

Oral magnesium sulfate is commonly used as a [saline laxative](#) or osmotic purgative. Magnesium sulfate is the main preparation of [intravenous magnesium](#).

Indications for internal use are:

- Replacement therapy for [hypomagnesemia](#).
- Magnesium sulfate is the first-line [antiarrhythmic](#) agent for [torsades de pointes](#) in [cardiac arrest](#) under the 2005 ECC guidelines and for managing [quinidine](#)-induced arrhythmias.
- As a [bronchodilator](#) after beta-agonist and [anticholinergic](#) agents have been tried, e.g. in severe exacerbations of [asthma](#). Studies conducted have revealed that magnesium sulfate can be nebulized to reduce the symptoms of acute asthma. It is commonly administered via the [intravenous](#) route for the management of severe [asthma](#) attacks.
- Magnesium sulfate can be used to treat [eclampsia](#) in pregnant women.
- Magnesium sulfate can also [delay labor](#) by inhibiting uterine muscle contraction in the case of premature labor, to delay [preterm birth](#). However, meta-analyses have failed to support it as a tocolytic agent. [And its use for prolonged periods \(more than 5 to 7 days\) may result in health problems for the baby.](#)
- [Intravenous](#) magnesium sulfate has been shown to [prevent cerebral palsy](#) in [preterm](#) babies. A recent systematic review suggests that antenatal intravenous magnesium sulphate can reduce the risk of cerebral palsy and gross motor dysfunction in preterm infants by on average 30%.

An overdose of magnesium causes [hypermagnesemia](#).

- • [Misoprostol \(Cytotec\)](#)
- Prescription drug
- Consult a doctor if you have a medical concern.
- • Prevents stomach ulcers and stomach irritation in patients taking pain and arthritis drugs, such as aspirin or ibuprofen, for long periods of time.
- [Side effects](#) - [Warnings](#) - [How to use](#)
- [National Library of Medicine](#)
- • [Brand name](#): Cytotec
- [Pregnancy risk](#): Category [X](#) (Should not be used during pregnancy)
- [May prevent](#): [Stomach ulcer](#)
- [Drug class](#): [Prostaglandin E1 Analog](#)

Misoprostol is a synthetic [prostaglandin E₁](#) (PGE₁) [analog](#) that is used with nonsteroidal anti-inflammatory drug ([NSAID](#)) to prevent [gastric ulcers](#), to treat [missed miscarriage](#), to [induce labor](#), and to induce [abortion](#). Misoprostol was invented and marketed by [G.D. Searle & Company](#) (now [Pfizer](#)) under the trade name [Cytotec](#), but other [brand-name](#) and [generic](#) formulations are now available.

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Ulcer prevention

Misoprostol is approved for use in the prevention of [NSAID](#) induced gastric ulcers. [It acts upon gastric parietal cells](#), inhibiting the secretion of [gastric acid](#) via [G-protein coupled](#)

[receptor](#) mediated inhibition of [adenylate cyclase](#), which leads to decreased intracellular [cyclic AMP](#) levels and decreased [proton pump](#) activity at the [apical](#) surface of the parietal cell. Because other classes of drugs, especially [H2-receptor antagonists](#) and [proton pump inhibitors](#), are more effective for the treatment of acute peptic ulcers, [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 coprescribed with NSAIDs to prevent their common adverse effect of [gastric ulceration](#) (e.g. with [diclofenac](#) in '[Arthrotec](#)').

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](#). However, these effects are not pronounced enough to warrant prescription of misoprostol at doses lower than those needed to achieve gastric acid suppression.

However, even in the treatment of NSAID induced ulcers, [omeprazole](#) proved to be at least as effective as misoprostol, but significantly better tolerated, and therefore misoprostol should not be considered a first choice treatment. [Misoprostol-induced diarrhea and the need of multiple daily doses \(typically four\) are the main issues impairing compliance with therapy](#).

Labor induction

Misoprostol is commonly used for [labor induction](#). [It causes uterine contractions and the ripening \(effacement or thinning\) of the cervix](#). It is significantly less expensive than the other commonly used ripening agent, [dinoprostone](#) (trade names *Cervidil* and *Prepidil*).

[Oxytocin](#) (trade names *Pitocin* and *Syntocinon*) has long been used as the standard agent for labor induction, [but doesn't work well when the cervix is not yet ripe](#). In addition to being used alone to induce labor, misoprostol may be used in conjunction with oxytocin.

Protocols for inducing labor with misoprostol typically call for [25 µg to be administered vaginally](#). In countries where the only approved use of misoprostol is ulcer prevention, misoprostol is not sold in tablets smaller than 100 µg. When used for induction, the 100 µg tablet is commonly split into two or four pieces.

As of October 2012, misoprostol was not approved by the United States FDA for use as a labor-induction drug; however, an NDA for that purpose has been filed and is under review.

Controversy

When Cytotec first came on the market, the label listed a contraindication that it not be used on pregnant women. In August 2000, due to increase of "off label" usage, [Searle](#) (the manufacturer of Cytotec) distributed a letter warning against the use of misoprostol in pregnant women. In addition to citing the [abortifacient](#) nature of the drug, the letter cited reports of [uterine rupture](#) and death associated with using misoprostol to induce labor. All cervical ripening and induction agents can cause [uterine hyperstimulation](#), which can negatively affect the blood supply to the fetus and increases the risk of complications such as uterine rupture. Concern has been raised that uterine hyperstimulation that occurs during a

misoprostol induced labor is more difficult to treat than hyperstimulation during labors induced by other drugs. Other rare complications include [amniotic fluid embolism](#); a 2006 study showed that the use of drugs to induce labor nearly doubled the risk. Because the complications are rare, it is difficult to determine if misoprostol causes a higher risk than do other cervical ripening agents. One estimate is that it would require approximately 61,000 patients enrolled in randomized controlled trials to detect a clinically significant difference in serious fetal complications and approximately 155,000 patients to detect a clinically significant difference in serious maternal complications.

Induced abortion

Earlier pregnancy

Misoprostol is used for [medical abortions](#) as an alternative to [surgical abortion](#). Medical abortion has the advantage of being cheaper, simpler, less invasive, not requiring anesthesia, as well as not having the risk of scarring and adhesions that can be associated with surgical abortion.

Most protocols recommend that misoprostol be used with another drug. The American Congress of Obstetricians and Gynecologists (ACOG) [recommends mifepristone/misoprostol 200 mg/800mcg](#).

Misoprostol is used for [self-induced abortions](#) in Brazil, where [black market](#) prices exceed US \$100 per dose.

Later pregnancy

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 [laminaria](#) stents).

Post-partum hemorrhage

Misoprostol is also used to prevent and treat [post-partum hemorrhage](#). Orally administered misoprostol at a dosage of 600 µg was tested versus [oxytocin](#) 10iu in a large randomised controlled study. The study which involved a substantial number of patients receiving either oral or intravenous [oxytocin](#) showed that misoprostol is marginally less effective for this purpose. The use of rectally administered misoprostol is optimal in cases of haemorrhage; it was shown to be associated with lower incidence of side effects compared to other routes for this particular indication. Rectally administered misoprostol at dosages of 800 µg or 1000 µg was reported in a variety of case reports and randomised controlled trials. However, it is inexpensive and thermostable (thus does not require refrigeration like oxytocin) making it a cost effective and valuable drug to use in the developing world. A randomised control trial of misoprostol use found a 38% reduction in maternal deaths due to post-partum haemorrhage in resource-poor communities. 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.

Pharmacology

Misoprostol, a prostaglandin, binds to myometrial cells to cause strong myometrial contractions leading to expulsion of tissue. This agent also causes cervical ripening with softening and dilation of the cervix.

Mifepristone is a synthetic [steroid](#) compound used as a [pharmaceutical](#). It is a [progesterone receptor antagonist](#) used as an [abortifacient](#) in the first months of pregnancy, and in smaller doses as an [emergency contraceptive](#). Mifepristone is also a powerful [glucocorticoid](#) receptor antagonist, and has occasionally been used in refractory [Cushing's Syndrome](#) (due to ectopic/neoplastic ACTH/Cortisol secretion). During early trials, it was known as RU-38486 or simply **RU-486**, its designation at the [Roussel Uclaf](#) company, which designed the drug. The drug was initially made available in France, and other countries then followed—often amid controversy. It is marketed under tradenames **Korlym** and **Mifeprex**, according to [FDA Orange Book](#).

Medication uses

According to the current [RCOG](#) abortion [evidence-based clinical guideline](#):

- All methods of first-trimester abortion carry a small risk of failure to terminate the pregnancy. The risk for surgical abortion is around 0.23% and for medical abortion between 0.1% and 1.4% (depending on the regimen used and the experience of the centre).
- [Medical abortion using mifepristone plus prostaglandin is the most effective method of abortion at gestations of less than 7 weeks.](#)
- Conventional [vacuum aspiration](#) below 7 weeks have a higher failure rate than at later gestations. Protocols should include examination of the aspirate for the presence of the gestational sac and/or follow-up serum human chorionic gonadotrophin estimation, to ensure abortion completion.
- Early vacuum aspiration using a rigorous protocol (which includes magnification of aspirated material and indications for serum [βhCG](#) follow-up) may be used at gestations below 7 weeks, although data suggest that the failure rate is higher than for medical abortion.
- [Medical abortion using mifepristone plus prostaglandin continues to be an appropriate method for women in the 7–9 week gestation band.](#)

Mifepristone is sold outside the United States by Exelgyn Laboratories as Mifegyne, made in France, and is approved for:

1. Medical termination of intrauterine pregnancies of up to 49 days [gestation](#) (up to 63 days gestation in Britain and Sweden)
2. Softening and dilatation of the cervix prior to mechanical cervical dilatation for pregnancy termination
3. Use in combination with [gemeprost](#) for termination of pregnancies between 13 and 24 weeks gestation
4. Labor induction in [fetal death](#) in utero.^[2]

Mifepristone is sold in the United States by Danco Laboratories as Mifeprex, made in China, and is U.S. [Food and Drug Administration](#)-approved to terminate intrauterine pregnancies of up to 49 days gestation. [Under the FDA-approved regimen, a 600 mg dose is administered by a clinician following a counseling session. Two days later, a clinician administers 400 µg of](#)

another medicine, [misoprostol](#), to induce contractions. In European studies, this method terminated 96 to 99% of pregnancies of up to 49 days gestation, but in one large [multicenter trial](#) in the United States conducted from September 1994 to September 1995, the efficacy was lower (92%), which the authors of the study suggested may have been due to lack of experience with this method in the United States and/or the design of their study. In Europe and China, an observation period of several hours is required after administration of misoprostol. If expulsion of fetal tissue does not occur during the observation period, surgical abortion is offered. There is no required observation period in the United States, but it is strongly recommended.

Mifepristone can also be used in smaller doses as an [emergency contraceptive](#); if taken after sex but before [ovulation](#), it can prevent ovulation and so prevent pregnancy. In this role, a 10 mg dose is not as effective as the 600 mg dose, but has fewer side-effects. ^[6] Mifeprex and Mifegyne are only available in 200 mg tablets.

Contraindications

In [clinical trials](#), nearly all women using mifepristone experienced abdominal pain, uterine cramping, and vaginal bleeding or spotting for an average of 9–16 days.

The FDA prescribing information states that there are no data on the safety and efficacy of mifepristone in women with chronic medical conditions, and that "women who are more than 35 years of age and who also smoke 10 or more cigarettes per day should be treated with caution because such patients were generally excluded from clinical trials of mifepristone."

Adverse effects

No long-term studies to evaluate the [carcinogenic](#) potential of mifepristone have been performed. Results from studies conducted [in vitro](#) and in animals have revealed no [genotoxic](#) potential for mifepristone.

Pharmacology

In the presence of [progesterone](#), mifepristone acts as a [competitive progesterone receptor antagonist](#) (in the absence of progesterone, mifepristone acts as a [partial agonist](#)).

In addition to being an antiprogestogen, mifepristone is also an antiglucocorticoid and a weak [antiandrogen](#).

Side effects and contraindications

The most commonly reported [adverse effect](#) of taking a misoprostol 200 µg tablet by mouth four times a day to reduce the risk of NSAID induced gastric ulcers is [diarrhea](#).

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Tocolytics (also called **anti-contraction medications** or **labor repressants**) are medications used to suppress **premature labor** (from the Greek *tokos*, childbirth, and *lytic*, capable of dissolving). They are given when delivery would result in **premature birth**. The therapy also buys time for the administration of **betamethasone**, a **glucocorticoid** drug which greatly accelerates fetal lung maturity, **but takes one to two days to work**.

The suppression of contractions is often only partial and tocolytics **can only be relied on to delay birth for several days**. Depending on the tocolytic used the mother or fetus may require monitoring, as for instance blood pressure monitoring when **nifedipine** is used as it reduces blood pressure. In any case the risk of preterm labor alone justifies hospitalization.

Types of agents

There is no clear **first-line** tocolytic agent.

Various types of agents are used, with varying success rates and side effects. Some medications are not specifically approved by the **U.S. Food and Drug Administration** (FDA) for use in stopping uterine contractions in preterm labor, instead being used **off label**.

Drug	Mechanism	Description	Possible contraindications	Maternal side effects	Fetal and neonatal side effects
Terbutaline (Brethine)	β2-agonist	Is often the drug given first, especially if there is only low risk of preterm birth.	Cardiac arrhythmias	Cardiac or cardiopulmonary arrhythmias, pulmonary edema, myocardial ischemia, hypotension, tachycardia, death	Fetal tachycardia, hyperinsulinemia, hypoglycemia, myocardial and septal hypertrophy, myocardial ischemia
Ritodrine (Yutopar)	β2-agonist	No longer FDA approved.	Poorly controlled thyroid disease and diabetes	Metabolic hyperglycemia, hyperinsulinemia, hypokalemia, antidiuresis, altered thyroid function, physiologic tremor, palpitations, nervousness, nausea or vomiting, fever, hallucinations	Neonatal tachycardia, hypoglycemia, hypocalcemia, hyperbilirubinemia, hypotension, intraventricular hemorrhage
Fenoterol	β2-agonist		diabetes		
Salbutamol	β2-agonist		diabetes		

<p>Nifedipine (Procardia, Adalat)</p>	<p>CCBs</p>	<p>Is one of the most commonly used tocolytic agents.</p>	<p>Cardiac disease. It should not be used concomitantly with magnesium sulfate.</p>	<p>Flushing, headache, dizziness, nausea, transient hypotension. Administration of calcium channel blockers should be used with care in patients with renal disease and hypotension. Concomitant use of calcium channel blockers and magnesium sulfate may result in cardiovascular collapse.</p>	<p>None noted as yet</p>
<p>Atosiban</p>	<p>oxytocin antagonist</p>	<p>Less side effects than B2 recap agonist</p>			
<p>Indomethacin</p>	<p>NSAIDs</p>		<p>late pregnancy (ductus arteriosus), significant renal or hepatic impairment</p>	<p>Nausea, heartburn</p>	<p>Constriction of ductus arteriosus, pulmonary hypertension, reversible decrease in renal function with oligohydramnios, intraventricular hemorrhage, hyperbilirubinemia, necrotizing enterocolitis</p>
<p>Sulindac</p>	<p>NSAIDs</p>		<p>Coagulation disorders or thrombocytopenia, nonsteroidal anti-inflammatory drug (NSAID)-sensitive asthma,</p>		

			other sensitivity to NSAIDs ^[4]		
IV Magnesium sulfate	myosin light chain inhibitor	Shown to be ineffective. Has been recommended for women at high risk. However, meta-analyses have failed to support it as a tocolytic agent.	myasthenia gravis	Flushing, lethargy, headache, muscle weakness, diplopia, dry mouth, pulmonary edema, cardiac arrest	Lethargy, hypotonia, respiratory depression, demineralization with prolonged use
Ethyl alcohol	?	Shown to be ineffective. Was frequently prescribed as a tocolytic in the mid-20th century, but later double-blind studies ^[10] found it was not effective.			

Calcium-channel blockers and an oxytocin antagonist can delay delivery by 2–7 days.

Otherwise, tocolysis is rarely successful beyond 24–48 hours because current medication do not alter the fundamentals of labor activation. However, just gaining 48 hours is sufficient to allow the pregnant women to be transferred to a center specialized for management of preterm deliveries and give administered corticosteroids the possibility to reduce neonatal organ immaturity.

Antibiotics may delay the onset of labor in women with [premature rupture of membranes](#), but this is not usually characterized as tocolysis.

Contraindications to tocolysis

In addition to drug-specific contraindications, several general factors may contraindicate delaying birth with the use of tocolytic medications.

- Fetus is older than 34 weeks gestation

- Fetus weighs less than 2500 grams or has [intrauterine growth restriction](#) (IUGR) or [placental insufficiency](#)
- Lethal congenital or chromosomal abnormalities
- [Cervical dilation](#) is greater than 4 centimeters
- [Chorioamnionitis](#) or intrauterine infection is present
- Mother has severe [pregnancy-induced hypertension](#), [eclampsia/preeclampsia](#), active [vaginal bleeding](#), [placental abruption](#), a [cardiac disease](#), or another condition which indicates that the pregnancy should not continue.