

MIOSTOL - 200mcg. TAB.

Composition :

Each uncoated tablet contains :
Misoprostol I.P 200mcg.

DESCRIPTION :

Misoprostol is a synthetic prostaglandin that has an effective anti-ulcer agent and also has oxytocic properties. This drug is used to start labor, cause an abortion, and treat postpartum bleeding due to poor contraction of the uterus. For abortions it is often used with mifepristone or methotrexate. This drug reduces the risk of stomach ulcers in patients treated with NSAIDs, that are used for pain and various inflammatory conditions, for example, arthritis. Misoprostol is used primarily in patients at high risk for stomach ulcers when treated with NSAIDs, for example, the elderly, patients with concomitant debilitating diseases, and patients with a history of ulcers.

MECHANISM OF ACTION

Misoprostol seems to inhibit gastric acid secretion by a direct action on the parietal cells through binding to the prostaglandin receptor. The activity of this receptor is mediated by G proteins which normally activate adenylate cyclase. The significant cytoprotective actions of misoprostol are related to several mechanisms. These include: 1. Increased secretion of bicarbonate, 2. Considerable decrease in the volume and pepsin content of the gastric secretions, 3. It prevents harmful agents from disrupting the tight junctions between the epithelial cells which stops the subsequent back diffusion of H⁺ ions into the gastric mucosa, 4. Increased thickness of mucus layer, 5. Enhanced mucosal blood flow as a result of direct vasodilatation, 6. Stabilization of tissue lysozymes and vascular endothelium, 7. Improvement of mucosal regeneration capacity, and 8. Replacement of prostaglandins that have been depleted as a result of damage to the area. Misoprostol has also been shown to increase the amplitude and frequency of uterine smooth muscle contractions during pregnancy via selective binding to the EP-2 and EP-3 prostanoid receptors.

PHARMACOLOGY

Misoprostol is a synthetic prostaglandin E1 analogue. In comparison to other prostaglandin analogues, misoprostol is economical, widely available, stable at room temperature, and has few side effects.

Its clinical applications include medical abortion, treatment of incomplete abortion and miscarriages, cervical priming prior to surgical procedures, induction of labor, and management of postpartum hemorrhage. As well as its obstetric and gynecological indications, it is also used in the prevention and treatment of peptic ulcers.

Pharmacokinetics :

After oral administration, Misoprostol is rapidly and almost completely absorbed from the gastrointestinal tract. However, the drug undergoes extensive and rapid first-pass metabolism to form Misoprostol Acid. Misoprostol Acid is further metabolized by oxidation, primarily in the liver. Following a single dose of 400mcg. oral Misoprostol, the plasma Misoprostol level increases rapidly and peaks at about 30 minutes and declines rapidly by 120 minutes and remain low thereafter. Food reduces the rate but not the extent of absorption. Concomitant antacid use reduces total availability. The plasma elimination half-life is 20-40 minutes. While Misoprostol is orally administered the onset of action is 8 minutes and the duration of action is approximately 2 hours.

No accumulation of Misoprostol is noted in multiple dose studies. Serum protein binding is less than 90%, concentration-independent in the therapeutic range.

This drug is mainly eliminated through urine. Misoprostol acid is distributed into breast milk.

Pharmacokinetic in breast milk – Breast feeding mothers may be given Misoprostol for post partum hemorrhage prevention and treatment. It is best to throw away the milk produced in the first 5 hours after ingestion of Misoprostol. As Misoprostol acid is distributed into breast milk, so it is a good idea for women who are breast feeding to discard milk they have produced during the medical abortion procedure.

Misoprostol was detected in breast milk within 30 minutes of oral administration. The peak concentration was attained in 60 minutes. The level in breast milk rapidly drops afterwards and is undetectable by 4-5 hours after ingestion. The Misoprostol Acid level in breast milk is only one-third of that in the plasma.

Pharmacokinetic on the uterus and cervix – The uterotonic and cervical softening effects on the female genital tract were considered as side effects rather than therapeutic effects when Misoprostol was first introduced. However, it is because of these effects that Misoprostol is widely used in Obstetric and Gynecologist practice today.

Action on Uterus – After a single oral dose of Misoprostol there is an increase in uterine tonus. To produce regular contraction, however, a sustained plasma level is required and this requires repeated oral dose rather than a high serum level. A very low serum level of Misoprostol is required for the development of regular uterine contraction. The clinical effects or actions required for different indications of use also vary. The strength of concentration that is required to achieve the clinical effects increases with gestation.

Action on the Cervix – There were many clinical studies that have demonstrated the cervical priming effect of Misoprostol in the pregnant state. This drug has been used widely for its cervical softening effect before induction of labor and surgical evacuation of the uterus. Studies have shown that less force was required for mechanical dilation of the cervix if Misoprostol was applied before the procedure. The softening effect on the cervix may be more likely to be due to the direct effect of Misoprostol on the cervix.

INDICATIONS

Misoprostol is used in a variety of indications in the practice of obstetrics and gynecology, including medication abortion, medical management of miscarriage, induction of labor, cervical ripening before surgical procedures, and the treatment of postpartum hemorrhage. Misoprostol is used in combination with mifepristone to end an early pregnancy.

Misoprostol is also used sometimes to prevent stomach ulcers while taking NSAIDs, especially if the patient is at risk for developing ulcers or has a history of ulcers. Misoprostol helps to decrease the risk of serious ulcer complications such as stomach bleeding. This medication protects the stomach lining by lowering the amount of acid that comes in contact with it.

Labor Induction:

Misoprostol is commonly used for labor induction. It causes uterine contractions and the ripening of the cervix. It can be less expensive than the other commonly used ripening agent like Dinoprostone. Oxytocin has long been used as the standard agent for labor induction, but does not work well when the cervix is not yet ripe. Misoprostol also may be used in conjunction with oxytocin.

Abortion:

Misoprostol is used either alone or in conjunction with another medication like mifepristone or methotrexate for medical abortions as an alternative to surgical abortion. It is preferable to users because it feels more "natural," as the drugs induce a miscarriage. Misoprostol is most effective when it is used with methotrexate or mifepristone but alone is less effective. With Misoprostol 1% of women may have heavy bleeding requiring medical attention, some women may have ectopic pregnancy, and the 12% of pregnancies that continue after Misoprostol failure are more likely to have birth defects.

Combined given Misoprostol with mifepristone or methotrexate are effective in around 95% for early pregnancies. Misoprostol alone may be more effective in earlier gestation. Misoprostol can also be used to dilate the cervix in preparation for a surgical abortion, particularly in the second trimester either alone or in combination with other drugs.

Missed miscarriage:

Misoprostol is sometimes used to treat early fetal death in the absence of spontaneous miscarriage. A low dose is used initially, and then doubled for the remaining doses until delivery.

Postpartum bleeding:

Misoprostol is also used to prevent and treat post-partum bleeding. Orally administered misoprostol is marginally less effective than oxytocin. The use of rectally administered misoprostol is optimal in cases of bleeding and lower rates of side effects compared to other routes. However, it is inexpensive and thermostable, thus does not require refrigeration like oxytocin, making it a cost-effective and valuable drug.

Misoprostol is recommended due to its cost, effectiveness, stability, and low rate of side effects. Oxytocin must also be given by injection, while Misoprostol can be given orally or

rectally for this use, making it much more useful in areas where nurses and physicians are less available.

Ulcer prevention:

Misoprostol is used for the prevention of NSAID-induced gastric ulcers. It acts upon gastric parietal cells, inhibiting the secretion of gastric acid by decreasing activity of proton pump at the apical surface of the parietal cell. Misoprostol is only indicated for use by people who are both taking NSAIDs and are at high risk for NSAID-induced ulcers, including the elderly and people with ulcer complications. Misoprostol is sometimes Co-prescribed with NSAIDs to prevent their common adverse effect of gastric ulceration.

Misoprostol has other protective actions, but is only clinically effective at doses high enough to reduce gastric acid secretion. For instance, at lower doses, Misoprostol may stimulate increased secretion of the protective mucus that lines the gastrointestinal tract and increase mucosal blood flow, thereby increasing mucosal integrity.

DOSAGE:

Postpartum haemorrhage:

3 tablets (600mcg) should be taken orally, with a glass of water, within one minute after all babies have been delivered, before the placenta is delivered.

Incomplete abortion:

3 tablets (600mcg) should be taken orally, with a glass of water.

Gynecologic Surgery:

400 mcg orally 12 to 24 hours before surgery.

Cervical Ripening Before Surgical Abortion:

First Trimester - 400 µg orally at least 8 to 12 hours prior to suction curettage.

Cervical Ripening Before Other gynecologic Procedures in non-pregnant:

Hysteroscopy- 400 µg of oral misoprostol given at least 9 to 12 hours prior to hysteroscopy.

Endometrial biopsy: 400 µg of oral 3 hours prior to endometrial biopsy.

Abortion – (Misoprostol alone)

Misoprostol for medical abortion works best in the first 12 weeks of pregnancy.

Four tablets Misoprostol-200mcg. are recommended to initiate an early abortion, and four more (rarely) may be required for its completion. It is best to use Misoprostol within nine weeks since the last menstruation that is, fewer than 63 days counting from the first day of the last regular period. The earlier in pregnancy Misoprostol is administered the better, because it is safer, more effective, and less painful. Women with an intrauterine contraceptive device (IUD) in place should have it removed before using misoprostol.

STEPS FOR ABORTION –

Step1. Place four 200-mcg tablets (or their equivalent) in the mouth under the tongue or in the cheek pouch. Hold tablets in the mouth for 20-30 minutes to allow them to dissolve, and then swallow the remaining fragments.

During this process, you may experience bleeding that is somewhat heavier than for a period. That is normal. You should have a supply of thick sanitary napkins on hand.

Bleeding and uterine contractions (cramping) may begin as quickly as 30 minutes following this first step. If bleeding and contractions do not start within 3 hours, then follow the **Step 2**.

Bleeding itself does not mean that an abortion has occurred. Close inspection of the sanitary pad or other receptacle can reveal whether the pregnancy has been terminated. This will be difficult to detect in the very early stages of pregnancy, however, because the embryonic tissue is indistinguishable from the normal clotting of menstrual blood.

If it is not clear that the pregnancy has been terminated within three hours of taking the first dose—for example, if the embryonic sac is not visible on the sanitary pad, or if cramping continues without diminishing then immediately go to **Step 2**.

Step 2: Place four more 200-mcg tablets under the tongue or in the cheek pouch and hold them there for 20-30 minutes until they dissolve.

Step 3: If the pregnancy has not been terminated three hours after using the second set of pills and bleeding, take four more 200 mcg tablets of misoprostol.

The majority of pregnancies up to 12 weeks duration are terminated within hours of the first administration of Misoprostol. Generally, more than three-quarters of women experience an abortion within the first 24 hours, although it sometimes takes longer.

Misoprostol alone is about 75-85 percent successful in inducing abortion in the first trimester when used as recommended. Although less effective alone than when combined with mifepristone.

Combination with Mifepristone- First Trimester of Pregnancy: 400 mcg orally once as a single dose 48 hours after administer Mifepristone.

Labor Induction -

The doses ranging from 25 mcg 3-hourly to 50 mcg 4-hourly and 100 mcg 6-12hourly.

Duodenal Ulcer, Gastric Ulcer and NSAID-Induced Ulcer Prophylaxis-

200 mcg orally 4 times a day after meals and at bedtime.

Alternatively, 400 mcg orally 2 times a day may be used.

Misoprostol tablet should be taken strictly as per doctor's advice.

MISSED DOSE

Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

RENAL DOSE ADJUSTMENT

No dose adjustment is routinely needed, but the dose may be reduced to 100 mcg orally 4 times a day or 200 mcg orally 2 times a day if the patient is unable to tolerate the recommended regimen or if the patient is maintained on chronic hemodialysis.

Misoprostol should not be administered more frequently than every 3 to 6 hours.

PRECAUTION

Use with caution who are having allergic to Misoprostol or any other drugs. Disclose to the doctor and pharmacist what prescription and nonprescription medicine are taking, especially antacids, aspirin, arthritis medications and vitamins.

Before using Misoprostol, tell to the doctor or pharmacist about your medical history especially if you have stomach or intestinal disease like inflammatory bowel disease. There are risk factors for uterine rupture when this drug is used vaginally in case of cesarean delivery, uterine surgery, five or more previous pregnancies.

Daily use of alcohol and tobacco may increase your risk for stomach bleeding. Limit alcohol beverages and stop smoking.

WARNING

Do not take Misoprostol to prevent ulcers if you are pregnant or plan to become pregnant. Misoprostol may cause miscarriages, premature labor, or birth defects.

If you are a woman of childbearing age, you may take Misoprostol to prevent ulcers only if you have had a negative pregnancy test in the past 2 weeks and if you use a reliable method of birth control while taking Misoprostol. You must begin taking misoprostol on the second or third day of your menstrual period. If you become pregnant while taking Misoprostol, stop taking it and call your doctor immediately.

SIDE EFFECTS

Misoprostol is a safe and well tolerated drug. No clinically significant adverse hematological, endocrine, biochemical, immunological, respiratory, ophthalmic, platelet or cardiovascular effects have been found with Misoprostol. Diarrhea is the major adverse reaction that has been reported constantly with Misoprostol, but is unusually mild and self limiting. Nausea and vomiting may occur and will resolve in 2-6 hours. Contact your doctor if these symptoms persist for more than 8 days.

Fever and chills have also been reported in 32–57 percent women and are common following high doses in the third trimester immediate post partum period. Hyperpyrexia has been reported in the several cases following 600mcg. and hyperpyrexia with delirium and ICU admission has been reported following 800mcg. orally.

Another concern about the use of Misoprostol is the risk of uterine rupture, especially in women with a previous uterine scar. Incidences of uterine rupture are rare in the first trimester medical abortion, but the risk seems to increase with gestation.

Exposure to Misoprostol in early pregnancy has been associated with multiple congenital defects. However, mutagenicity studies of Misoprostol have been negative and has been shown to be embryotoxic, fetotoxic or teratogenic. This malformation therefore, may be due to a disturbed blood supply to the developing embryo during Misoprostol induced contraction of uterus.

Stop taking misoprostol and seek emergency medical attention if you experience an allergic reaction, like difficulty of breathing, closing of the throat, swelling of the lips, tongue and face.

Taking care of side effects:

Management adverse effects include:

Low grade fever and headache – May take antipyretic or NSAID.

Dizziness - Take rest and an increase in fluid intake.

Nausea/vomiting – May take an anti-emetic and rest.

Diarrhoea – May take an anti-diarrhoeal.

Abdomen pain and cramping – May take an NSAID or antipyretic and heat pack.

DRUG INTERACTIONS

Misoprostol has not been shown to have an effect on hepatic P450 enzyme systems.

Antacids may decrease the bioavailability of misoprostol, and antacids containing magnesium may aggravate diarrhea caused by Misoprostol.

Otherwise, no clinically significant drug interactions have been identified with Misoprostol.

OVERDOSE

May suffer from drowsiness, seizures, severe dizziness, slow or irregular heartbeats. If overdose is suspected consult to the doctor immediately.

STORAGE

Store at room temperature and away from excess heat and moisture.

PRESENTATION

1x4's x10 tablets in a box.