

Mifeprex® (Mifepristone)

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[➔ Instructions for Use](#)

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| Table of Contents | Page |
| Coverage Rationale | 1 |
| Applicable Codes | 1 |
| Background | 2 |
| Benefit Considerations | 2 |
| Clinical Evidence | 2 |
| U.S. Food and Drug Administration | 3 |
| Centers for Medicare and Medicaid Services | 4 |
| References | 4 |
| Policy History/Revision Information | 6 |
| Instructions for Use | 6 |

| Related Policies |
|------------------|
| None |

Coverage Rationale

[➔ See Benefit Considerations](#)

Mifeprex (mifepristone), in combination with misoprostol, is proven and medically necessary for the medical termination of intrauterine pregnancy through 70 days gestation when administered under the supervision of a qualified physician.³ For purposes of this treatment, pregnancy is dated from the first day of the last menstrual period in a presumed 28 day cycle with ovulation occurring at mid-cycle.³

Mifeprex should be prescribed only by physicians who have read and understood the prescribing information. Mifeprex may be administered only in a clinic, medical office, or hospital, by or under the supervision of a physician, able to assess the gestational age of an embryo and to diagnose ectopic pregnancies. Physicians must also be able to provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through others, and be able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.^{3,25}

Mifeprex is unproven and not medically necessary for treatment of:

- Breast cancer
- Endometriosis
- Induction of labor
- Leiomyomata
- Meningioma
- Oral contraception
- Ovarian cancer
- Psychotic major depression

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service.

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

| HCPCS Code | Description |
|------------|----------------------------|
| S0190 | Mifepristone, oral, 200 mg |
| S0191 | Misoprostol, oral, 200 mcg |

Background

Mifeprex (mifepristone) is a synthetic steroid with antiprogesterone effects. The anti-progesterone 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.³

Benefit Considerations

Although Mifeprex (mifepristone) is an orally administered drug product, the Risk Evaluation and Mitigation Strategy associated with its use requires administration in the physician's office clinic, or hospital.

The US Food and Drug Administration has granted approval of another mifepristone product, Korlym[®], for the treatment of endogenous Cushing's syndrome.²⁴ Notification criteria for Korlym are administered under the pharmacy benefit.

The member specific Certificate of Coverage must be referenced as some COCs contain explicit exclusions for abortion and related services. Mifepristone is a covered health service in Certificates of Coverage that do not explicitly exclude coverage for abortion and related services. Although most Certificates of Coverage explicitly exclude oral drugs administered in a physician office for non-emergency purposes, that exclusion does not apply to mifepristone.

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. See the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

Proven

Medical Termination of Intrauterine Pregnancy Through 70 Days' Pregnancy

Mifeprex, in combination with misoprostol, is indicated for the medical termination of intrauterine pregnancy through 70 days' pregnancy.³

Unproven

Mifepristone has also been used in the treatment of endometriosis, breast and ovarian cancer, meningioma, induction of labor, and psychotic major depression.^{4-6,11,13-19} In addition, modest efficacy has been shown for the use of mifepristone in treatment of symptomatic leiomyomata.^{10,21-22} To date, the studies published on these diseases have been small and most have been open-label trials. The use of mifepristone for any of these indications is considered unproven at this time. Mifepristone has also been studied as an estrogen-free oral contraceptive in small trials.^{9,20,23} Further study will need to be undertaken before mifepristone can be considered proven as an oral contraceptive.

Technology Assessment

In 2011, a Cochrane Database review was published which compared different medical methods for first trimester abortion. The authors concluded that there are safe and effective medical abortion methods available.⁷

- Combined regimens (mifepristone & misoprostol) are more effective than single agents. In the combined regimen, the dose of mifepristone can be lowered to 200 mg without significantly decreasing the method effectiveness.
- Vaginal misoprostol is more effective than oral administration and has fewer side effects than sublingual or buccal.

Professional Societies

World Health Organization

In 2018, the World Health Organization (WHO) published its recommendations for the medical management of abortion. The evidence-based recommendations on the medical management of abortion include:

- For the treatment of incomplete abortion at < 13 weeks uterine size - the use of 600 µg misoprostol administered orally or 400 µg misoprostol administered sublingually.
- For the treatment of incomplete abortion at ≥ 13 weeks uterine size – the use of repeat doses of 400 µg misoprostol administered sublingually, vaginally or buccally every 3 hours.
- For the medical management for intrauterine fetal demise at ≥ 14 to ≤ 28 weeks of gestation:
 - The use of 200 mg mifepristone administered orally, followed 1 to 2 days later by repeat doses of 400 µg misoprostol administered sublingually or vaginally every 4 to 6 hours. The minimum recommended interval between use of mifepristone and misoprostol is 24 hours.
 - Where sublingual misoprostol is not used, the use of repeat doses of 400 µg misoprostol administered vaginally every 4 to 6 hours is suggested.
- For the medical management of induced abortion at < 12 weeks gestation:
 - The use of 200 mg mifepristone administered orally, followed 1 to 2 days later by 800 µg misoprostol administered vaginally, sublingually or buccally. The minimum recommended interval between use of mifepristone and misoprostol is 24 hours.
 - For the misoprostol-only regimen, the use of 800 µg misoprostol administered vaginally, sublingually or buccally is recommended.
- For the medical management of induced abortion at ≥ 12 weeks gestation:
 - The use of 200 mg mifepristone administered orally, followed 1 to 2 days later by repeat doses of 400 µg misoprostol administered vaginally, sublingually or buccally every 3 hours. The minimum recommended interval between use of mifepristone and misoprostol is 24 hours.
 - For the misoprostol-only regimen, the use of repeat doses of 400 µg misoprostol administered vaginally, sublingually or buccally is recommended.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Although Mifeprex is an orally administered drug product, the Risk Evaluation and Mitigation Strategy associated with its use requires administration in the physician's office.

Mifeprex, in combination with misoprostol, is indicated for the medical termination of intrauterine pregnancy through 70 days' pregnancy. For purposes of this treatment, pregnancy is dated from the first day of the last menstrual period in a presumed 28 day cycle with ovulation occurring at mid-cycle. The duration of pregnancy may be determined from menstrual history and by clinical examination. Ultrasonographic scan should be used if the duration of pregnancy is uncertain, or if ectopic pregnancy is suspected. Patients taking Mifeprex must take 800 mcg, buccally, of misoprostol within 24 to 48 hours after taking Mifeprex unless a complete abortion has already been confirmed before that time. Pregnancy termination by surgery is recommended in cases when Mifeprex and misoprostol fail to cause termination of intrauterine pregnancy.³

Prior to a physician using mifepristone in his/her practice, the physician must sign and return to Danco Laboratories the Prescriber's Agreement, indicating that they meet the qualifications and will observe the guidelines outlined below.²⁵ Danco

Laboratories will not ship Mifeprex until they have the signed Prescriber Agreement on file. Under Federal law, Mifeprex must be provided by or under the supervision of a physician who meets the following qualifications:

- Ability to assess the duration of pregnancy accurately
- Ability to diagnose ectopic pregnancies
- Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through others, and are able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Has read and understood the prescribing information of Mifeprex. The prescribing information is attached to the letter, and is also available by calling 1-877-4 Early Option (1-877-432-7596) or website: www.earlyoptionpill.com.

In addition to these qualifications, the physician must provide Mifeprex in a manner consistent with the following guidelines:²⁵

- Under federal law, each patient must be provided with a Medication Guide. The physician must fully explain the procedure to each patient, provide her with a copy of the Medication Guide and Patient Agreement, give her an opportunity to read and discuss them, obtain her signature on the Patient Agreement and sign it themselves.
- The patient's follow-up visit at approximately 14 days is very important to confirm that a complete termination of pregnancy has occurred and that there have been no complications. The physician must notify Danco Laboratories in writing as discussed in the Package Insert under the heading Dosage and Administration in the event of an on-going pregnancy, which is not terminated subsequent to the conclusion of the treatment procedure.
- While serious adverse events associated with the use of Mifeprex are rare, the physician must report any hospitalization, blood transfusion, or other serious event to Danco Laboratories by providing a brief clinical and administrative synopsis of any such adverse events, and identifying the patient solely by package serial number to ensure patient confidentiality.
- The prescriber must follow additional specific requirements imposed by the distributor, including procedures for storage, dosage tracking, damaged product returns and other matters.

The FDA has published post-market drug safety information for patients and providers regarding Mifeprex and the risk for sepsis associated with its use.¹² Physicians and their patients should fully discuss early potential signs and symptoms that may warrant immediate medical evaluation. All providers of medical abortion and emergency room health care providers should investigate the possibility of sepsis in patients who are undergoing medical abortion and present with nausea, vomiting, or diarrhea and weakness with or without abdominal pain, and without fever or other signs of infection more than 24 hours after taking misoprostol. The FDA recommends that physicians suspect infection in patients with this presentation and consider immediately initiating treatment with antibiotics that includes coverage of anaerobic bacteria such as *Clostridium sordellii*.

Another mifepristone product, Korlym[®], is indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.²⁴

Centers for Medicare and Medicaid Services (CMS)

Medicare does not have a National Coverage Determination (NCD) for Mifeprex (mifepristone). Local Coverage Determinations (LCDs) do not exist at this time.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the [Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals](#). (Accessed March 6, 2020)

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Policy History/Revision Information

| Date | Summary of Changes |
|------------|--|
| 08/01/2020 | Template Update <ul style="list-style-type: none"> ● Reformatted policy; transferred content to new template |
| 05/01/2020 | Supporting Information <ul style="list-style-type: none"> ● Updated <i>References</i> section to reflect the most current information ● Archived previous policy version 2019D0012P |

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence ([Medicare IOM Pub. No. 100-16, Ch. 4, §90.5](#)).

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.