PRESCRIBING INFORMATION

[Pr]Oxytocin Injection, USP

Synthetic

10 USP Oxytocin Units per mL

Sterile Solution

For Intravenous Infusions or Intramuscular Use

Oxytocic

Fresenius Kabi Canada Ltd.
165 Galaxy Blvd, Suite 100
Toronto, ON M9W 0C8

Date of Preparation:
May 22, 2020

Submission Control Number: 225475

[Pr]Oxytocin Injection, USP
10 USP units/mL
Sterile Solution
Oxytocic

ACTIONS AND CLINICAL PHARMACOLOGY

Oxytocin Injection, USP, synthetic, acts on the smooth muscle of the uterus to stimulate contractions; response depends on the uterine threshold of excitability. It exerts a selective action on the smooth musculature of the uterus, particularly towards the end of pregnancy, during labour and immediately following delivery. Oxytocin stimulates rhythmic contractions of the uterus, increases the frequency of existing contractions and raises the tone of the uterine musculature. Synthetic oxytocin elicits only slight pressor and antidiuretic activity due to the absence of vasopressin. (Hypertension has been observed resulting from concomitant use of oxytocics and continuous caudal block anesthesia).

INDICATIONS AND CLINICAL USE

IMPORTANT NOTICE

Oxytocin Injection, USP is **not** indicated for the **elective** induction of labour. Elective induction of labour is defined as the initiation of labour for convenience in an individual with a term pregnancy, who is free of medical indications for the initiation of labour. Oxytocin Injection, USP is indicated in the following:

Antepartum

- For induction of labour in patients with a medical indication for the initiation of labour, such as Rh problems, maternal diabetes, mild pre-eclampsia at or near term, when delivery is in the best interest of mother and fetus, or when membranes are prematurely ruptured and delivery indicated.
- For stimulation or reinforcement of labour as in selected cases of uterine inertia.
- As adjunctive therapy in the management of incomplete or inevitable abortion.

Postpartum

- To produce uterine contractions during the third stage of labour and to control postpartum bleeding and hemorrhage.

CONTRAINDICATIONS

Oxytocin Injection, USP is contraindicated in the following:

- Significant cephalopelvic disproportion.
- Severe toxemia.
- Malpresentation or malposition of the fetus or placenta previa.

- Prematurity or unripe cervix.
- Predisposition to uterine rupture (grand multiparity, overdistention of the uterus, previous cesarean section or other surgery involving the uterus).
- Hypertonic labour patterns.
- Prolonged use in uterine inertia.
- Factors predisposing to thromboplastin or amniotic fluid embolism (prolonged retention of dead fetus, *abruptio placentae*).
- Serious medical and obstetric conditions and any conditions in which fetal distress already occurs.
- Inability of physician to be in attendance.
- Hypersensitivity to oxytocin.

WARNINGS AND PRECAUTIONS

Oxytocin Injection, USP, when given for induction or stimulation of labour, must be administered only by the intravenous route and with adequate medical supervision in a hospital.

Cardiovascular disorders

Oxytocin should be used with caution in patients who have a pre-disposition to myocardial ischaemia due to pre-existing cardiovascular disease (such as hypertrophic cardiomyopathy, valvular heart disease and/or ischaemic heart disease including coronary artery vasospasm), to avoid significant changes in blood pressure and heart rate in these patients.

QT Syndrome

Oxytocin should be given with caution to patients with known 'long QT syndrome' or related symptoms and to patients taking drugs that are known to prolong the QTc interval (see DRUG INTERACTIONS).

The following should be borne in mind when using Oxytocin Injection, USP:

1. **Use only under close medical/obstetrical supervision.**
2. **Never administer undiluted oxytocin intravenously, and/or use in high concentrations.**
3. **Oxytocin must not be used by more than one route simultaneously, e.g., parenteral and buccal, or parenteral and nasal.**

When given for **induction** and **stimulation** of labour, Oxytocin Injection, USP must only be used as **intravenous drip infusion**, and not by intramuscular, nor by direct intravenous injection.

Careful monitoring (blood pressure, fetal heart rate, possible tocometry) is vital, in order to adjust dosage according to the individual response: if uterine activity interferes at any time with fetal heart rate, the infusion should be discontinued.

In patients with cardiovascular disorders, the infusion volume should be kept low by using a more concentrated solution.

All patients receiving intravenous oxytocin must be under continuous observation by trained personnel with a thorough knowledge of the drug and qualified to identify complications. A physician qualified to manage any complications should be immediately available.

When properly administered, oxytocin should stimulate uterine contractions similar to those seen in normal labour. Overstimulation of the uterus by improper administration can be hazardous to both mother and fetus. Even with proper administration and adequate supervision, hypertonic contractions can occur in patients whose uteri are hypersensitive to oxytocin.

Carcinogenesis, Mutagenesis, Impairment of Fertility

There are no animal or human studies on the carcinogenicity and mutagenicity of this drug, nor is there any information on its effect on fertility.

Pregnancy

Animal reproduction studies have not been conducted with oxytocin. Based on the wide experience with this drug and its chemical structure and pharmacological properties, it would not be expected to present risk of fetal abnormalities when used as indicated.

DRUG INTERACTIONS

Oxytocin should be used with special caution in conjunction with cyclopropane anesthesia since the risk of arrhythmias may be increased. In instances where a vasoconstrictor drug is administered prophylactically in conjunction with continuous caudal block anesthesia, severe hypertension may occur when oxytocin is given within 3 to 6 hours of administration of the vasoconstrictor drug. Sudden, marked elevation of blood pressure occurring under these circumstances has been reported to respond to intravenous administration of chlorpromazine.

Prostaglandin E_2 acts synergistically with oxytocin and the simultaneous parenteral administration of this product usually results in a substantial reduction in the quantity of oxytocin required. When oral prostaglandin E_2 has been employed, the infusion of oxytocin should not be started until at least one hour has elapsed following the last dose of prostaglandin E_2. A suitable time period should elapse, usually the following day, before prostaglandin E_2 is to be administered to patients who have previously received oxytocin.

Oxytocin should be considered as potentially arrhythmogenic, particularly in patients with other risk factors for Torsades de Pointes such as drugs which prolong the QT interval or in patients with history of long QT syndrome (see WARNINGS AND PRECAUTIONS).

ADVERSE EFFECTS

Water intoxication with headaches and nausea has been reported after prolonged or too rapid intravenous infusion of oxytocin (see SYMPTOMS AND TREATMENT OF OVERDOSAGE). Premature ventricular contractions, fetal bradycardia and cardiac arrhythmia have been noted. Hypotension, tachycardia and ECG changes have been observed following intravenous administration of concentrated solutions. Anxiety, dyspnea, precordial pain, edema, cyanosis or reddening of the skin and cardiovascular spasm and collapse have occurred on rare occasions. In very few cases, anaphylactoic reactions (dyspnea, hypotension shock) occurred. Overdosage may give rise to the following complications: slowing of fetal heart, meconium staining of the amniotic fluid and asphyxia; hypertonic contractions, uterine rupture, retention of the placenta, postpartum uterine inertia.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Intravenous infusion of oxytocin in nonpregnant subjects given at a rate greater than 45 mU/min (4.5 mL/min = 90 drops/min using 10 USP units/L dilution) has been shown to have an antidiuretic effect comparable to that of vasopressin but of shorter duration.

There are also a number of cases reported in the literature where high intravenous doses of oxytocin administered along with a large volume of electrolyte-free fluid have resulted in the development of water intoxication.

However, high doses of oxytocin can be given without danger of water intoxication provided that the daily fluid intake is limited at this time. Acute overdosage of oxytocin, therefore, is unlikely in any circumstances and adverse reactions are to be expected only if the concomitant fluid intake is excessive.

Symptoms of Water Intoxication

Headache, anorexia, nausea, vomiting, abdominal pain, lethargy, drowsiness, unconsciousness, and grand mal type seizures have been reported.

Owing to the excessive retention of water, the serum electrolyte concentration is low.

Treatment

Discontinue oxytocin and restrict all fluid intake. Encourage diuresis by administration of a diuretic such as furosemide. The use of intravenous hypertonic sodium chloride solution should be reserved for severe water intoxication with frank CNS disturbance. Careful supervision and, where necessary, correction of electrolyte imbalance should be undertaken, particularly in the diuretic phase. At the end of the diuretic phase, the hypertonic infusion, if used, should be stopped to avoid water retention due to excessive sodium.

Control convulsions with judicious use of diazepam or barbiturates. Good nursing care is of prime importance, particularly in the comatose patient; it should include regular observation and accurate recording of the vital signs and depth of coma, maintenance of a free airway, frequent turning and other routine measures usually adopted with unconscious patients.

Prophylactic antibiotic therapy in the comatose patient is a matter of individual physician preference.

DOSAGE AND ADMINISTRATION

Induction of Labour

Intravenous infusion (drip method) is the only acceptable method of administration for the induction or stimulation of labour. Accurate control of the rate of infusion flow is essential. An infusion pump or other such device and frequent monitoring of strength of contractions and fetal heart rate are necessary for the safe administration of oxytocin for the induction or stimulation of labour. If uterine contractions become too powerful, the infusion can be abruptly stopped, and oxytocic stimulation of the uterine musculature will soon wane.

Note

Oxytocin is stable in 0.9% sodium chloride or 5% dextrose solution for 24 hours. It is unstable in any solution containing preservatives such as bisulfites and metabisulfites. 10 USP units of oxytocin are dissolved in 1 L of 5% dextrose solution (= 10 mU/mL). To

ensure the homogeneity of the drip solution, the bottle or bag must be turned upside down at least once before use.

The **initial** dose should be no more than 1 to 4 mU/min = 0.1 to 0.4 mL/min = 2 to 8 drops/min. The dose may be increased in increments of no more than 1 to 2 mU/min = 0.1 to 0.2 mL/min = 2 to 4 drops/min, until a contraction pattern has been established, which is similar to normal labour, to a maximum of 20 mU/min = 2 mL/min = 40 drops/min, provided fetal heart rate, resting uterine tone and the frequency, duration and force of contractions are carefully monitored.

The oxytocin infusion should be discontinued immediately in the event of uterine hyperactivity or fetal distress.

If regular contractions are not established after the infusion of 500 mL (= 5 USP units oxytocin), the attempt to induce labour should be broken off; it can generally be repeated on the following day.

Once labour is initiated, the infusion rate is adjusted (usually reduced) according to need. Intravenous infusion should be administered only when strictly medically indicated, rather than for convenience.

Stimulation of Labour
Intravenous infusion (see **Induction of Labour** above). Cases must be strictly selected and doses rigidly controlled.

Postpartum Hemorrhage, Postpartum Atony
a) Intravenous infusion (see **Induction of Labour** above).
b) Administer 5 to 10 USP units by **slow intravenous** injection.
c) Administer 5 to 10 USP units by intramuscular injection.

Stability and Storage Recommendations
DO NOT FREEZE. Store at 15 °C to 25 °C.
Oxytocin is stable in 0.9% sodium chloride or 5% dextrose solution for 24 hours. It is unstable in any solution containing preservatives such as bisulfites and metabisulfites.
Oxytocin Injection USP, 10 mL vial is intended for single puncture (multidose vial) only.

AVAILABILITY OF DOSAGE FORMS

Oxytocin Injection, USP is a sterile solution of oxytocin prepared by synthesis in water for injection USP. Use only if solution is clear.

Each mL possesses an oxytocin activity equivalent to 10 IU (10 USP Units). Also contains chlorobutanol 5 mg as preservative and water for injection. pH adjusted with glacial acetic acid. Oxytocin Injection, USP is packaged in USP type I tubular glass vials with latex free stoppers.

Product Number	USP Oxytocin units per mL, synthetic	Volume
C912011	10	1 mL in a 2 mL vial
C1210	10	10 mL in a 10 mL vial

1 mL size is a single use vial, packaged 25 vials per tray. Discard unused portion.

10 mL size is a single-puncture, multidose vial, packaged 25 vials per tray. Use only if solution is clear and seal intact.

If you want more information about Oxytocin Injection, USP:

- Talk to your healthcare professional
- Find the full prescribing information that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp); the manufacturer's website (https://www.fresenius-kabi.ca), or by calling 1-877-821-7724.

This prescribing Information was prepared by:

Fresenius Kabi Canada Ltd.
165 Galaxy Blvd, Suite 100
Toronto, ON M9W 0C8

Last Revised: May 22, 2020