

MIFEPREX® (MIFEPRISTONE)

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Related Policy
<ul style="list-style-type: none"> Abortions (Therapeutic and Elective)

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines 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.

CONDITIONS OF COVERAGE

Applicable Lines of Business/ Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	General Benefits Package
Referral Required (Does not apply to non-gatekeeper products)	Yes - Office No – Outpatient, Inpatient
Authorization Required (Precertification always required for inpatient admission)	Yes – Outpatient, Inpatient No - Office
Precertification with Medical Director Review Required	No
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	Office, Inpatient, Outpatient

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

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.

This policy applies to Oxford Commercial plan membership. Certain groups may exclude Mifeprex from coverage if such coverage would be contrary to the Group's bona fide religious tenets. Healthy NY Plans do not have an elective abortion benefit.

Please refer to the member specific benefit plan document and [Coverage Rationale](#) below for specific benefit coverage guidelines.

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

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

Mifeprex (mifepristone), in combination with misoprostol, is proven and medically necessary for termination of 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:

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

Recommended Guidelines

Therapeutic Abortions

Coverage of therapeutic abortions is subject to benefit availability and any specific limitations/maximums as outlined in the member's certificate of coverage/health benefits plan.

Oxford covers therapeutic abortions that may include the following indications:

- Medical conditions which cause pregnancy to pose substantial risk to maternal health such as cardiac or cardiovascular anomalies, cardiovascular disease, renal disease, malignancy, and severe diabetes mellitus
- The certain diagnosis of:
 - Chromosomal abnormalities inconsistent with normal life in the fetus
 - Major structural defects such as severe neural tube defects, severe cardiac abnormalities, severe ventral wall defects, or other severe structural defects
 - Major metabolic abnormalities such as sickle cell disease, Tay Sachs disease, cystic fibrosis, or major biochemical abnormalities
- Pregnancy which is the result of rape or incest

- Exposure to known teratogenic agents, which pose significant risk of fetal developmental abnormalities

Elective Abortions

Coverage of elective abortions is subject to benefit availability and any specific limitations/maximums as outlined in the member's certificate of coverage/health benefits plan.

Notes:

- Treatment of complications of elective and therapeutic abortions is considered medically necessary and therefore not subject to annual and dollar limits.
- If an abortion CPT code is billed, it is reimbursed according to the elective abortion benefit, unless the diagnosis code is listed as a therapeutic procedure in the policy titled [Abortions \(Therapeutic and Elective\)](#).

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

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,TM 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

BACKGROUND

Mifeprex (mifepristone) is a synthetic steroid with anti-progestational effects. 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.³

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 may apply.

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

CLINICAL EVIDENCE

Proven/Medically Necessary

Medical Termination of Intrauterine Pregnancy through 49 Days' Pregnancy

Mifeprex, in combination with misoprostol, is indicated for the medical termination of intrauterine pregnancy through 49 days' pregnancy.³

Unproven/Not Medically Necessary Uses

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. 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 less side effects than sublingual or buccal.

Professional Societies

World Health Organization, Department of Reproductive Health and Research

In 2012, the World Health Organization (WHO) updated its 2003 publication 'Safe abortion: technical and policy guidance for health systems.' Recommended methods for medical abortion between 63 and 84 days gestational age are as follows:⁸

- The recommended method for medical abortion is mifepristone followed by misoprostol.
- For pregnancies of gestational age between 9 and 12 weeks (63 and 84 days), the recommended method for medical abortion is mifepristone followed 36 to 48 hours later by misoprostol. (Strength of recommendation: weak.; Quality of evidence based on one randomized controlled trial and one observational study: low.)
- Dosages and routes of administration for mifepristone followed by misoprostol.
- Mifepristone should always be administered orally. The recommended dose is 200 mg.
- Administration of misoprostol is recommended 36 to 48 hours following ingestion of mifepristone.
 - The recommended dose of misoprostol is 800 µg vaginally.

- Subsequent misoprostol doses should be 400 µg, administered either vaginally or sublingually, every 3 hours up to four further doses, until expulsion.
- This recommendation is likely to be affected as studies are completed.

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The foregoing Oxford policy has been adapted from an existing UnitedHealthcare Pharmacy Clinical Pharmacy Program that was researched, developed and approved by the UnitedHealth Group National Pharmacy & Therapeutics Committee [2018D00120]

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
06/01/2018	<ul style="list-style-type: none"> Routine review; no content changes Archived previous policy version PHARMACY 286.4 T1