

## UTEROTONIC AGENTS FACT SHEET

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**Oxytocin (Pitocin®):** Oxytocin is a synthetic version of the natural nonapeptide produced in the posterior pituitary. The drug comes in solution at a concentration of 10 U/ml. For postpartum use, including third stage of labor, oxytocin is dosed at 10-40 U per liter of IV fluid and given as an IV infusion. The rate of infusion should be sufficient to maintain uterine contractility. The plasma half-life of oxytocin is 1-6 minutes and the clinical response is rapid after IV infusion. Alternatively, the agent may be given as an IM injection (10 units). Intramuscular response to the drug occurs within 3-5 minutes, with a clinical response lasting about 2-3 hours. The drug may be stored at room temperature.

- **Side Effects:** Side effects are rare in the absence of prolonged use. Nausea and vomiting have been reported. The most serious side effect from prolonged use of IV oxytocin is water intoxication with subsequent dilutional hyponatremia. Rapid IV infusion is associated with hypotension and tachycardia. The drug should not to be given as an IV bolus.
- **Contraindications:** The only postpartum contraindication to use of oxytocin would be hypersensitivity to the drug.

**Hemabate® (carboprost or 15 methyl PGF<sub>2</sub> alpha):** Hemabate is FDA-approved for the treatment of postpartum hemorrhage secondary to uterine atony not responsive to conventional treatment (massage and oxytocin). The drug is supplied in 1 ml ampoules containing 250 mcg of the drug. The dose is one ampoule given as an IM injection. The peak plasma level of the drug is reached about 30 minutes after injection. A successful clinical response is expected after a single injection in about 75% of cases. In refractory cases, additional dosing at 15-90 minute intervals may be beneficial. The total amount of drug given should not exceed 2 mg (8 doses). The clinical response may be enhanced with concomitant use of oxytocin. It may be less effective when used in the setting of chorioamnionitis. It should be noted that other uterotonic agents are also less effective in the setting of chorioamnionitis. The drug must be refrigerated when stored.

- **Side Effects:** Recognized side effects include nausea, vomiting, diarrhea, fever (up to 1 degree Celsius), bronchospasm, and hypertension.
  - **Contraindications:** It is recommended that the drug be given with caution to patients with active hepatic or cardiovascular disease, asthma, or hypersensitivity to the drug.
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**Methergine® (methylergonovine maleate):** Methergine is a semi-synthetic ergot alkaloid that is FDA-approved for routine management of the third stage of labor and postpartum atony. It is supplied in ampoules containing 0.2 mg of active drug in a volume of 1 mL or as a single tablet of 0.2 mg of active drug. The drug is given either as an intramuscular injection (1 ampoule) or orally (single tablet). When given as an oral agent, the onset of action is within 5-10 minutes with a bioavailability of 60%. When given as an intramuscular injection, the onset of action is 2-5 minutes and the bioavailability is 78% (about 25% greater than when given orally). The plasma half-life is about 3.4 hours. The agent should not be given by intravascular injection. The frequency of administration is 2-4 hours for IM administration and 6-8 hours when given orally. The drug must be refrigerated when stored.

- **Side Effects:** Side effects are rare in the absence of prolonged use. Most common side effects are nausea and vomiting. Chest pain, arterial spasm, myocardial infarction, and hallucination have been reported in cases of toxicity.
- **Contraindications:** Methergine should be used with extreme caution in the setting of hypertension or preeclampsia. Care should be exercised when there has been recent administration of other vasoconstrictive agents (i.e. ephedrine). In these settings, there may be an exaggerated blood pressure response to the use of this agent. Care should also be taken when CYP 3A3 inhibiting agents, such as macrolide antibiotics, protease inhibitors, or azole antifungals, have recently been used.

**Cytotec® (misoprostol):** This agent is a synthetic prostaglandin E<sub>1</sub> analog. This agent is FDA-approved for reducing the risk of NSAID-induced gastric ulcers. It comes in either 100 or 200 mcg tablets. This agent is not FDA-approved for uterine atony or obstetrical hemorrhage, although its effectiveness has been clearly demonstrated in the obstetrical literature. The drug is water-soluble and is quickly absorbed after sublingual, oral, vaginal, and rectal use. The most common method of administering misoprostol for postpartum hemorrhage is rectally, although in a conscious patient sublingual use would also be reasonable. The dose usually ranges between 800-1000 mcg. The time to peak plasma concentration is shortest for sublingual administration and the plasma concentration is higher than when given rectally. However, after rectal administration, plasma concentrations are maintained for a longer period. The drug undergoes a series of chemical reactions after ingestion, converting the agent to a prostaglandin F analog, making the drug very similar to hemabate (15 methyl PGF<sub>2</sub> alpha). Therefore, it is unlikely that misoprostol would be effective if hemabate has failed, or vice versa. Unlike hemabate, misoprostol does not appear to exacerbate bronchoconstriction in patients with asthma. One of the major advantages of this agent is that the drug does not need to be refrigerated and may be easily stored on labor and delivery hospital units.

- **Side Effects:** Diarrhea, shivering, pyrexia and headaches are the most common side effects.
- **Contraindications:** Hypersensitivity to the drug.

## REFERENCE

1. <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.LabelApprovalHistory> (Accessed 4/2009).