 2025 ANDA Approval must be held unlawful, stayed, set aside, vacated, and preliminarily and permanently enjoined under the APA and the Court's inherent equitable power to enjoin ultra vires actions, *Larson v. Domestic & Foreign Com. Corp.*, 337 U.S. 682, 689–91 (1949).

SEVENTH CLAIM

2025 ANDA APPROVAL

ADMINISTRATIVE PROCEDURE ACT (5 U.S.C. § 706)

IN EXCESS OF STATUTORY JURISDICTION, AUTHORITY, OR LIMITATIONS, OR SHORT OF STATUTORY RIGHT; ARBITRARY, CAPRICIOUS, AN ABUSE OF DISCRETION, OR OTHERWISE NOT IN ACCORDANCE WITH LAW

33. Plaintiffs re-allege and incorporate paragraphs 1–32 above and all paragraphs in the Amended Complaint as if fully set forth in this paragraph.

34. Defendants lacked legal authority to issue the 2025 ANDA Approval.

35. Because the FDA relied on the unlawful 2016 Major Changes labeling and the 2021/2023 Removal of the In-Person Dispensing Protection as a means to approve Evita's generic drug, Mifepristone Tablets, 200 mg, the 2025 ANDA Approval was unlawfully approved.

36. Unable to rely on an unlawful approval, the FDA's 2025 ANDA Approval violated the FDCA because it lacked the clinical investigations, adequate testing, sufficient information, and substantial evidence to show the safety and effectiveness

of mifepristone under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof as required by 21 U.S.C. § 355(d).

37. Therefore, the 2025 ANDA Approval must be held unlawful, set aside, vacated, and preliminarily and permanently enjoined.

38. Evita may submit an application with proposed labeling consistent with the pre-2016 Major Changes labeling, but, unlike Danco, Evita cannot simply revert to a previously approved label.

SUPPLEMENTAL PRAYER FOR RELIEF

For these reasons, Plaintiffs respectfully request that the Court enter an order and judgment against Defendants, including their employees, agents, successors, and all persons in active concert or participation with them, in which it includes the following supplemental relief:

A. Issues a preliminary injunction, or stay of the effective dates, that rescinds the 2025 ANDA Approval;

B. Holds unlawful, sets aside, and vacates the 2025 ANDA Approval;

C. Any other relief the Court deems proper.

Date: November 19, 2025

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on November 19, 2025, a true and accurate copy of the foregoing was electronically filed by using the Court's CM/ECF system to be served on all counsel of record entered in the case.

/s/ *Louis J. Capozzi, III*
Louis J. Capozzi, III

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use MIFEPREX safely and effectively. See full prescribing information for MIFEPREX.

MIFEPREX® (mifepristone) tablets, for oral use
Initial U.S. Approval: 2000

WARNING: SERIOUS AND SOMETIMES FATAL INFECTIONS OR BLEEDING

See full prescribing information for complete boxed warning.

Serious and sometimes fatal infections and bleeding occur very rarely following spontaneous, surgical, and medical abortions, including following MIFEPREX use.

- **Atypical Presentation of Infection. Patients with serious bacterial infections and sepsis can present without fever, bacteremia or significant findings on pelvic examination. A high index of suspicion is needed to rule out serious infection and sepsis. (5.1)**
- **Bleeding. Prolonged heavy bleeding may be a sign of incomplete abortion or other complications and prompt medical or surgical intervention may be needed. (5.2)**

MIFEPREX is only available through a restricted program called the Mifepristone REMS Program (5 3).
Before prescribing MIFEPREX, inform the patient about these risks. Ensure the patient knows whom to call and what to do if they experience sustained fever, severe abdominal pain, prolonged heavy bleeding, or syncope, or if they experience abdominal pain or discomfort or general malaise for more than 24 hours after taking misoprostol.

----------INDICATIONS AND USAGE----------
MIFEPREX is a progestin antagonist indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. (1)

----------DOSAGE AND ADMINISTRATION----------
- 200 mg MIFEPREX on Day 1, followed 24-48 hours after MIFEPREX dosing by 800 mcg buccal misoprostol. (2.1)
- Instruct the patient what to do if significant adverse reactions occur. (2.2)
- Follow-up is needed to confirm complete termination of pregnancy. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Tablets containing 200 mg of mifepristone each, supplied as 1 tablet on one blister card (3)

----------CONTRAINDICATIONS----------
- Confirmed/suspected ectopic pregnancy or undiagnosed adnexal mass (4)
- Chronic adrenal failure (4)
- Concurrent long-term corticosteroid therapy (4)
- History of allergy to mifepristone, misoprostol, or other prostaglandins (4)
- Hemorrhagic disorders or concurrent anticoagulant therapy (4)
- Inherited porphyria (4)
- Intrauterine device (IUD) in place (4)

----------WARNINGS AND PRECAUTIONS----------
- Ectopic pregnancy: Exclude before treatment. (5.4)
- Rhesus immunization: Prevention needed as for surgical abortion. (5.5)

----------ADVERSE REACTIONS----------
Most common adverse reactions (>15%) are nausea, weakness, fever/chills, vomiting, headache, diarrhea, and dizziness. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Danco Laboratories, LLC at 1-877-432-7596 or medicaldirector@earlyoptionpill.com or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------DRUG INTERACTIONS----------
- CYP3A4 inducers can lower mifepristone concentrations. (7.1)
- CYP3A4 inhibitors can increase mifepristone concentrations. Use with caution. (7.2)
- CYP3A4 substrate concentrations can be increased. Caution with coadministration of substrates with narrow therapeutic margin. (7.3)

----------USE IN SPECIFIC POPULATIONS----------
- Pregnancy: Risk of fetal malformations in ongoing pregnancy if not terminated is unknown. (8.1)

See 17 for PATIENT COUNSELING INFORMATION, Medication Guide.

Revised: 01/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: SERIOUS AND SOMETIMES FATAL INFECTIONS OR BLEEDING

Serious and sometimes fatal infections and bleeding occur very rarely following spontaneous, surgical, and medical abortions, including following MIFEPREX use. No causal relationship between the use of MIFEPREX and misoprostol and these events has been established.

- **Atypical Presentation of Infection. Patients with serious bacterial infections (e.g., *Clostridium sordellii*) and sepsis can present without fever, bacteremia, or significant findings on pelvic examination following an abortion. Very rarely, deaths have been reported in patients who presented without fever, with or without abdominal pain, but with leukocytosis with a marked left shift, tachycardia, hemoconcentration, and general malaise. A high index of suspicion is needed to rule out serious infection and sepsis *[see Warnings and Precautions (5.1)]*.**
- **Bleeding. Prolonged heavy bleeding may be a sign of incomplete abortion or other complications and prompt medical or surgical intervention may be needed. Advise patients to seek immediate medical attention if they experience prolonged heavy vaginal bleeding *[see Warnings and Precautions (5.2)]*.**

Because of the risks of serious complications described above, MIFEPREX is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Mifepristone REMS Program *[see Warnings and Precautions (5.3)]*.

Before prescribing MIFEPREX, inform the patient about the risk of these serious events. Ensure that the patient knows whom to call and what to do, including going to an Emergency Room if none of the provided contacts are reachable, if they experience sustained fever, severe abdominal pain, prolonged heavy bleeding, or syncope, or if they experience abdominal pain or discomfort, or general malaise (including weakness, nausea, vomiting, or diarrhea) for more than 24 hours after taking misoprostol.

1 INDICATIONS AND USAGE

MIFEPREX is indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Regimen

For purposes of this treatment, pregnancy is dated from the first day of the last menstrual period. The duration of pregnancy may be determined from menstrual history and clinical examination. Assess the pregnancy by ultrasonographic scan if the duration of pregnancy is uncertain or if ectopic pregnancy is suspected.

Remove any intrauterine device (“IUD”) before treatment with MIFEPREX begins [*see Contraindications (4)*].

The dosing regimen for MIFEPREX and misoprostol is:

- MIFEPREX 200 mg orally + misoprostol 800 mcg buccally
  - *Day One:* MIFEPREX Administration
    One 200 mg tablet of MIFEPREX is taken in a single oral dose.
  - *Day Two or Three:* Misoprostol Administration (minimum 24-hour interval between MIFEPREX and misoprostol)
    Four 200 mcg tablets (total dose 800 mcg) of misoprostol are taken by the buccal route.

    Tell the patient to place two 200 mcg misoprostol tablets in each cheek pouch (the area between the cheek and gums) for 30 minutes and then swallow any remnants with water or another liquid (see Figure 1).

    Figure 1

    2 pills between cheek and gum on left side + 2 pills between cheek and gum on right side

Patients taking MIFEPREX must take misoprostol within 24 to 48 hours after taking MIFEPREX. The effectiveness of the regimen may be lower if misoprostol is administered less than 24 hours or more than 48 hours after mifepristone administration.

Because most women will expel the pregnancy within 2 to 24 hours of taking misoprostol *[see Clinical Studies (14)]*, discuss with the patient an appropriate location for them to be when taking the misoprostol, taking into account that expulsion could begin within 2 hours of administration.

2.2 Patient Management Following Misoprostol Administration

During the period immediately following the administration of misoprostol, the patient may need medication for cramps or gastrointestinal symptoms *[see Adverse Reactions (6)].*

Give the patient:

- Instructions on what to do if significant discomfort, excessive vaginal bleeding or other adverse reactions occur
- A phone number to call if the patient has questions following the administration of the misoprostol
- The name and phone number of the healthcare provider who will be handling emergencies.

2.3 Post-treatment Assessment: Day 7 to 14

Patients should follow-up with their healthcare provider approximately 7 to 14 days after the administration of MIFEPREX. This assessment is very important to confirm that complete termination of pregnancy has occurred and to evaluate the degree of bleeding. Termination can be confirmed by medical history, clinical examination, human Chorionic Gonadotropin (hCG) testing, or ultrasonographic scan. Lack of bleeding following treatment usually indicates failure; however, prolonged or heavy bleeding is not proof of a complete abortion.

The existence of debris in the uterus (e.g., if seen on ultrasonography) following the treatment procedure will not necessarily require surgery for its removal.

Patients should expect to experience vaginal bleeding or spotting for an average of 9 to 16 days. Women report experiencing heavy bleeding for a median duration of 2 days. Up to 8% of women may experience some type of bleeding for more than 30 days. Persistence of heavy or moderate vaginal bleeding at the time of follow-up, however, could indicate an incomplete abortion.

If complete expulsion has not occurred, but the pregnancy is not ongoing, patients may be treated with another dose of misoprostol 800 mcg buccally. There have been rare reports of uterine rupture in women who took MIFEPREX and misoprostol, including women with prior uterine rupture or uterine scar and women who received multiple doses of misoprostol within 24 hours. Patients who choose to use a repeat dose of misoprostol should have a follow-up visit with their healthcare provider in approximately 7 days to assess for complete termination.

Surgical evacuation is recommended to manage ongoing pregnancies after medical abortion *[see Use in Specific Populations (8.1)]*. Advise the patient whether you will provide such care or will refer them to another provider as part of counseling prior to prescribing MIFEPREX.

2.4 Contact for Consultation

For consultation 24 hours a day, 7 days a week with an expert in mifepristone, call Danco Laboratories at 1-877-4 Early Option (1-877-432-7596).

3 DOSAGE FORMS AND STRENGTHS

Tablets containing 200 mg of mifepristone each, supplied as 1 tablet on one blister card. MIFEPREX tablets are light yellow, cylindrical, and bi-convex tablets, approximately 11 mm in diameter and imprinted on one side with “MF.”

4 CONTRAINDICATIONS

- Administration of MIFEPREX and misoprostol for the termination of pregnancy (the “treatment procedure”) is contraindicated in patients with any of the following conditions:
  - Confirmed or suspected ectopic pregnancy or undiagnosed adnexal mass (the treatment procedure will not be effective to terminate an ectopic pregnancy) *[see Warnings and Precautions (5.4)]*
  - Chronic adrenal failure (risk of acute adrenal insufficiency)
  - Concurrent long-term corticosteroid therapy (risk of acute adrenal insufficiency)
  - History of allergy to mifepristone, misoprostol, or other prostaglandins (allergic reactions including anaphylaxis, angioedema, rash, hives, and itching have been reported *[see Adverse Reactions (6.2)]*)
  - Hemorrhagic disorders or concurrent anticoagulant therapy (risk of heavy bleeding)

- Inherited porphyrias (risk of worsening or of precipitation of attacks)

- Use of MIFEPREX and misoprostol for termination of intrauterine pregnancy is contraindicated in patients with an intrauterine device ("IUD") in place (the IUD might interfere with pregnancy termination). If the IUD is removed, MIFEPREX may be used.

5 WARNINGS AND PRECAUTIONS

5.1 Infection and Sepsis

As with other types of abortion, cases of serious bacterial infection, including very rare cases of fatal septic shock, have been reported following the use of MIFEPREX *[see Boxed Warning]*. Healthcare providers evaluating a patient who is undergoing a medical abortion should be alert to the possibility of this rare event. A sustained (> 4 hours) fever of 100.4°F or higher, severe abdominal pain, or pelvic tenderness in the days after a medical abortion may be an indication of infection.

A high index of suspicion is needed to rule out sepsis (e.g., from *Clostridium sordellii*) if a patient reports abdominal pain or discomfort or general malaise (including weakness, nausea, vomiting, or diarrhea) more than 24 hours after taking misoprostol. Very rarely, deaths have been reported in patients who presented without fever, with or without abdominal pain, but with leukocytosis with a marked left shift, tachycardia, hemoconcentration, and general malaise. No causal relationship between MIFEPREX and misoprostol use and an increased risk of infection or death has been established. *Clostridium sordellii* infections have also been reported very rarely following childbirth (vaginal delivery and caesarian section), and in other gynecologic and non-gynecologic conditions.

5.2 Uterine Bleeding

Uterine bleeding occurs in almost all patients during a medical abortion. Prolonged heavy bleeding (soaking through two thick full-size sanitary pads per hour for two consecutive hours) may be a sign of incomplete abortion or other complications, and prompt medical or surgical intervention may be needed to prevent the development of hypovolemic shock. Counsel patients to seek immediate medical attention if they experience prolonged heavy vaginal bleeding following a medical abortion *[see Boxed Warning]*.

Women should expect to experience vaginal bleeding or spotting for an average of 9 to 16 days. Women report experiencing heavy bleeding for a median duration of 2 days. Up to 8% of all subjects may experience some type of bleeding for 30 days or more. In general, the duration of bleeding and spotting increased as the duration of the pregnancy increased.

Decreases in hemoglobin concentration, hematocrit, and red blood cell count may occur in patients who bleed heavily.

Excessive uterine bleeding usually requires treatment by uterotonics, vasoconstrictor drugs, surgical uterine evacuation, administration of saline infusions, and/or blood transfusions. Based on data from several large clinical trials, vasoconstrictor drugs were used in 4.3% of all subjects, there was a decrease in hemoglobin of more than 2 g/dL in 5.5% of subjects, and blood transfusions were administered to ≤ 0.1% of subjects. Because heavy bleeding requiring surgical uterine evacuation occurs in about 1% of patients, special care should be given to patients with hemostatic disorders, hypocoagulability, or severe anemia.

5.3 Mifepristone REMS Program

MIFEPREX is available only through a restricted program under a REMS called the Mifepristone REMS Program, because of the risks of serious complications *[see Warnings and Precautions (5.1, 5.2)]*.

Notable requirements of the Mifepristone REMS Program include the following:

- Prescribers must be certified with the program by completing the Prescriber Agreement Form.
- Patients must sign a Patient Agreement Form.
- MIFEPREX must only be dispensed to patients by or under the supervision of a certified prescriber, or by certified pharmacies on prescriptions issued by certified prescribers.

Further information is available at 1-877-4 Early Option (1-877-432-7596).

5.4 Ectopic Pregnancy

MIFEPREX is contraindicated in patients with a confirmed or suspected ectopic pregnancy because MIFEPREX is not effective for terminating ectopic pregnancies *[see Contraindications (4)]*. Healthcare providers should remain alert to the possibility that a patient who is undergoing a medical abortion could have an undiagnosed ectopic pregnancy because some of the expected symptoms experienced with a medical abortion (abdominal pain, uterine bleeding) may be similar to those of a ruptured ectopic pregnancy. The presence of an ectopic pregnancy may have been missed even if the patient underwent ultrasonography prior to being prescribed MIFEPREX.

Patients who became pregnant with an IUD in place should be assessed for ectopic pregnancy.

5.5 Rhesus Immunization

The use of MIFEPREX is assumed to require the same preventive measures as those taken prior to and during surgical abortion to prevent rhesus immunization.

6 ADVERSE REACTIONS

The following adverse reactions are described in greater detail in other sections:

- Infection and sepsis *[see Warnings and Precautions (5.1)]*
- Uterine bleeding *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Information presented on common adverse reactions relies solely on data from U.S. studies, because rates reported in non-U.S. studies were markedly lower and are not likely generalizable to the U.S. population. In three U.S. clinical studies totaling 1,248 women through 70 days gestation who used mifepristone 200 mg orally followed 24-48 hours later by misoprostol 800 mcg buccally, women reported adverse reactions in diaries and in interviews at the follow-up visit. These studies enrolled generally healthy women of reproductive age without contraindications to mifepristone or misoprostol use according to the MIFEPREX product label. Gestational age was assessed prior to study enrollment using the date of the woman's last menstrual period, clinical evaluation, and/or ultrasound examination.

About 85% of patients report at least one adverse reaction following administration of MIFEPREX and misoprostol, and many can be expected to report more than one such reaction. The most commonly reported adverse reactions (>15%) were nausea, weakness, fever/chills, vomiting, headache, diarrhea, and dizziness (see Table 1). The frequency of adverse reactions varies between studies and may be dependent on many factors, including the patient population and gestational age.

Abdominal pain/cramping is expected in all medical abortion patients and its incidence is not reported in clinical studies. Treatment with MIFEPREX and misoprostol is designed to induce uterine bleeding and cramping to cause termination of an intrauterine pregnancy. Uterine bleeding and cramping are expected consequences of the action of MIFEPREX and misoprostol as used in the treatment procedure. Most patients can expect bleeding more heavily than they do during a heavy menstrual period *[see Warnings and Precautions (5.2)]*.

Table 1 lists the adverse reactions reported in U.S. clinical studies with incidence >15% of women.

Table 1
Adverse Reactions Reported in Women Following Administration of Mifepristone (oral) and Misoprostol (buccal) in U.S. Clinical Studies

Adverse Reaction	# U.S. studies	Number of Evaluable Women	Range of frequency (%)	Upper Gestational Age of Studies Reporting Outcome
Nausea	3	1,248	51-75%	70 days
Weakness	2	630	55-58%	63 days
Fever/chills	1	414	48%	63 days
Vomiting	3	1,248	37-48%	70 days
Headache	2	630	41-44%	63 days
Diarrhea	3	1,248	18-43%	70 days
Dizziness	2	630	39-41%	63 days

One study provided gestational-age stratified adverse reaction rates for women who were 57-63 and 64-70 days; there was little difference in frequency of the reported common adverse reactions by gestational age.

Information on serious adverse reactions was reported in six U.S. and four non-U.S. clinical studies, totaling 30,966 women through 70 days gestation who used mifepristone 200 mg orally followed 24-48 hours later by misoprostol 800 mcg buccally. Serious adverse reaction rates were similar between U.S. and non-U.S. studies, so rates from both U.S. and non-U.S. studies are presented. In the U.S. studies, one studied women through 56 days gestation, four through 63 days gestation, and one through 70 days gestation, while in the non-U.S. studies, two studied women through 63 days gestation, and two through 70 days gestation. Serious adverse reactions were reported in <0.5% of women. Information from the U.S. and non-U.S. studies is presented in Table 2.

Table 2
Serious Adverse Reactions Reported in Women Following Administration of Mifepristone (oral) and Misoprostol (buccal) in U.S. and Non-U.S. Clinical Studies

Adverse Reaction	U.S.			Non-U.S.		
	# of studies	Number of Evaluable Women	Range of frequency (%)	# of studies	Number of Evaluable Women	Range of frequency (%)
Transfusion	4	17,774	0.03-0.5%	3	12,134	0-0.1%
Sepsis	1	629	0.2%	1	11,155	<0.01%*
ER visit	2	1,043	2.9-4.6%	1	95	0
Hospitalization Related to Medical Abortion	3	14,339	0.04-0.6%	3	1,286	0-0.7%
Infection without sepsis	1	216	0	1	11,155	0.2%
Hemorrhage	NR	NR	NR	1	11,155	0.1%

NR= Not reported
* This outcome represents a single patient who experienced death related to sepsis.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of MIFEPREX and misoprostol. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Infections and infestations: post-abortal infection (including endometritis, endomyometritis, parametritis, pelvic infection, pelvic inflammatory disease, salpingitis)
Blood and the lymphatic system disorders: anemia
Immune system disorders: allergic reaction (including anaphylaxis, angioedema, hives, rash, itching)
Psychiatric disorders: anxiety
Cardiac disorders: tachycardia (including racing pulse, heart palpitations, heart pounding)
Vascular disorders: syncope, fainting, loss of consciousness, hypotension (including orthostatic), light-headedness
Respiratory, thoracic and mediastinal disorders: shortness of breath
Gastrointestinal disorders: dyspepsia
Musculoskeletal, connective tissue and bone disorders: back pain, leg pain
Reproductive system and breast disorders: uterine rupture, ruptured ectopic pregnancy, hematometra, leukorrhea
General disorders and administration site conditions: pain

7 DRUG INTERACTIONS

7.1 Drugs that May Reduce MIFEPREX Exposure (Effect of CYP 3A4 Inducers on MIFEPREX)

CYP450 3A4 is primarily responsible for the metabolism of mifepristone. CYP3A4 inducers such as rifampin, dexamethasone, St. John's Wort, and certain anticonvulsants (such as phenytoin, phenobarbital, carbamazepine) may induce mifepristone metabolism (lowering serum concentrations of mifepristone). Whether this action has an impact on the efficacy of the dose

regimen is unknown. Refer to the follow-up assessment *[see Dosage and Administration (2.3)]* to verify that treatment has been successful.

7.2 Drugs that May Increase MIFEPREX Exposure (Effect of CYP 3A4 Inhibitors on MIFEPREX)

Although specific drug or food interactions with mifepristone have not been studied, on the basis of this drug's metabolism by CYP 3A4, it is possible that ketoconazole, itraconazole, erythromycin, and grapefruit juice may inhibit its metabolism (increasing serum concentrations of mifepristone). MIFEPREX should be used with caution in patients currently or recently treated with CYP 3A4 inhibitors.

7.3 Effects of MIFEPREX on Other Drugs (Effect of MIFEPREX on CYP 3A4 Substrates)

Based on *in vitro* inhibition information, coadministration of mifepristone may lead to an increase in serum concentrations of drugs that are CYP 3A4 substrates. Due to the slow elimination of mifepristone from the body, such interaction may be observed for a prolonged period after its administration. Therefore, caution should be exercised when mifepristone is administered with drugs that are CYP 3A4 substrates and have narrow therapeutic range.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

MIFEPREX is indicated, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. Risks to pregnant patients are discussed throughout the labeling.

Refer to misoprostol labeling for risks to pregnant patients with the use of misoprostol.

The risk of adverse developmental outcomes with a continued pregnancy after a failed pregnancy termination with MIFEPREX in a regimen with misoprostol is unknown; however, the process of a failed pregnancy termination could disrupt normal embryo-fetal development and result in adverse developmental effects. Birth defects have been reported with a continued pregnancy after a failed pregnancy termination with MIFEPREX in a regimen with misoprostol. In animal reproduction studies, increased fetal losses were observed in mice, rats, and rabbits and skull deformities were observed in rabbits with administration of mifepristone at doses lower than the human exposure level based on body surface area.

Data

Animal Data

In teratology studies in mice, rats and rabbits at doses of 0.25 to 4.0 mg/kg (less than 1/100 to approximately 1/3 the human exposure based on body surface area), because of the antiprogestational activity of mifepristone,fetal losses were much higher than in control animals. Skull deformities were detected in rabbit studies at approximately 1/6 the human exposure, although no teratogenic effects of mifepristone have been observed to date in rats or mice. These deformities were most likely due to the mechanical effects of uterine contractions resulting from inhibition of progesterone action.

8.2 Lactation

MIFEPREX is present in human milk. Limited data demonstrate undetectable to low levels of the drug in human milk with the relative (weight-adjusted) infant dose 0.5% or less as compared to maternal dosing. There is no information on the effects of MIFEPREX in a regimen with

misoprostol in a breastfed infant or on milk production. Refer to misoprostol labeling for lactation information with the use of misoprostol. The developmental and health benefits of breast-feeding should be considered along with any potential adverse effects on the breast-fed child from MIFEPREX in a regimen with misoprostol.

8.4 Pediatric Use

Safety and efficacy of MIFEPREX have been established in pregnant females. Data from a clinical study of MIFEPREX that included a subset of 322 females under age 17 demonstrated a safety and efficacy profile similar to that observed in adults.

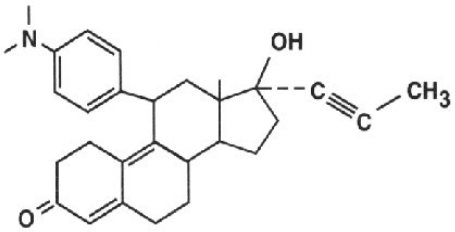
10 OVERDOSAGE

No serious adverse reactions were reported in tolerance studies in healthy non-pregnant female and healthy male subjects where mifepristone was administered in single doses greater than 1800 mg (ninefold the recommended dose for medical abortion). If a patient ingests a massive overdose, the patient should be observed closely for signs of adrenal failure.

11 DESCRIPTION

MIFEPREX tablets each contain 200 mg of mifepristone, a synthetic steroid with antiprogestational effects. The tablets are light yellow in color, cylindrical, and bi-convex, and are intended for oral administration only. The tablets include the inactive ingredients colloidal silica anhydrous, corn starch, povidone, microcrystalline cellulose, and magnesium stearate.

Mifepristone is a substituted 19-nor steroid compound chemically designated as 11ß-[*p*-(Dimethylamino)phenyl]-17ß-hydroxy-17-(1-propynyl)estra-4,9-dien-3-one. Its empirical formula is $C_{29}H_{35}NO_2$. Its structural formula is:



The compound is a yellow powder with a molecular weight of 429.6 and a melting point of 192-196°C. It is very soluble in methanol, chloroform and acetone and poorly soluble in water, hexane and isopropyl ether.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The anti-progestational activity of mifepristone results from competitive interaction with progesterone at progesterone-receptor sites. Based on studies with various oral doses in several animal species (mouse, rat, rabbit, and monkey), the compound inhibits the activity of endogenous or exogenous progesterone, resulting in effects on the uterus and cervix that, when combined with misoprostol, result in termination of an intrauterine pregnancy.

During pregnancy, the compound sensitizes the myometrium to the contraction-inducing activity

of prostaglandins.

12.2 Pharmacodynamics

Use of MIFEPREX in a regimen with misoprostol disrupts pregnancy by causing decidual necrosis, myometrial contractions, and cervical softening, leading to the expulsion of the products of conception.

Doses of 1 mg/kg or greater of mifepristone have been shown to antagonize the endometrial and myometrial effects of progesterone in women.

Antiglucocorticoid and antiandrogenic activity: Mifepristone also exhibits antiglucocorticoid and weak antiandrogenic activity. The activity of the glucocorticoid dexamethasone in rats was inhibited following doses of 10 to 25 mg/kg of mifepristone. Doses of 4.5 mg/kg or greater in human beings resulted in a compensatory elevation of adrenocorticotropic hormone (ACTH) and cortisol. Antiandrogenic activity was observed in rats following repeated administration of doses from 10 to 100 mg/kg.

12.3 Pharmacokinetics

Mifepristone is rapidly absorbed after oral ingestion with non-linear pharmacokinetics for Cmax after single oral doses of 200 mg and 600 mg in healthy subjects.

Absorption

The absolute bioavailability of a 20 mg mifepristone oral dose in females of childbearing age is 69%. Following oral administration of a single dose of 600 mg, mifepristone is rapidly absorbed, with a peak plasma concentration of 1.98 ± 1.0 mg/L occurring approximately 90 minutes after ingestion.

Following oral administration of a single dose of 200 mg in healthy men (n=8), mean Cmax was 1.77 ± 0.7 mg/L occurring approximately 45 minutes after ingestion. Mean $AUC_{0-\infty}$ was 25.8 ± 6.2 mg*hr/L.

Distribution

Mifepristone is 98% bound to plasma proteins, albumin, and α_1-acid glycoprotein. Binding to the latter protein is saturable, and the drug displays nonlinear kinetics with respect to plasma concentration and clearance.

Elimination

Following a distribution phase, elimination of mifepristone is slow at first (50% eliminated between 12 and 72 hours) and then becomes more rapid with a terminal elimination half-life of 18 hours.

Metabolism

Metabolism of mifepristone is primarily via pathways involving N-demethylation and terminal hydroxylation of the 17-propynyl chain. *In vitro* studies have shown that CYP450 3A4 is primarily responsible for the metabolism. The three major metabolites identified in humans are: (1) RU 42 633, the most widely found in plasma, is the N-monodemethylated metabolite; (2) RU 42 848, which results from the loss of two methyl groups from the 4-dimethylaminophenyl in position 11ß; and (3) RU 42 698, which results from terminal hydroxylation of the 17-propynyl chain.

Excretion

By 11 days after a 600 mg dose of tritiated compound, 83% of the drug has been accounted for by the feces and 9% by the urine. Serum concentrations are undetectable by 11 days.

Specific Populations

The effects of age, hepatic disease and renal disease on the safety, efficacy and pharmacokinetics of mifepristone have not been investigated.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

No long-term studies to evaluate the carcinogenic potential of mifepristone have been performed.

Mutagenesis

Results from studies conducted *in vitro* and in animals have revealed no genotoxic potential for mifepristone. Among the tests carried out were: Ames test with and without metabolic activation; gene conversion test in *Saccharomyces cerevisiae* D4 cells; forward mutation in *Schizosaccharomyces pompe* P1 cells; induction of unscheduled DNA synthesis in cultured HeLa cells; induction of chromosome aberrations in CHO cells; *in vitro* test for gene mutation in V79 Chinese hamster lung cells; and micronucleus test in mice.

Impairment of Fertility

In rats, administration of 0.3 mg/kg mifepristone per day caused severe disruption of the estrus cycles for the three weeks of the treatment period. Following resumption of the estrus cycle, animals were mated and no effects on reproductive performance were observed.

14 CLINICAL STUDIES

Safety and efficacy data from clinical studies of mifepristone 200 mg orally followed 24-48 hours later by misoprostol 800 mcg buccally through 70 days gestation are reported below. Success was defined as the complete expulsion of the products of conception without the need for surgical intervention. The overall rates of success and failure, shown by reason for failure based on 22 worldwide clinical studies (including 7 U.S. studies) appear in Table 3.

The demographics of women who participated in the U.S. clinical studies varied depending on study location and represent the racial and ethnic variety of American females. Females of all reproductive ages were represented, including females less than 18 and more than 40 years of age; most were 27 years or younger.

Table 3
Outcome Following Treatment with Mifepristone (oral) and Misoprostol (buccal) Through 70 Days Gestation

	U.S. Trials	Non-U.S. Trials
N	16,794	18,425
Complete Medical Abortion	97.4%	96.2%
Surgical Intervention*	2.6%	3.8%
Ongoing Pregnancy**	0.7%	0.9%

* Reasons for surgical intervention include ongoing pregnancy, medical necessity, persistent or heavy bleeding after treatment, patient request, or incomplete expulsion.
** Ongoing pregnancy is a subcategory of surgical intervention, indicating the percent of women who have surgical intervention due to an ongoing pregnancy.

The results for clinical studies that reported outcomes, including failure rates for ongoing pregnancy, by gestational age are presented in Table 4.

Table 4
Outcome by Gestational Age Following Treatment with Mifepristone and Misoprostol (buccal) for U.S. and Non-U.S. Clinical Studies

	≤49 days			50-56 days			57-63 days			64-70 days		
	N	%	Number of Evaluable Studies	N	%	Number of Evaluable Studies	N	%	Number of Evaluable Studies	N	%	Number of Evaluable Studies
Complete medical abortion	12,046	98.1	10	3,941	96.8	7	2,294	94.7	9	479	92.7	4
Surgical intervention for ongoing pregnancy	10,272	0.3	6	3,788	0.8	6	2,211	2	8	453	3.1	3

One clinical study asked subjects through 70 days gestation to estimate when they expelled the pregnancy, with 70% providing data. Of these, 23-38% reported expulsion within 3 hours and over 90% within 24 hours of using misoprostol.

16 HOW SUPPLIED/STORAGE AND HANDLING

is only available through a restricted program called the Mifepristone REMS Program *[see Warnings and Precautions (5.3)].*

MIFEPREX is supplied as light yellow, cylindrical, and bi-convex tablets imprinted on one side with “MF.” Each tablet contains 200 mg of mifepristone. One tablet is individually blistered on one blister card that is packaged in an individual package (National Drug Code 64875-001-01).

Store at 25°C (77°F); excursions permitted to 15 to 30°C (59 to 86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide), included with each package of MIFEPREX. Additional copies of the Medication Guide are available by contacting Danco Laboratories at 1-877-4 Early Option (1-877-432-7596) or from www.earlyoptionpill.com.

Serious Infections and Bleeding

- Inform the patient that uterine bleeding and uterine cramping will occur [*see Warnings and Precautions (5.2)*].
- Advise the patient that serious and sometimes fatal infections and bleeding can occur very rarely [*see Warnings and Precautions (5.1, 5.2)*].
- MIFEPREX is only available through a restricted program called the Mifepristone REMS Program [*see Warnings and Precautions (5.3)*]. Under the Mifepristone REMS Program:
    - Patients must sign a Patient Agreement Form.
    - MIFEPREX is only dispensed by or under the supervision of certified prescribers or by certified pharmacies on prescriptions issued by certified prescribers.

Provider Contacts and Actions in Case of Complications

- Ensure that the patient knows whom to call and what to do, including going to an Emergency Room if none of the provided contacts are reachable, or if the patient experiences complications including prolonged heavy bleeding, severe abdominal pain, or sustained fever *[see Boxed Warning]*.
-

Compliance with Treatment Schedule and Follow-up Assessment

- Advise the patient that it is necessary to complete the treatment schedule, including a follow-up assessment approximately 7 to14 days after taking MIFEPREX *[see Dosage and Administration (2.3)]*.
- Explain that
    - prolonged heavy vaginal bleeding is not proof of a complete abortion,
    - if the treatment fails and the pregnancy continues, the risk of fetal malformation is unknown,
    - it is recommended that ongoing pregnancy be managed by surgical termination *[see Dosage and Administration (2.3)]*. Advise the patient whether you will provide such care or will refer them to another provider.

Subsequent Fertility

- Inform the patient that another pregnancy can occur following medical abortion and before resumption of normal menses.
- Inform the patient that contraception can be initiated as soon as pregnancy expulsion has been confirmed, or before resuming sexual intercourse.

MIFEPREX is a registered trademark of Danco Laboratories, LLC.

Manufactured for:
Danco Laboratories, LLC
P.O. Box 4816
New York, NY 10185
1-877-4 Early Option (1-877-432-7596)
www.earlyoptionpill.com

03/2023

MEDICATION GUIDE

Mifeprex (MIF-eh-prex) (mifepristone tablets, for oral use

Read this information carefully before taking Mifeprex and misoprostol. It will help you understand how the treatment works. This Medication Guide does not take the place of talking with your healthcare provider.

What is the most important information I should know about Mifeprex?

What symptoms should I be concerned with? Although cramping and bleeding are an expected part of ending a pregnancy, rarely, serious and potentially life-threatening bleeding, infections, or other problems can occur following a miscarriage, surgical abortion, medical abortion, or childbirth. Seeking medical attention as soon as possible is needed in these circumstances. Serious infection has resulted in death in a very small number of cases. There is no information that use of Mifeprex and misoprostol caused these deaths. If you have any questions, concerns, or problems, or if you are worried about any side effects or symptoms, you should contact your healthcare provider. You can write down your healthcare provider's telephone number here _____.

Be sure to contact your healthcare provider promptly if you have any of the following:

- **Heavy Bleeding.** Contact your healthcare provider right away if you bleed enough to soak through two thick full-size sanitary pads per hour for two consecutive hours or if you are concerned about heavy bleeding. In about 1 out of 100 women, bleeding can be so heavy that it requires a surgical procedure (surgical aspiration or D&C).
- **Abdominal Pain or "Feeling Sick."** If you have abdominal pain or discomfort, or you are "feeling sick," including weakness, nausea, vomiting, or diarrhea, with or without fever, more than 24 hours after taking misoprostol, you should contact your healthcare provider without delay. These symptoms may be a sign of a serious infection or another problem (including an ectopic pregnancy, a pregnancy outside the womb).
- **Fever.** In the days after treatment, if you have a fever of 100.4°F or higher that lasts for more than 4 hours, you should contact your healthcare provider right away. Fever may be a symptom of a serious infection or another problem.

If you cannot reach your healthcare provider, go to the nearest hospital emergency room.

What to do if you are still pregnant after Mifeprex with misoprostol treatment. If you are still pregnant, your healthcare provider will talk with you about a surgical procedure to end your pregnancy. In many cases, this surgical procedure can be done in the office/clinic. The chance of birth defects if the pregnancy is not ended is unknown.

Talk with your healthcare provider. Before you take Mifeprex, you should read this Medication Guide and you and your healthcare provider should discuss the benefits and risks of your using Mifeprex.

What is Mifeprex?

Mifeprex is used in a regimen with another prescription medicine called misoprostol, to end an early pregnancy. Early pregnancy means it is 70 days (10 weeks) or less since your last menstrual period began. Mifeprex is not approved for ending pregnancies that are further along. Mifeprex blocks a hormone needed for your pregnancy to continue. When you use Mifeprex on Day 1, you also need to take another medicine called misoprostol 24 to 48 hours after you take Mifeprex, to cause the pregnancy to be passed from your uterus.

The pregnancy is likely to be passed from your uterus within 2 to 24 hours after taking Mifeprex and misoprostol. When the pregnancy is passed from the uterus, you will have bleeding and cramping that will likely be heavier than your usual period. About 2 to 7 out of 100 women taking Mifeprex will need a surgical procedure because the pregnancy did not completely pass from the uterus or to stop bleeding.

Who should not take Mifeprex?

Some patients should not take Mifeprex. Do not take Mifeprex if you:

- Have a pregnancy that is more than 70 days (10 weeks). Your healthcare provider may do a clinical examination, an ultrasound examination, or other testing to determine how far along you are in pregnancy.
- Are using an IUD (intrauterine device or system). It must be taken out before you take Mifeprex.
- Have been told by your healthcare provider that you have a pregnancy outside the uterus (ectopic pregnancy).
- Have problems with your adrenal glands (chronic adrenal failure).
- Take a medicine to thin your blood.
- Have a bleeding problem.
- Have porphyria.
- Take certain steroid medicines.
- Are allergic to mifepristone, misoprostol, or medicines that contain misoprostol, such as Cytotec or Arthrotec.

Ask your healthcare provider if you are not sure about all your medical conditions before taking this medicine to find out if you can take Mifeprex.

What should I tell my healthcare provider before taking Mifeprex?

Before you take Mifeprex, tell your healthcare provider if you:

- cannot follow-up within approximately 7 to 14 days of your first visit
- are breastfeeding. Mifeprex can pass into your breast milk. The effect of the Mifeprex and misoprostol regimen on the breastfed infant or on milk production is unknown.
- are taking medicines, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
  Mifeprex and certain other medicines may affect each other if they are used together. This can cause side effects.

How should I take Mifeprex?

- Mifeprex will be given to you by a healthcare provider or pharmacy.
- You and your healthcare provider will plan the most appropriate location for you to take the misoprostol, because it may cause bleeding, cramps, nausea, diarrhea, and other symptoms that usually begin within 2 to 24 hours after taking it.
- Most women will pass the pregnancy within 2 to 24 hours after taking the misoprostol tablets.

Follow the instruction below on how to take Mifeprex and misoprostol:

Mifeprex (1 tablet) orally + misoprostol (4 tablets) buccally

Day 1:

- Take 1 Mifeprex tablet by mouth.

24 to 48 hours after taking Mifeprex:

- Take 4 misoprostol tablets by placing 2 tablets in each cheek pouch (the area between your teeth and cheek - see Figure A) for 30 minutes and then swallow anything left over with a drink of water or another liquid.
- The medicines may not work as well if you take misoprostol sooner than 24 hours after Mifeprex or later than 48 hours after Mifeprex.
- Misoprostol often causes cramps, nausea, diarrhea, and other symptoms. Your healthcare provider may send you home with medicines for these symptoms.

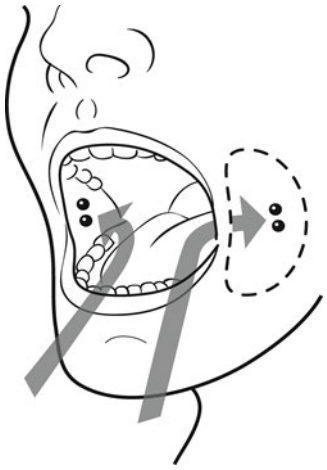


Figure A (2 tablets between your left cheek and gum and 2 tablets between your right cheek and gum).

Follow-up Assessment at Day 7 to 14:

- This follow-up assessment is very important. You must follow-up with your healthcare provider about 7 to 14 days after you have taken Mifeprex to be sure you are well and that you have had bleeding and the pregnancy has passed from your uterus.
- Your healthcare provider will assess whether your pregnancy has passed from your uterus. If your pregnancy continues, the chance that there may be birth defects is unknown. If you are still pregnant, your healthcare provider will talk with you about a surgical procedure to end your pregnancy.
- If your pregnancy has ended, but has not yet completely passed from your uterus, your provider will talk with you about other choices you have, including waiting, taking another dose of misoprostol, or having a surgical procedure to empty your uterus.

When should I begin birth control?

You can become pregnant again right after your pregnancy ends. If you do not want to become pregnant again, start using birth control as soon as your pregnancy ends or before you start having sexual intercourse again.

What should I avoid while taking Mifeprex and misoprostol?

Do not take any other prescription or over-the-counter medicines (including herbal medicines or supplements) at any time during the treatment period without first asking your healthcare provider about them because they may interfere with the treatment. Ask your healthcare provider about what medicines you can take for pain and other side effects.

What are the possible side effects of Mifeprex and misoprostol?

Mifeprex may cause serious side effects. See "What is the most important information I should know about Mifeprex?"

Cramping and bleeding. Cramping and vaginal bleeding are expected with this treatment. Usually, these symptoms mean that the treatment is working. But sometimes you can get cramping and bleeding and still be pregnant. This is why you must follow-up with your healthcare provider approximately 7 to 14 days after taking Mifeprex. See "How should I take Mifeprex?" for more information on your follow-up assessment. If you are not already bleeding after taking Mifeprex, you probably will begin to bleed once you take misoprostol, the medicine you take 24 to 48 hours after Mifeprex. Bleeding or spotting can be expected for an average of 9 to16 days and may last for up to 30 days. Your bleeding may be similar to, or greater than, a normal heavy period. You may see blood clots and tissue. This is an expected part of passing the pregnancy.

The most common side effects of Mifeprex treatment include: nausea, weakness, fever/chills, vomiting, headache, diarrhea and dizziness. Your provider will tell you how to manage any pain or other side effects. These are not all the possible side effects of Mifeprex.

Call your healthcare provider for medical advice about any side effects that bother you or do not go away. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of Mifeprex.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. This Medication Guide summarizes the most important information about Mifeprex. If you would like more information, talk with your healthcare provider. You may ask your healthcare provider for information about Mifeprex that is written for healthcare professionals.

For more information about Mifeprex, go to www.earlyoptionpill.com or call 1-877-4 Early Option (1-877-432-7596).

Manufactured for: *Danco Laboratories, LLC*
P.O. Box 4816
New York, NY 10185
1-877-4 Early Option (1-877-432-7596) www.earlyoptionpill.com

This Medication Guide has been approved by the U.S. Food and Drug Administration. Approval 03/2023

FDA U.S. FOOD & DRUG ADMINISTRATION

ANDA 216616

ANDA APPROVAL

Evita Solutions, LLC
(b) (6), (b) (4)

Dear (b) (6), (b) (4):

This letter is in reference to your abbreviated new drug application (ANDA) received for review on October 1, 2021, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Mifepristone Tablets, 200 mg.

Reference is also made to any amendments submitted prior to the issuance of this letter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug meets the requirements for approval under the FD&C Act. Accordingly the ANDA is **approved**, effective on the date of this letter. We have determined your Mifepristone Tablets, 200 mg to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Mifeprex (mifepristone) tablets, 200 mg, of Danco Laboratories, LLC NDA - 020687.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FD&C Act authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a) of the FD&C Act]. In accordance with section 505-1(i) of the FD&C Act, a drug that is the subject of an ANDA under section 505(j) of the FD&C Act is subject to certain elements of the REMS required for the applicable listed drug.

The details of the REMS requirements were outlined in our REMS notification letter dated January 26, 2022.

The Mifepristone REMS Program is an approved single, shared system (SSS) REMS for mifepristone 200 mg tablets, in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation; it includes Elements to Assure Safe Use (ETASU) and an implementation system.

Your final proposed REMS, received on April 16, 2025 is approved. Your product will be included in the Mifepristone REMS Program and will be posted on the FDA REMS website: http://www.fda.gov/rems.

Other products may be added to the Mifepristone REMS Program in the future if additional NDAs or ANDAs are approved.

Your REMS must be fully operational before you introduce your drug into interstate commerce.

Under section 505-1(g)(2)(C) of the FD&C Act, FDA can require the submission of a REMS assessment if FDA determines an assessment is needed to evaluate whether the REMS should be modified to ensure the benefits of the drug outweigh the risks or to minimize the burden on the healthcare delivery system of complying with the REMS.

We remind you that you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FD&C Act.

We also remind you that section 505-1(f)(8) of the FD&C Act prohibits holders of an approved covered application from using any element to assure safe use to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) of the FD&C Act could result in enforcement action.

Prominently identify any submission containing a REMS assessment or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

ANDA 216616 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR ANDA 216616/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR ANDA 216616/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR ANDA 216616/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISION FOR ANDA 216616

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but Word format is preferred.

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standard for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website as https://www.uspnf.com/.

REQUIREMENTS AND RECOMMENDATIONS POST APPROVAL

Under applicable statutes, regulations, and guidances, your ANDA may be subject to certain requirements and recommendations post approval, including requirements regarding changes to approved ANDAs, postmarketing reporting, promotional materials, and annual facility fees, among others. For information on post-approval requirements and recommendations for ANDAs and a list of resources for ANDA holders, we refer you to https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/requirements-and-resources-approved-andas.

Sincerely yours,

{See appended electronic signature page}

(b) (6)

Center for Drug Evaluation and Research

(b) (6)

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