A cost-effective generic

Methylergonovine Maleate Tablets, USP (0.2 mg)

AB rated to Methergine®

Approved by the U.S. FDA
Packaged 100 Tablets per bottle
NDC# 63704-006-01

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Please see accompanying prescribing information

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Methylergonovine Maleate Tablets, USP
Rx Only

DESCRIPTION
Methylergonovine Maleate is a semi-synthetic ergot alkaloid used for the prevention and control of postpartum hemorrhage.

Methylergonovine Maleate Tablets, USP is available in tablets for oral ingestion containing 0.2 mg methylergonovine maleate.

Tablets
Active Ingredients: methylergonovine maleate, USP, 0.2 mg.
Inactive Ingredients: acacia, cornstarch, gelatin, lactose monohydrate, methylparaben, microcrystalline cellulose, povidone, propylparaben, saccharin acid, and tartaric acid.

CLINICAL PHARMACOLOGY
Methylergonovine maleate acts directly on the smooth muscle of the uterus and increases the tone, rate and amplitude of rhythmic contractions. Thus, it produces a rapid and sustained tonic uterine effect which shortens the third stage of labor and reduces blood loss. The onset of action after I.V. administration is immediate; after I.M. administration, 2-5 minutes, and after oral administration, 5-10 minutes.

Pharmacokinetic studies following an I.V. injection have shown that methylergonovine is rapidly distributed from plasma to peripheral tissues within 2-3 minutes or less. The bioavailability after oral administration was reported to be about 60%, with no accumulation after repeated doses. During delivery, with intramuscular injection, bioavailability increased to 76%. Ergot alkaloids are mostly eliminated by hepatic metabolism and excretion, and the decrease in bioavailability following oral administration is probably a result of first-pass metabolism in the liver.

Bioavailability studies conducted in fasting healthy female volunteers have shown that oral absorption of a 0.2 mg methylergonovine maleate tablet was fairly rapid, with an average peak plasma concentration of 3243 ± 1306 pg/mL observed at 1.12 ± 0.82 hours. For a 0.2 mg intramuscular injection, a mean peak plasma concentration of 5918 ± 1952 pg/mL was observed at 0.41 ± 0.21 hours. The extent of absorption of the tablet, based upon methylergonovine plasma concentrations, was found to be equivalent to that of the I.M. solution given orally, and the extent of oral absorption of the I.M. solution was proportional to the dose following administration of 0.1, 0.2, and 0.4 mg. When given intramuscularly, the extent of absorption of methylergonovine maleate solution was about 25% greater than the tablet. The volume of distribution (Vdss/F) of methylergonovine was calculated to be 58.1 ± 17.0 liters, and the plasma clearance (CL/F) was calculated to be 14.4 ± 4.5 liters per hour.

The plasma level decline was biphasic, with a mean elimination half-life of 3.39 hours (range 1.5 to 12.7 hours). A delayed gastrointestinal absorption (Tmax about 3 hours) of methylergonovine maleate tablet might be observed in postpartum women during continuous treatment with this oxytocic agent.

INDICATIONS AND USAGE
For routine management after delivery of the placenta; postpartum atony and hemorrhage; subinvolution. Under full obstetric supervision, it may be given in the second stage of labor following delivery of the anterior shoulder.

CONTRAINdications
Hypertension; toxemia; pregnancy; and hypersensitivity.

WARNINGS
This drug should not be administered I.V. routinely because of the possibility of inducing sudden hypertensive and cerebrovascular accidents. If I.V. administration is considered essential, the drug should be administered slowly and under close observation. Blood pressure should be continuously monitored. On rare occasions, this drug has caused anaphylactic reactions.

The most common adverse reaction is hypertension, associated in several cases with seizure and/or headache. Hypotension has also been reported. Nausea and vomiting have occurred occasionally.

ADVERSE REACTIONS
Methylergonovine maleate has not been associated with drug abuse or dependence of either a psychological or physical nature.

OVERDOSE
Symptoms of acute overdose may include: nausea, vomiting, abdominal pain, numbness, tingling of the extremities, rise in blood pressure, in severe cases followed by hypotension, respiratory depression, hypothermia, convulsions, and coma.

Drug interactions
CYP 3A4 inhibitors (e.g., Macrolide Antibiotics and Protease Inhibitors)

There have been rare reports of serious adverse events in connection with the coadministration of certain ergot alkaloids drugs (e.g., dihydroergotamine and ergotamine) and potent CYP 3A4 inhibitors, resulting in vasoospasm leading to cerebral ischemia and/or ischemia of the extremities. Although there have been no reports of such interactions with methylergonovine alone, potent CYP 3A4 inhibitors should not be coadministered with methylergonovine. Examples of some of the more potent CYP 3A4 inhibitors include macrolide antibiotics (e.g., erythromycin, troleandomycin, clarithromycin), HIV protease or reverse transcriptase inhibitors (e.g., ritonavir, indinavir, nelfinavir, delavirdine) or azole antifungals (e.g., ketoconazole, itraconazole, voriconazole). Less potent CYP 3A4 inhibitors should be administered with caution. Less potent inhibitors include saquinavir, nefazodone, fluconazole, grapefruit juice, fluoxetine, fluvoxamine, zileuton, and clotrimazole. These lists are not exhaustive, and the prescriber should consider the effects on CYP 3A4 of other agents being considered for concomitant use with methylergonovine.

No pharmacokinetic interactions involving other cytochrome P450 isoenzymes are known.

Caution should be exercised when methylergonovine maleate is used concurrently with other vasconstrictors or ergot alkaloids.

Carcinogenesis, Mutagenesis, Impairment of Fertility
No long-term studies have been performed in animals to evaluate carcinogenic potential. The effect of the drug on mutagenesis or fertility has not been determined.

Pregnancy
Category C. Animal reproductive studies have not been conducted with methylergonovine maleate. It is also not known whether methylergonovine maleate can cause fetal harm or can affect reproductive capacity. Use of methylergonovine maleate is contraindicated during pregnancy because of its uterotic effects. (See INDICATIONS AND USAGE.)

Labor and Delivery
The uterotonic effect of methylergonovine maleate is utilized after delivery to assist involution and decrease hemorrhage, shortening the third stage of labor.

Nursing Mothers
Methylergonovine maleate may be administered orally for a maximum of 1 week postpartum to control uterine bleeding. Recommended dosage is 1 tablet (0.2 mg) 3 or 4 times daily. At this dosage level, a small quantity of drug appears in mothers’ milk. Caution should be exercised when methylergonovine maleate is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
Clinical studies of methylergonovine maleate did not include sufficient number of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in response between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

DOSAGE AND ADMINISTRATION
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Intramuscularly
1 mL, 0.2 mg, after delivery of the anterior shoulder, after delivery of the placenta, or during the puerperium. May be repeated as required, at intervals of 2-4 hours.

Intravenously
Dosage same as intramuscular. (See WARNINGS.)

Orally
One tablet, 0.2 mg, 3 to 4 times daily in the puerperium for a maximum of 1 week.

HOW SUPPLIED
White, round, biconvex compressed tablets debossed with “N” on one side and “01” on the other side.

Available in bottles of 28 and 100 tablets.

Manufactured for:
ErgoJect LLC Pharmacist Pharmaceutical LLC
Salem, VA 24153

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References
1. Information on Adverse Reactions supplied by Medical Services Dept., Novartis Pharmaceuticals, E. Hanover, N.J., based on computerized clinical reports.