METHYLERGONOVINE b (Systemic)

Category

Uterine stimulant.

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Hemorrhage, postpartum and postabortal (prophylaxis and treatment)¾Methylergonovine is indicated in the prevention or treatment of postpartum or postabortal uterine bleeding due to uterine atony or subinvolution. Its use is not recommended prior to delivery of the placenta since placental entrapment may occur. 18, 25

[Abortion, incomplete (treatment)]¾In cases of incomplete abortion, methylergonovine may be used to hasten expulsion of uterine contents.

Unaccepted

Methylergonovine is not as effective in treatment of migraine as other ergot alkaloids and use is not recommended. 15

Methylergonovine is not indicated for induction or augmentation of labor, to induce abortion, or in cases of threatened spontaneous abortion because of its propensity to produce nonphysiologic, tetanic contractions and its long duration of action. 11, 12, 15, 18, 22, 25

Pharmacology

Mechanism of action/Effect:

Uterine stimulant¾
Methylergonovine directly stimulates the uterine muscle to increase force and frequency of contractions 11, 12, 22, 23, 25.

When usual doses of methylergonovine are used, these contractions precede periods of relaxation; when larger doses are used, basal uterine tone is elevated and these relaxation periods will be decreased 11, 12, 25, 27.

Contraction of the uterine wall around bleeding vessels at the placental site produces hemostasis 14.

The sensitivity of the uterus to the oxytocic effect is much greater toward the end of pregnancy. 11, 12, 15, 22 The oxytocic actions of methylergonovine are greater than its vascular effects. 12, 17

Vasoconstriction¾

Methylergonovine, like other ergot alkaloids, produces arterial vasoconstriction by stimulation of alpha-adrenergic and serotonin receptors and inhibition of endothelial-derived relaxation factor release 12, 13, 22, 23, 25, 26.

It is a less potent vasoconstrictor than ergotamine. 12

Other actions/effects:

Methylergonovine has minor actions on the central nervous system (CNS). 12 In the CNS, methylergonovine is a partial agonist and partial antagonist at some serotonin and dopamine receptors. 12 Methylergonovine also possesses weak dopaminergic antagonist actions in certain blood vessels 12 and partial agonist actions at serotonin receptors in umbilical and placental blood vessels 12.

It does not possess significant alpha-adrenergic blocking activity. 12

Precautions to Consider

Cross-sensitivity and/or related problems

Patients sensitive to other ergot derivatives may be sensitive to this medication also, although there is some degree of variation among ergot alkaloids in their ability to elicit oxytocic, CNS, or vasoconstrictive effects. 12

Pregnancy/Reproduction

Pregnancy¾Methylergonovine is contraindicated during pregnancy. 11, 16, 22, 23, 27 Tetanic contractions may result in decreased uterine blood flow and fetal distress. 11, 27

Labor and delivery¾High doses of methylergonovine administered prior to delivery may cause uterine tetany and fetal distress 11, 35.

Methylergonovine should not be administered prior to delivery of the placenta 25.

Administration prior to delivery of the placenta may cause captivation of the placenta or missed diagnosis of twin gestation, due to excessive uterine contraction 14, 25.

Breast-feeding

Problems in humans have not been documented. Ergot alkaloids are excreted in breast milk 25.

However, very little passes into breast milk in humans 10, 15, 16, 25.

In a study in women who had received 125 mcg of methylergonovine orally 3 times a day for 5 days, concentrations in breast milk ranged from less than 0.5 (limit of detection) to 1.3 nanograms per mL at 1 hour after a 250 mcg oral dose and from 0 to 1.2 nanograms per mL at 8 hours 10, 15, 16.

Inhibition of lactation has not been reported for methylergonovine 32.

However, studies have shown that methylergonovine may interfere with the secretion of prolactin (to a lesser degree than bromocriptine) in the immediate postpartum period. 12, 16, 22, 25 This could result in delayed or diminished lactation with prolonged use. 12, 14, 16, 22, 25

Ergot alkaloids have the potential to cause chronic ergot poisoning in the infant only if used in the mother in higher-than-recommended doses or if used for a longer period of time than is generally recommended. 12, 16

Pediatrics

In newborns, elimination of methylergonovine may be prolonged 25.

Neonates inadvertently administered ergonovine in overdose amounts have developed respiratory depression, myoclonic movements, purpuric symptoms, mild jaundice, and severe peripheral vasoconstriction. 15, 25, 28

Geriatrics

No information is available on the effects of methylergonovine in geriatric patients.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication. 2

Anesthetics, general, especially halothane 15, 17, 18

(peripheral vasoconstriction may be potentiated by the concurrent use of general anesthetics with methylergonovine 17)
(concurrent use of halothane in concentrations greater than 1% may interfere with the oxytocic actions of methylergonovine, resulting in severe uterine hemorrhage 15, 18)

Bromocriptine 13 or

Ergot alkaloids, other 13, 28

(the incidence of rare cases of hypertension, strokes, seizures, and myocardial infarction associated with the postpartum use of bromocriptine or other ergot alkaloids may be increased with the use of ergot alkaloids 3, 4, 13)

Nicotine or

Smoking, tobacco

(nicotine absorption from heavy smoking may result in enhanced vasoconstriction)

Nitroglycerin 21, 29 or

Antianginal agents, other 29

(ergot alkaloids may induce coronary vasospasm, lowering the efficacy of nitroglycerin or other antianginal agents 21, 29 ; increased doses of nitroglycerin or antianginal agents and/or use of intracoronary nitroglycerin may be necessary 30)

Vasoconstrictors, other, including those present in local anesthetics or 12, 14, 15, 25

Vasopressors 12, 15, 21

(concurrent use may result in enhanced vasoconstriction; dosage adjustments may be necessary 12, 15)
(the pressor effect of sympathomimetic pressor amines may be potentiated, resulting in potentially severe hypertension, headache, and rupture of cerebral blood vessels 15, 25 ; gangrene developed in a patient receiving both dopamine and ergonovine infusions 15, 21)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):
With physiology/laboratory test values

Blood pressure or 12, 13, 14, 22, 25, 29

Central venous pressure 25

(may be elevated due to peripheral vasoconstriction primarily of postcapillary vessels 12, 13, 25 ; less likely with methylergonovine than ergonovine 18, 22, 25 ; has sometimes been associated with preeclampsia, history of hypertension, intravenous administration of methylergonovine, or concurrent use of local anesthetics containing vasoconstrictors 13 ; hypotension has also been reported 12, 13, 25)

Heart rate 12, 13, 15, 17

(may be decreased due primarily to an increase in vagal tone, and possibly to decreased central sympathetic activity and direct depression of the myocardium 12, 13, 17)

Prolactin 22, 25, 27

(serum concentrations may be decreased 22, 25, 27)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Except under special circumstances, this medication should not be used when the following medical problems exist

>> Angina pectoris, unstable or 15, 19, 25, 29, 34

>> Myocardial infarction, recent 15, 19, 25, 26, 29, 34

(vasospasm caused by methylergonovine may precipitate angina or myocardial infarction 3, 7, 16, 29, 31, 34)

>> Cardiovascular disease or 34, 35, 36

>> Coronary artery disease 12, 15, 23, 25, 26, 29, 31, 34, 35, 36

(patients may be more susceptible to angina or myocardial infarction caused by methylergonovine-induced vasospasm 31, 34)

>> Cerebrovascular accident, history of or 19, 26, 29, 34

>> Transient ischemic attack, history of 19, 26, 29, 34

(patients may be susceptible to recurrence due to increases in blood pressure)

>> Eclampsia or 15, 28, 29, 34

>> Preeclampsia 13, 14, 15, 25, 28, 29, 34

(may be exacerbated 15, 25, 26, 28, 31, 34 ; patients may be more likely to develop methylergonovine-induced hypertension 14, 18, 28, 34 ; headaches, severe cardiac arrhythmias, seizures, and cerebrovascular accidents have occurred 18, 25, 28, 29, 34)

>> Hypertension, severe, or history of 13, 14, 15, 18, 23, 25, 26, 28, 29, 34

(may be exacerbated 15, 25, 26, 28, 31, 34)

>> Occlusive peripheral vascular disease 12, 15, 18, 23, 25, 29, 34 or

>> Raynaud's phenomenon, severe 12, 26, 29, 34

(may be exacerbated 12, 26, 34 ; a patient with Raynaud's phenomenon developed impalpable arterial pulses with use of ergonovine 12, 17, 18, 34)

Risk-benefit should be considered when the following medical problems exist

Allergy or sensitivity to methylergonovine or other ergot alkaloids 18, 25, 34

>> Hepatic function impairment 12, 15, 18, 22, 23, 25, 34

(impaired metabolism of methylergonovine may result in ergot overdose 34)

Hypocalcemia 25, 34

(oxytocic response to methylergonovine may be reduced 25, 34 ; cautious use of intravenous calcium gluconate may restore oxytocic response to methylergonovine 25, 34)

>> Mitral valve stenosis or 25, 29, 34

>> Venoatrial shunts 25, 29, 34

(vasospasm caused by methylergonovine may precipitate angina or myocardial infarction 29, 31, 34)

>> Renal function impairment 15, 18, 23, 25, 31, 34

>> Sepsis 12, 15, 23, 25, 34

(possible increased sensitivity to effects of methylergonovine 12, 34)

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):
Blood pressure determinations and 22, 23, 25

Pulse rate determinations and 23

Uterine response 25

(recommended at frequent intervals after parenteral therapy to monitor for adverse reactions; especially important with intravenous administration or before repeating doses 35)

Side/Adverse Effects

Note: Because the duration of therapy with methylergonovine is generally short, many of the side effects seen with other ergot alkaloids do not occur 25.

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention

Incidence less frequent

Bradycardia 12, 14, 15, 28 (slow heartbeat); coronary vasospasm 12, 13, 14, 15, 21, 23, 25 (chest pain)
Incidence rare

Allergic reaction, including shock 25; cardiac arrest 13, 14, 19, 26, 28 or ventricular arrhythmias, including fibrillation and tachycardia (irregular heartbeat) 14, 15, 19, 22, 25, 28; dyspnea 15, 22, 25 (unexplained shortness of breath); hypertension, sudden and severe 12, 13, 14, 15, 17, 18, 20, 22, 25 (sudden, severe headache; blurred vision; seizures); myocardial infarction 13, 14, 15, 19 (crushing chest pain; unexplained shortness of breath)¾has occurred with the use of ergot preparations in the postpartum period 13, 14; peripheral vasospasm (itching of skin; pain in arms, legs, or lower back; pale or cold hands or feet; weakness in legs)¾dose-related 22, 25, 37

Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Nausea¾especially after intravenous use 12, 15, 18, 19, 22, 25; uterine cramping 11, 15, 19, 25; vomiting¾especially after intravenous use 12, 15, 18, 19, 22, 25

Note: Uterine cramping will occur to some degree in all patients and is indicative of efficacy. However, dosage reduction may be required in occasional patients with severe or intolerable uterine cramps. 25

Incidence less frequent

Abdominal or stomach pain 15; diarrhea 12, 25; dizziness 12, 15, 22, 25; sweating 22, 25; tinnitus 15, 22, 25 (ringing in the ears)

Overdose

For specific information on the agents used in the management of methylergonovine overdose, see:
- Charcoal, Activated (Oral-Local) monograph;
- Chlorpromazine in Phenothiazines (Systemic) monograph;
- Diazepam in Benzodiazepines (Systemic) monograph;
- Hydralazine (Systemic) monograph;
- Laxatives (Local) monograph;
- Nitroglycerin in Nitrates (Systemic) monograph;
- Nitroprusside (Systemic) monograph;
- Phentolamine (Systemic) monograph;
- Phenytoin in Anticonvulsants, Hydantoin (Systemic) monograph; and/or
- Tolazoline (Parenteral-Systemic) monograph.

For more information on the management of overdose or unintentional ingestion, contact a Poison Control Center (see Poison Control Center Listing).

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Acute

Angina 12, 25 (chest pain); bradycardia 12 (slow heartbeat); confusion 12; drowsiness 12; fast, weak pulse 12, 25; miosis 12 (small pupils); peripheral vasoconstriction, severe (coolness, paleness, or

numbness of arms or legs; muscle pain; weak or absent arterial pulse in arms or legs; tingling, itching, and coolness of skin 12, 17, 25); respiratory depression 15, 25 (decreased breathing rate or trouble in breathing; bluish color of skin or inside of nose or mouth); seizures 12, 15; tachycardia 12 (fast heartbeat); unconsciousness 12, 25; unusual thirst 12; uterine tetany 11, 12 (severe cramping of the uterus)

Chronic

Formication 12, 17, 25 (false feeling of insects crawling on the skin); gangrene 12, 15, 20, 25 (dry, shriveled appearance of skin on hands, lower legs, or feet); hemiplegia 12 (paralysis of one side of the body); thrombophlebitis 12, 20, 25 (pain and redness in an arm or leg)

Note: Chronic overdose symptoms are unlikely with proper use since treatment is of short duration. 12, 15, 14, 25

Treatment of overdose

Immediate discontinuation of methylergonovine. 12, 14 Since there is no specific antidote for the management of methylergonovine overdose, treatment is primarily supportive and symptomatic and may include the following: 12, 15, 26, 38

To decrease absorption¾

Gastrointestinal decontamination for oral overdose, preferably with multiple doses of activated charcoal and an appropriate cathartic. 3, 23, 25 Gastric lavage may also be considered. 3, 15, 23, 25

Specific treatment¾

Use of nitroglycerin for treatment of myocardial ischemia 3, 12, 15, 19.

Intracoronary nitroglycerin may be necessary. 15, 19

Use of diazepam or phenytoin for treatment of seizures. 3, 15, 23, 25

Use of sodium nitroprusside, tolazoline, or phentolamine for treatment of peripheral ischemia. 3, 12, 15, 23, 25

Use of sodium nitroprusside, chlorpromazine 15 mg, or hydralazine for treatment of severe hypertension. 7, 12, 15, 23, 25

Monitoring¾

Frequent monitoring of vital signs, arterial blood gases, and electrolytes. 3, 23 Electrocardiogram monitoring to assess cardiac function and perfusion. 3 Monitoring of serum methylergonovine levels is not predictive of the outcome of overdose. 3

Supportive care¾

May include maintaining an open airway and breathing, maintaining proper fluid and electrolyte balance, correcting hypertension, and controlling seizures. Patients in whom intentional overdose is known or suspected should be referred for psychiatic consultation.

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Ergonovine/Methylergonovine (Systemic).
In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):
Before using this medication

>> Conditions affecting use, especially:

Allergies or sensitivity to methylergonovine or other ergot alkaloids
Pregnancy¾Should not be used prior to delivery or delivery of the placenta
Breast-feeding¾Ergot alkaloids are excreted in breast milk
Other medical problems, especially cardiac or vascular disease, hepatic function impairment, severe hypertension or history of hypertension, renal function impairment, and sepsis
Proper use of this medication

>> Importance of not using more medication or using for longer than prescribed; risk of ergotism and gangrene with prolonged use

>> Proper dosing
Missed dose: Not taking missed dose; not doubling doses
>> Proper storage
Precautions while using this medication

Notifying physician if infection develops, since infection may cause increased sensitivity to medication

Side/adverse effects

Signs of potential side effects, especially allergic reaction, coronary vasospasm or other cardiovascular complications, dyspnea, severe hypertension, or peripheral vasospasm

General Dosing Information

Antiemetic medications such as prochlorperazine may be administered prior to use of methylergonovine. 12, 15, 25

For parenteral dosage forms only

Because the risk of severe adverse effects is increased with intravenous use of methylergonovine, such use is recommended only for emergencies such as excessive uterine bleeding. 14, 15, 18, 19, 22, 24, 25, 28

If intravenous use is warranted, administration must be done slowly, over a period of at least 1 minute 15, 22, 24, 25 ; some clinicians recommend dilution of the solution with normal saline before administration. 14, 24, 25

In some patients who do not respond to methylergonovine because of hypocalcemia, cautious intravenous administration of calcium gluconate (provided the patient is not receiving digitalis) may restore the oxytocic action. 25

Oral Dosage Forms

METHYLERGONOVINE MALEATE TABLETS USP

Usual adult and adolescent dose

Uterine stimulant¾
Oral, 200 to 400 mcg (0.2 to 0.4 mg) two to four times a day (every six to twelve hours) until the danger of uterine atony and hemorrhage has passed. 15, 18, 19, 22, 25

Note: Generally, a treatment course of 48 hours is sufficient 18, 25.

However, in some patients, treatment for up to 7 days may be necessary, especially when used for treatment of incomplete abortion 15, 25.

Oral administration usually follows an initial parenteral dose. 25

Strength(s) usually available

U.S.¾200 mcg (0.2 mg) (Rx)[Methergine]

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container. Protect from light.

Parenteral Dosage Forms

METHYLERGONOVINE MALEATE INJECTION USP

Usual adult and adolescent dose

Uterine stimulant¾
Intramuscular or intravenous, 200 mcg (0.2 mg), repeated in two to four hours if necessary, up to five doses. 15, 18, 19, 24, 25

Strength(s) usually available

U.S.¾200 mcg (0.2 mg) per mL (Rx)[Methergine]

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

Stability:

Discolored solutions or solutions containing visible particles should not be used. 24