MISOPROST 25 / 200 / 600 Tablets (Misoprostol)

**Composition**

Misoprost 25  
Each uncoated tablet contains:  
Misoprostol ............. 25 mcg  

Misoprost 200  
Each uncoated tablet contains:  
Misoprostol ............. 200 mcg  

Misoprost 600  
Each uncoated tablet contains:  
Misoprostol ............. 600 mcg  

**Dosage Form**

Tablets for oral and vaginal use.

**Pharmacology**

- **Pharmacodynamics**

  Misoprostol is a synthetic prostaglandin E1 analogue, which is a potent inhibitor of gastric acid secretion in humans. It also causes the cervix to soften and the uterus to contract. Prostaglandin E1 causes myometrial contractions by interacting with specific receptors on myometrial cells. This interaction results in a change in calcium concentration, thereby initiating muscle contraction. By interacting with prostaglandin receptors, misoprostol causes the cervix to soften and the uterus to contract, resulting in the expulsion of the uterine contents.

- **Pharmacokinetics**

  Misoprostol is extensively absorbed, and undergoes rapid de-esterification to its free acid (misoprostol acid), which is responsible for its clinical activity and, unlike the parent compound, is detectable in plasma. The alpha side chain undergoes beta-oxidation and the beta side chain undergoes omega oxidation followed by reduction of the ketone to give prostaglandin F analogues. In normal volunteers, misoprostol is rapidly absorbed after oral administration, with a $T_{\text{max}}$ of misoprostol acid of $12 \pm 3$ minutes and a terminal half-life of 20 - 40 minutes. There is high variability of plasma levels of misoprostol acid between and within studies but mean values after single doses show a linear relationship with dose over the range of 200-400 mcg. No accumulation of misoprostol acid was noted in multiple-dose studies; plasma steady state was achieved within 2 days. Maximum plasma concentrations of misoprostol acid are diminished when the dose is taken with food and total availability of misoprostol acid is reduced by use of concomitant antacid. Clinical trials were conducted...
with concomitant antacid, however, so this effect does not appear to be clinically important. After oral administration of radiolabelled misoprostol, about 80% of detected radioactivity appears in urine.

In contrast, after vaginal administration, the plasma concentration gradually increased, reaching maximum levels after 70-80 minutes and slowly declined with detectable levels present after 6 hours. Vaginal misoprostol was present in the circulation longer than oral misoprostol and, hence, its duration of stimulation of the uterus exceeds that of oral misoprostol. When misoprostol is administered vaginally, the plasma concentrations of misoprostol acid peak in 1-2 hours and then decline slowly. Vaginal application of misoprostol results in slower increases and lower peak plasma concentrations of misoprostol acid than does oral administration, but overall exposure to the drug is increased.

In a pharmacokinetic study comparing misoprostol 600 mcg given orally and rectally, it was seen that in all the subjects receiving oral misoprostol, the serum concentration rose quickly, peaked between 7.5 and 30 minutes (mean = 18 minutes) after administration, fell steeply by 60 minutes, and remained low thereafter, which may be of clinical significance in postpartum haemorrhage (PPH) treatment. On the other hand, serum concentration of misoprostol acid in subjects receiving the rectal doses rose gradually, reached a maximum level between 15 and 60 minutes (mean = 40.5 minutes), and declined slowly in 5 patients and faster in the others. The longer half-life of rectally administered misoprostol could prolong uterine contraction, thus preventing a delayed haemorrhage.

### Indications

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<tr>
<th>First Trimester Abortion</th>
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MISOPROST with mifepristone is indicated for the medical termination of intrauterine pregnancy through 49 days of pregnancy. For this purpose, pregnancy is dated from the first day of the last menstrual period in a presumed 28-day cycle with ovulation occurring at mid-cycle.

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<tr>
<th>Cervical Ripening</th>
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Cervical ripening prior to uterine instrumentation
- Cervical ripening for induction of labour in live foetus and intrauterine foetal death

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<tr>
<th>Prevention of PPH (Postpartum Haemorrhage)</th>
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### Dosage And Administration

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Mifepristone is administered prior to MISOPROST. Treatment with mifepristone and MISOPROST for the termination of pregnancy requires three visits to the healthcare provider by the patient. Mifepristone may be administered only in a clinic, medical office or hospital, by or under the supervision of a gynaecologist, able to assess the gestational age of an embryo and to diagnose ectopic pregnancies. The gynaecologist 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 the patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.

**Day 1: Mifepristone Administration**

Three 200 mg tablets (600 mg) of mifepristone are taken as a single oral dose.

**Day 3: MISOPROST Administration**

The patient should return to the clinic 2 days after ingesting mifepristone. Unless abortion has occurred and has been confirmed by clinical examination or ultrasonographic scan, the patient should be given two 200
mcg tablets (400 mcg) of MISOPROStorally. During intake and for 3 hours following the intake, the patient should be monitored in the treatment centre, in order not to miss possible acute effects of misoprostol administration. During the period immediately following the administration of misoprostol, the patient may need medication for cramps or gastrointestinal symptoms. The patient should be given instructions on what to do if significant discomfort, excessive bleeding or other adverse reactions occur and should be given a phone number to call if she has questions following the administration of misoprostol. In addition, the name and phone number of the healthcare provider who will be handling emergencies should be provided to the patient.

Day 14: Post-treatment Examination
The patient should return for a follow-up visit approximately 14 days after the administration of mifepristone. This visit is very important to confirm by clinical examination or ultrasonographic scan that a complete termination of pregnancy has occurred. Patients who have an ongoing pregnancy at this visit have a risk of foetal malformation resulting from the treatment. Surgical termination is recommended to manage medical abortion treatment failures.

<table>
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<tr>
<th>Cervical Ripening</th>
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<tbody>
<tr>
<td>Cervical Ripening Prior to Uterine Instrumentation</td>
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<tr>
<td>400 mcg MISOPROST vaginally, 2-3 hours before the procedure.</td>
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<tr>
<td>Cervical Ripening for Induction of Labour(Live Baby&gt;28 Weeks)</td>
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<tr>
<td>MISOPROST 25 vaginally, every 3-4 hours until contractions; maximum six doses.</td>
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<tr>
<td>MISOPROST 25should be used in institutions that are able to perform caesarean sections. Foetal well-being and uterine contractions should be monitored. Beware of uterine hyperstimulation with the risk of uterine rupture and foetal distress.</td>
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<tr>
<td>Cervical Ripening for Induction of Labour(Intrauterine Foetal Death&gt;28 Weeks)</td>
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<tr>
<td>50 mcg MISOPROST vaginally, every 3-4 hours until delivery; maximum six doses.</td>
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<th>Prevention of PPH</th>
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<tr>
<td>For prevention of PPH, one tablet ofMISOPROST 600is administered orally immediately after cord clamping.</td>
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<th>Contraindications</th>
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<td>First Trimester Abortion</td>
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<tr>
<td>Administration of mifepristone and misoprostol for the termination of pregnancy (the ‘treatment procedure’) is contraindicated in patients with any one of the following conditions:</td>
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<tr>
<td>Confirmed or suspected ectopic pregnancy or undiagnosed adnexal mass (the treatment procedure will not be effective to terminate an ectopic pregnancy)</td>
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<td>Intrauterine device (IUD) in place</td>
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<td>Chronic adrenal failure</td>
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<td>Pregnancy not confirmed</td>
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<td>Concurrent long-term corticosteroid therapy</td>
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<td>Severe asthma uncontrolled by therapy</td>
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<td>History of allergy/hypersensitivity to mifepristone, misoprostol or other prostaglandin analogue</td>
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<tr>
<td>Haemorrhagic disorders or concurrent anticoagulant therapy</td>
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<tr>
<td>Inherited porphyria</td>
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| Because it is important to have access to appropriate medical care if an emergency develops, the treatment
procedure is contraindicated if a patient does not have adequate access to medical facilities equipped to provide emergency treatment of incomplete abortion, blood transfusions, and emergency resuscitation during the period from the first visit until discharged by the administering healthcare provider.

### Cervical Ripening

- Severe bronchial asthma or active cardiac disease
- Cephalopelvic disproportion
- Foetal malpresentations
- Previous caesarean section
- Previous uterine surgery
- Acute foetal distress
- Abruptio placenta
- Unexplained vaginal bleeding

When there is suspicion or evidence of foetal compromise prior to induction (e.g. failed non-stress or stress test, meconium staining or diagnosis or history of non-reassuring foetal status)

When there is uterine abnormality (e.g. bicornate uterus)

When there is placenta praevia or unexplained vaginal bleeding after 24 weeks gestation with this pregnancy

When there are signs or symptoms of chorioamnionitis, unless adequate prior treatment has been instituted

### PPH

**Pregnancy**

### Warnings And Precautions

#### General

The patient should not give misoprostol to anyone else. Misoprostol has been prescribed for the patient’s specific condition, it may not be the correct treatment for another person, and may be dangerous to the other person if she is or were to become pregnant.

**When Used for First Trimester Abortion**

During intake and for 3 hours following the intake, the patient should be monitored in the treatment centre, in order not to miss possible acute effects of misoprostol administration. During the period immediately following the administration of misoprostol, the patient may need medication for cramps or gastrointestinal symptoms. The patient should be given instructions on what to do if significant discomfort, excessive bleeding or other adverse reactions occur and should be given the phone number to call if she has questions following the administration of misoprostol.

Any IUD should be removed before treatment with mifepristone / misoprostol begins.

Patients with prosthetic heart valves or who have had one previous episode of infective endocarditis should receive appropriate prophylactic antibiotic treatment.

The use of mifepristone (before misoprostol administration) is assumed to require the same preventive measures as those taken prior to and during surgical abortion to prevent rhesus immunization.

Although there is no clinical evidence, the effectiveness of mifepristone may be lower if misoprostol is administered more than 2 days after mifepristone administration.

The expulsion may take place before prostaglandin administration (in about 3% of cases). This does not
preclude the control visit in order to check for the complete expulsion and the uterine vacuity.

During clinical trials, pregnancies occurred between embryo expulsion and the resumption of menses. To avoid potential exposure of a subsequent pregnancy to mifepristone, it is recommended that conception be avoided during the next menstrual cycle. Contraception can be initiated as soon as the termination of the pregnancy has been confirmed, or before the woman resumes sexual intercourse.

Before mifepristone and misoprostol are given to a woman who has undergone genital mutilation (FGM), a physical examination must be performed by a qualified, trained medical professional to exclude any anatomical obstacles to medical abortion.

Pregnancy-related symptoms such as nausea and vomiting may increase after mifepristone and increase further after misoprostol administration, and they will weaken and disappear during the abortion process. Lower abdominal pain and cramping are the most common symptoms and they are related to misoprostol administration and the abortion process. If pain persists after expulsion of the products of conception, its origin should be investigated. Diarrhoea is the most common dose-related side effect related to misoprostol use, which normally does not require treatment. Some women also report chills, shivering and/or temperature rise after misoprostol administration.

Any reproductive tract infections should be treated before the medical abortion regimen is administered.

A decrease of the efficacy of the method can theoretically occur due to the anti-prostaglandin properties of non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin (acetyl salicylic acid). Limited evidence suggests that co-administration of NSAIDs on the day of misoprostol administration does not adversely influence the effects of mifepristone or misoprostol and does not reduce the clinical efficacy of medical termination of pregnancy.

Rare but serious cardiovascular accidents have been reported following the intramuscular administration of a prostaglandin analogue. For this reason, women with risk factors for cardiovascular disease or established cardiovascular disease should be treated with caution.

Information for Patients

Patients should be fully advised of the treatment procedure and its effects. Each patient must understand the necessity to combine treatment with prostaglandin to be administered at a second visit; the necessity of completing the treatment schedule, including a follow-up visit approximately 14 days after taking mifepristone to check for complete expulsion; that vaginal bleeding and uterine cramping probably will occur; that prolonged heavy vaginal bleeding is not proof of a complete abortion; that if the treatment fails, there is a risk of foetal malformation; that medical abortion treatment failures are managed by surgical termination; and the steps to take in an emergency situation, including precise instructions and a telephone number that she can call if she has any problems or concerns.

Laboratory Tests

Clinical examination is necessary to confirm the complete termination of pregnancy after the treatment procedure. Changes in quantitative human chorionic gonadotropin (hCG) levels will not be decisive until at least 10 days after the administration of mifepristone. A continuing pregnancy can be confirmed by ultrasonographic scan.

Decreases in haemoglobin concentration, haematocrit and red blood cell count occur in some women who bleed heavily. Clinically significant changes in serum enzyme (serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, alkaline phosphatase, gamma-glutamyltransferase) activities were rarely reported.

The existence of debris in the uterus following the treatment procedure will not necessarily require surgery.
for its removal.

**Method of Prostaglandin Administration**

During intake and for 3 hours following the intake, the patient should be monitored in the treatment centre, in order not to miss the possible acute effects of prostaglandin administration. The treatment centre must be equipped with adequate medical facilities. On discharge from the treatment centre, the woman should be provided with appropriate medications as necessary and be fully counselled regarding the likely signs and symptoms she may experience and have direct access to the treatment centre by telephone, or local access.

**Monitoring**

Patients must be monitored and undergo appropriate medical evaluation and intervention should any of the serious adverse events, mentioned below, occur following a spontaneous abortion, or surgical or medical abortion, including following mifepristone use:

**Vaginal Bleeding**

The patient must be informed of the occurrence of prolonged vaginal bleeding (an average of about 12 days or more after mifepristone intake), which may be heavy.

Vaginal bleeding occurs in almost all patients during a medical abortion and is not in any way a proof of complete expulsion. The bleeding can occur very quickly after misoprostol intake, and sometimes later:

- In 60%, expulsion occurs within 4 hours following misoprostol intake.
- In 40%, expulsion occurs within 24 to 72 hours following misoprostol intake.

Patients should be counselled to seek immediate medical attention in case of persistence of vaginal bleeding (soaking through two thick full-size sanitary pads per hour for 2 consecutive hours) which may be a sign of incomplete abortion, or other complications, or an unnoticed extra-uterine pregnancy, and prompt medical or surgical intervention may be considered.

According to data from the US and French trials, women should expect to experience vaginal bleeding or spotting for an average of 9-16 days, while 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.

The patient should be informed not to travel far away from the prescribing centre as long as complete expulsion has not been recorded. She should be given precise instructions as to whom she should contact and where to go in the event of any problems, particularly in the case of very heavy vaginal bleeding.

Since heavy bleeding requiring haemostatic curettage occurs in 0-1.4% of the cases during the medical method of pregnancy termination, special care should be given to patients with haemostatic disorders with hypocoagulability, or with anaemia. The decision to use the medical or the surgical method should be decided with specialized consultants according to the type of haemostatic disorder and the level of anaemia. Excessive vaginal bleeding usually requires treatment by uterotonics, vasoconstrictor drugs, curettage, administration of saline infusions, and/or blood transfusions.

A follow-up visit must take place within a period of 14-21 days after administration of mifepristone to verify by the appropriate means (clinical examination, ultrasound scan, and beta-hCG measurement) that expulsion has been completed and that vaginal bleeding has stopped. In case of persistent bleeding (even light) beyond the control visit, its disappearance should be checked within a few days. If an ongoing pregnancy is suspected, a further ultrasound scan may be required to evaluate its viability.

**Infection and Sepsis**

Very rare cases of fatal toxic shock caused by Clostridium sordelli and endometritis, presenting without fever or other obvious symptoms of infection, have been reported after medical abortion with the use of 200 mg mifepristone followed by unauthorized vaginal administration of misoprostol tablets for oral use. No causal relationship between these events and the use of mifepristone and misoprostol has been established. The
gynaecologist evaluating a patient who is undergoing a medical abortion should be alert to the possibility of this potentially fatal complication. In particular, a sustained 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. Clostridium sordellii) if a patient reports abdominal pain or discomfort or general malaise (including weakness, nausea, vomiting or diarrhoea) 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 leucocytosis with a marked left shift, tachycardia, haemoconcentration, and general malaise. These deaths occurred in women who used vaginally administered misoprostol, but no causal relationship between vaginal 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 caesarean section), and in other gynaecologic and non-gynaecologic conditions.

**Failures and Confirmation of Pregnancy Termination**

The non-negligible risk of failure, which occurs in 1.3-7.5 % of the cases, makes the control visit mandatory in order to check that the expulsion is completed. Patients should be scheduled for and return for a follow-up visit at approximately 14 days after administration of mifepristone to confirm that the pregnancy is completely terminated and to assess the degree of bleeding. Termination can be confirmed by clinical examination or ultrasonographic scan. Lack of bleeding following treatment usually indicates failure; however, prolonged or heavy bleeding is not proof of a complete abortion. Rare case of incomplete expulsion or medical abortion failures/ongoing pregnancies should be managed with surgical termination. The patient should be advised whether such care will be provided by the same health care provider or will be referred to another health care provider. The efficacy of the method decreases with parity, and consequently increasing age of the woman.

**Ectopic Pregnancy**

Gynaecologists should remain alert to the possibility that a patient who is undergoing a medical abortion could have an undiagnosed ectopic pregnancy since some of the expected symptoms of a medical abortion 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 mifepristone.

**When Used for Cervical Ripening for Induction of Labour**

Some authors suggest moistening misoprostol with 3-4 drops of saline/distilled water when used for vaginal administration.

When used for cervical ripening for a pregnant woman with a live foetus, it is important that misoprostol 25 mcg should be used in institutions that are able to perform caesarean sections. Foetal well-being and uterine contractions should be monitored. Beware of uterine hyperstimulation with the risk of uterine rupture and foetal distress. Continuous monitoring of uterine contractions and foetal heart sounds should be done to rule out uterine hyperstimulation, foetal distress and meconium stained liquor.

Oxytocin should not be used for 6 hours after the administration of the last dose of misoprostol as it may lead to hyperstimulation of the uterus.

The risk factors for uterine rupture include later trimester pregnancies, larger doses of the drug, prior caesarean section or uterine surgery, and a history of five or more previous pregnancies. This information may allow the healthcare providers to better identify patients at risk and thereby improve the safe use of misoprostol.

The patient should be examined prior to the administration of misoprostol 25 mcg. The foetus should be in vertex presentation.
Multifoetal pregnancies are not excluded as long as the leading foetus is vertex. Misoprostol can be used with intact or ruptured membranes. There may be an increased risk of uterine tachysystole, uterine rupture, meconium passage, meconium staining of amniotic fluid, and caesarean delivery due to uterine hyperstimulation with the use of higher doses of misoprostol.

For Prevention of PPH
Misoprostol 600 mcg should be administered orally immediately after cord clamping. Exclude second twin before using misoprostol 600 mcg. Misoprostol 600 mcg should be used with caution in the following conditions:
- Bronchial asthma
- Heart diseases

### Drug Interactions
Misoprostol has not been shown to interfere with the beneficial effects of aspirin on signs and symptoms of rheumatoid arthritis. Misoprostol does not exert clinically significant effects on the absorption, blood levels, and antiplatelet effects of therapeutic doses of aspirin.

Misoprostol is predominantly metabolized via fatty acid-oxidizing systems and has shown no adverse effect on the hepatic microsomal mixed function oxidase (P450) enzyme system. In specific studies, no clinically significant pharmacokinetic interaction has been demonstrated with antipyrene or diazepam. A modest increase in propranolol concentrations (mean approximately 20% in AUC, 30% in $C_{\text{max}}$) has been observed with multiple dosing of misoprostol. In extensive clinical studies, no drug interactions have been attributed to misoprostol. Drug interaction studies with misoprostol and several NSAIDs showed no clinically significant effect on the kinetics of ibuprofen, diclofenac, piroxicam, aspirin, naproxen or indomethacin. Concomitant administration of NSAIDs and misoprostol in rare cases can cause a transaminase increase and peripheral oedema.
Magnesium-containing antacids should be avoided during treatment with misoprostol as this may worsen the misoprostol-induced diarrhoea.

### Renal Impairment
Pharmacokinetic studies in patients with varying degrees of renal impairment showed an approximate doubling of $T_{1/2}$, $C_{\text{max}}$, and AUC compared to normal, but no clear correlation between the degree of impairment and AUC. In subjects over 64 years of age, the AUC for misoprostol acid is increased. No routine dosage adjustment is recommended in older patients or patients with renal impairment, but dosage may need to be reduced if the usual dose is not tolerated.

### Hepatic Impairment
Misoprostol is metabolized by fatty acid-oxidizing systems present in organs throughout the body. Its metabolism and plasma levels are, therefore, unlikely to be affected markedly in patients with hepatic impairment.

### Pregnancy
When Mifepristone and Misoprostolate are used for Abortion (upto 49 days)
Patients who have an ongoing pregnancy at the last visit have a risk of foetal malformation resulting from the treatment. Surgical termination is recommended to manage medical abortion treatment failures. In animals, the abortifacient effect of mifepristone precludes the proper assessment of any teratogenic effect of the molecule. With sub-abortive doses, isolated cases of malformations are observed in rabbits, but not in...
rats or mice, and are too few to be considered significant, or attributable to mifepristone.
In clinical practice, rare cases of malformations of the extremity of lower limbs (out of them, clubfoot) have
been reported in case of mifepristone administered alone or associated with prostaglandins. The few
reported cases of malformations do not allow a causality assessment for mifepristone alone or associated to
prostaglandin. However, data is too limited to determine whether the molecule is a human teratogen.
There is currently no relevant clinical data that suggest the possible occurrence of malformation after the
vaginal use of misoprostol during pregnancy. However, in a few cases where misoprostol was self-
administered (orally or vaginally) in order to induce an abortion, the following deleterious effects of
misoprostol have been suggested: malformations of limbs, of foetus movements and of cranial nerves
(hypomimia, abnormalities in suckling, deglutition, and eye movements). To date, a risk of malformation
cannot be excluded.
Consequently:
Women should be informed, that due to the risk of failure of the medical method of pregnancy
termination and due to the unknown risk to the foetus, the post-treatment visit is mandatory.
Should a failure of the method be diagnosed at the post-treatment visit (viable ongoing pregnancy),
and should the patient still agree, pregnancy termination should be completed by another method.
Should the patient wish to continue with her pregnancy, the available data are too limited to justify a
systematic termination of an exposed pregnancy. In that event, a careful ultrasonographic
monitoring of the pregnancy should be carried out.

Teratogenic Effects
Patients who decide to continue the pregnancy after treatment must be informed of the risk of
teratogenicity. This risk is inherent to the mifepristone and misoprostol regimen objective and is enhanced
when regimens other than the one mentioned is used. Exposure of the foetus to misoprostol or
mifeprostone increases the risk of developing Moebius syndrome and/or an amniotic band syndrome. A
second termination of pregnancy procedure shall be considered. In case of continuation of the pregnancy,
close monitoring by ultrasound scan must be performed in specialized centres.
Cases of ongoing pregnancies not terminated by surgical abortion at the end of treatment with mifepristone
alone have reported of sirenomelia and cleft palate.
Several reports in the literature indicate that prostaglandins, including misoprostol, may have teratogenic
effects in human beings. Skull defects, cranial nerve palsies, delayed growth and psychomotor development,
facial malformation and limb defects have all been reported after exposure during the first trimester.

Non-teratogenic Effects
The indication for use of mifepristone in conjunction with misoprostol is for the termination of pregnancy
through 49 days' duration of pregnancy (as dated from the first day of the last menstrual period). These
drugs together disrupt pregnancy by causing decidual necrosis, myometrial contractions and cervical
softening, leading to the expulsion of the products of conception.

When MISOPROSTOL is used for Cervical Ripening for Labour and Delivery
There may be an increased risk of uterine tachysystole, uterine rupture, meconium passage, meconium
staining of amniotic fluid and caesarean delivery due to uterine hyperstimulation with the use of higher
doses of misoprostol. The risk of uterine rupture increases with advancing gestational ages and with prior
uterine surgery, including caesarean delivery. Grand multiparity also appears to be a risk factor for uterine
rupture.

When MISOPROSTOL is used for Prevention of PPH
MISOPROSTOL 600 mcg is not to be administered during pregnancy. For prevention of PPH, misoprostol 600
mcg should be administered orally immediately after cord clamping.
Lactation

Misoprostol is rapidly metabolized in the mother to misoprostol acid, which is biologically active and is excreted in breast milk. There are no published reports of adverse effects of misoprostol in breastfeeding infants of mothers taking misoprostol. Misoprostol should not be administered to nursing mothers because the excretion of misoprostol acid could cause undesirable effects such as diarrhoea in nursing infants.

Paediatric Use

Safety and effectiveness of misoprostol in paediatric patients have not been established.

Undesirable Effects

General

Gastrointestinal side effects like diarrhoea (usually dose-related and self-limiting), abdominal pain, nausea, flatulence, dyspepsia, headache, vomiting, constipation
Shivering
Hyperthermia
Dizziness

Obstetrics and Gynaecological Use

Patient may experience pain due to uterine contractions
Severe genital bleeding
Shock
Pelvic pain
Uterine rupture (requiring surgical repair, hysterectomy, and/or salpingo-oophorectomy)

Women who received misoprostolduring clinical trials reported the following gynaecological disorders:
Spotting (0.7%), cramps (0.6%), hypermenorrhoea (0.5%), menstrual disorder (0.3%), and dysmenorrhoea (0.1%). Postmenopausal vaginal bleeding may be related to misoprostoladministration. If it occurs, diagnostic workup should be undertaken to rule out gynaecological pathology.
The following adverse events were infrequently reported. Causal relationships between misoprostol and these events have not been established but cannot be excluded. The adverse reaction terms were then categorized utilizing the incidence rate as follows:

- Causal Relationship Unknown or Incidence Very Common: ≥1/10 (≥10%) / Common: ≥1/100 and <1/10, (≥1% and <10%) / Uncommon: ≥1/1000 and <1/100, (≥0.1% and <1%) / Rare: ≥1/10,000 and <1/1000, (≥0.01% and <0.1%) / Very Rare: <1/10,000, (<0.01%)

- Body as a Whole: Aches/pains, asthenia, fatigue, fever, rigors, weight changes, chills.
- Skin: Rash, dermatitis, alopecia, pallor, breast pain.
- Special Senses: Abnormal taste, abnormal vision, conjunctivitis, deafness, tinnitus, earache.
- Respiratory: Upper respiratory tract infection, bronchitis, bronchospasm, dyspnoea, pneumonia, epistaxis.
- Cardiovascular: Chest pain, oedema, diaphoresis, hypotension, hypertension, arrhythmia, phlebitis, increased cardiac enzymes, syncope, myocardial infarction (some fatal), thromboembolic events (e.g. pulmonary embolism, arterial thrombosis, and CVA).
- Gastrointestinal: bleeding, inflammation/infection, rectal disorder, abnormal hepatobiliary function, gingivitis, reflux, dysphagia, amylase increase.
Hypersensitivity: Anaphylactic reaction.

Metabolic: Glycosuria, gout, increased nitrogen, increased alkaline phosphatase.

Genitourinary: Polyuria, dysuria, haematuria, urinary tract infection.

Nervous system/Psychiatric: Anxiety, change in appetite, depression, drowsiness, dizziness, thirst, impotence, loss of libido, sweating increase, neuropathy, neurosis, confusion.

Musculoskeletal: Arthralgia, myalgia, muscle cramps, stiffness, back pain.


Reproductive System and Breast Disorders: Vaginal haemorrhage (including postmenopausal bleeding), intermenstrual bleeding, menstrual disorder, uterine cramping, menorrhagia, dysmenorrhoea, uterine haemorrhage.

Congenital, Familial and Genetic Disorders: Birth defects.

Very rare cases of fatal toxic shock caused by Clostridium sordellii endometritis, presenting without fever or other obvious symptoms of infection, have been reported. Clinicians should be aware of this potentially fatal complication

When Used for Cervical Ripening for Labour and Delivery

Hyperstimulation of the uterus, which may progress to uterine tetany with marked impairment of uteroplacental blood flow.
Retained placenta
Amniotic fluid embolism
Foetal and maternal death

Common (≥1/100 to <1/10): Foetal heart rate disorder*, Abnormal labour affecting foetus, Meconium in amniotic fluid, Uterine contractions abnormal.

Uncommon (≥1/1,000 to <1/100): Hypoxic-ischaemic encephalopathy, neonatal respiratory depression, neonatal respiratory distress syndrome, transient tachypnoea of the newborn, nausea, vomiting, rash, antepartum haemorrhage, foetal acidosis, PPH, premature separation of placenta, uterine hypertonus, pruritus genital, APGAR score low, blood pressure increased, uterine rupture.

*(Foetal heart rate disorder was reported as foetal heart rate abnormalities, foetal bradycardia, foetal tachycardia, unexplained absence of normal variability, foetal heart rate decreased, foetal heart rate deceleration, early or late decelerations, variable decelerations, prolonged decelerations)

Overdosage

The toxic dose of misoprostol in humans has not been determined. Cumulative total daily doses of 1,600 mcg have been tolerated, with only symptoms of gastrointestinal discomfort being reported. Clinical signs that may indicate an overdose are sedation, tremor, convulsions, dyspnoea, abdominal pain, diarrhoea, fever, palpitations, hypotension, or bradycardia. Symptoms should be treated with supportive therapy. It is not known if misoprostol acid is dialysable. However, because misoprostol is metabolized like a fatty acid, it is unlikely that dialysis would be appropriate treatment for overdose. In cases of overdose, standard supportive measures should be adopted as required.

Storage And Handling Instructions

Store below 25°C.

Packaging Information
Misoprost 25 ...Pack of 4 tablets
Misoprost 200 ...Pack of 4 tablets
Misoprost 600 ...Pack of 1 tablet

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MISOPROST 25 / 200 / 600 Tablets

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