1. **Name of the drug product:**

   EVATOCIN
   Oxytocin Injection B.P.

2. **Qualitative and quantitative composition:**
   Each vial contains Oxytocin B.P. as Oxytocin solution (synthetic) equivalent to 10 I.U. /ml - 1ml

   For full list of excipients, see section 6.1

3. **Pharmaceutical form:**
   Solution for Injection

   A clear, colourless liquid.

4. **Clinical Particulars:**

4.1 Therapeutic indications:

Important Notice: Oxytocin is indicated for the medical rather than the elective induction of labour. available data and information are inadequate to define the benefit to risk considerations in the use of drug products for elective induction. 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.

Antepartum: Oxytocin injection (synthetic) is indicated for the initiation or improvement of uterine contractions, where this is desirable and considered suitable for reasons of fetal or maternal concern, in order to achieve early vaginal delivery for fetal or maternal reasons.

It is indicated for:

1. Induction of labour in patients with a medical indication for the initiation of labour, such as Rh problems, maternal diabetes, preeclampsia at or near term, when delivery is in the best interest of both mother and fetus or when membranes are prematurely ruptured and delivery is indicated.
2. Stimulation of reinforcement of labour, as in selective cases of uterine inertia.
3. As adjunctive therapy in the management of incomplete or inevitable abortion. In the first trimester, curettage is generally considered primary therapy.

In the second trimester abortion, Oxytocin infusion will often be successful in emptying the uterus. Other means of therapy, however may be required in such cases.

Postpartum:
Oxytocin injection (synthetic) is indicated to produce uterine contractions during the third stage of labour and to control postpartum bleeding or hemorrhage.

4.2 Posology and method of administration:

Induction or augmentation of labor:
Oxytocin should only be administered as an intravenous infusion, preferably by means of a variable speed infusion pump, or by drip infusion. It should not be administered by subcutaneous, intramuscular or intravenous bolus injection.
The initial infusion rate should be set at 1-4 milliunits/min. This rate may be gradually increased at intervals of not shorter than 20 min, until a contraction pattern similar to that of normal labor is established. In pregnancy near term, this can often be achieved with an infusion of less than 10 milliunits/min. The recommended maximum rate is 20 milliunits/min. The increments in infusion rate should not be as high once contractions have been established, as those used to initiate contractions. Once an adequate level of uterine activity is attained, the infusion rate can often be reduced.
The frequency and duration of contractions and foetal heart rate must be carefully monitored during oxytocin administration, the latter preferably by electronic means, and the infusion must be discontinued immediately in the event of uterine hyperactivity, foetal distress or foetal heart abnormalities.
If regular contractions are not established after the infusion of 5 IU oxytocin, the attempt to induce labour should be terminated. It can generally be repeated on the following day, starting again from a rate of 1-4 milliunits/min. In general, the dose of Oxytocin required for the augmentation of labor is less than that required for induction. Therefore, the initial infusion rate should be at the lower end of the recommended range.

Third stage of labour and puerperium (haemorrhage, subinvolution of the uterus):
5-10 IU by intramuscular injection or 5 IU by slow bolus intravenous injection. In patients given Oxytocin by drip to induce or stimulate labour, the infusion should be continued during the third stage.

Caesarean section:
5 IU by intravenous infusion or slow bolus intravenous injection after delivery of the foetus.

Preparation of infusion solution:
For drip infusion, the preparation of a solution containing 10 IU Oxytocin per 1 litre infusion fluid is recommended. To ensure even mixing of the drip solution, the bottle or bag must be turned upside down several times before use. Using this concentration, the recommended initial infusion rate of 1-4 mU/min corresponds to 0.1-0.4 mL/min, and the recommended maximum rate of 20 mU/min is reached at a rate of 2 mL/min. When using a mechanical infusion pump which delivers smaller volumes than those given by drip infusion, a more concentrated oxytocin solution will be

required.

The concentration suitable for infusions within the recommended dosage range (1-20 MU/ min) must be calculated according to the specification of the pump used.

Treatment of Incomplete or Inevitable Abortion:

Intravenous infusion with physiologic saline solution, 500 mL, or 5% dextrose in physiologic saline solution to which 10 units of oxytocin have been added should be infused at a rate of 20 to 40 drops/minute. Parenteral drug products should be inspected Visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

4.3 Contraindications:

Oxytocin injection (synthetic) is contraindicated in any one of the following circumstances.

- When there is significant cephalopelvic disproportion.
- Unfavorable fetal positions or presents, such as transverse lies, which are undeliverable without conversion prior to delivery
- In obstetrical emergencies where benefit-to-risk ratio for either the fetus or the mother favors
- Surgical intervention
- In cases of fetal distress where delivery is not imminent
- Prolonged use in uterine inertia or severe toxemia;
- Hypertonic uterine patterns;
- Patients with hypersensitivity to the drug;
- Induction or augmentation of labor in those cases where vaginal delivery is contraindicated, such as cord presentation or prolapse, total placenta previa, and vasa previa.

4.4 Precautions and Warnings:

WARNINGS

Oxytocin injection (synthetic), when given for the induction of labor or stimulation of labor must be administered only by the intravenous route and with adequate medical supervision in a hospital.

PRECAUTIONS

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

When properly administered, Oxytocin should stimulate uterine contractions, comparable 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.

Except in unusual circumstances, Oxytocin should not be administered in the following conditions; prematurity, borderline cephalopelvic disproportion previous major surgery on the cervix or uterine including caesarean section, over distention of uterus, grand multiparity or invasive cervical carcinoma.

Because of the variability of the combinations of factors which may be present in conditions listed above the definition of “unusual circumstances” must be left to the judgment of the physician. The decision can be made by carefully weighing the potential benefits which Oxytocin can provide in a given case against the rare but definite potential for the drug to produce hyper tonicity or tetanic spasm.

Maternal deaths due to hypertensive episodes, subarachnoid hemorrhage, rupture of the uterus and fetal deaths due to various causes have been reported associated with the use of parenteral oxytocic drugs for induction of labour or for augmentation in the first and second stages of labour.

Oxytocin has been shown to have an intrinsic antidiuretic effect, acting to increase water reabsorption from the glomerular filtrate. Consideration should therefore be given to the

possibility of water intoxication, particularly when Oxytocin is administered continuously by infusion and the patient is receiving fluids by mouth.

4.5 Interaction with other drugs:

Severe hypertension has been reported when oxytocin was given three to four hours following prophylactic administration of a vascoconstrictor in conjuction with caudal block anesthesia. Cyclopropane anesthesia may modify oxytocin's cardiovascular effects, so as to produce unexpected results such as hypotension. Maternal sinus bradycardia with abnormal atrioventricular rhythms has also been noted when oxytocin was used concomitantly with cyclopropane anesthesia.

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.

4.6 Pregnancy and Lactation:

There are no known indications for use in the first and second trimester of pregnancy other than in relation to spontaneous or induced abortion. Based on the wide experience with this drug and its chemical structure and pharmacological properties, it would not be expected to present a risk of foetal abnormalities when used as indicated.

Oxytocin may be found in small quantities in mother's breast milk. However, oxytocin is not expected to cause harmful effects in the newborn because it passes into the alimentary tract where it undergoes rapid inactivation.

4.7 Effects on ability to drive and operate machine:

Evatocin can induce labour, therefore caution should be exercised when driving or operating machines. Women with uterine contractions should not drive or use machines

4.8 Adverse effects:

The following adverse reactions have been reported in the mother:

- Anaphylactic reaction
- Postpartum hemorrhage
- Cardiac arrhythmia
- Fatal afibrinogenemia
- Nausea
- Premature ventricular contractions
- Pelvic hematoma

Excessive dosage or hypersensitivity to the drug may result in uterine hypertonicity, spasm, titanic contraction or rupture of the uterus. The possibility of increased blood loss and afibrinogenemia should be kept in mind when administering the drug. Severe water intoxication with convulsions and coma has occurred, and is associated with a slow oxytocin infusion over a 24-hour period. Maternal death due to oxytocin-induced water intoxication has been reported.

The following adverse reactions have been reported in the fetus or infant:

1. **Due to induced uterine motility**

Bradycardia
Premature ventricular contractions and other arrhythmias Permanent CNS or brain damage
Fetal death

Due to use of Oxytocin in mother
Neonatal retinal hemorrhage
Low Apgar scores at five minutes Neonatal jaundice

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board,Pharmacovigilance Electronic Reporting System (PvERS)
https://pv.pharmacyboardkenya.org

4.9 Over dosage:

Overdosage with oxytocin injection (synthetic) depends essentially on uterine hyperactivity whether or not due to hypersensitivity to this agent. Hyperstimulation with strong (hypertonic) or prolonged (tetanic) contractions, or a resting tone of 15 to 20 mm H_2O or more between contractions can lead to tumultuous labor, uterine rupture, cervical and vaginal lacerations, postpartum hemorrhage, uteroplacental hypoperfusion and variable deceleration of fetal heart, fetal hypoxia, hypercapnia or death. Water intoxication with convulsions, which is caused by the inherent antidiuretic effect of oxytocin, is a serious complication that may occur if large doses (40 to 50 milliunits/ minute) are infused for long periods. Management consists of immediate discontinuation of oxytocin, and symptomatic and supportive therapy.

5. Pharmacological properties:

5.1 Pharmacodynamic properties:

Oxytocin injection (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 toward the end of the pregnancy, during labor 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 does not possess the cardiovascular effects, such as elevation of blood pressure, as exhibited by vasopressin found in posterior pituitary injection**.**

5.2 Pharmacokinetic properties:

Plasma levels and onset/duration of effect:
Intravenous infusion: When Oxytocin is given by continuous intravenous infusion at doses appropriate for induction or augmentation of labor, the uterine response sets in gradually and usually reaches a steady state within 20 to 40 minutes. The corresponding plasma levels of oxytocin are comparable to those measured during spontaneous first stage labor. For example, oxytocin plasma levels in 10 pregnant women at term, receiving

an intravenous infusion at a rate of 4 milliunits/minute, were 2 to 5 micro units/mL.
Intravenous injection and intramuscular injection: When administered by intravenous or intramuscular injection for prevention or treatment of post-partum haemorrhage, Oxytocin acts rapidly, with a latency period of less than 1 minute by intravenous injection and of 2 to 4 minutes by intramuscular injection. The Oxytocic response lasts for 30 to 60 minutes after intramuscular administration and possibly less after intravenous injection.

Distribution:
Oxytocin distributes throughout the extracellular fluid, with minimal amounts reaching the foetus. The steady-state distribution volume determined in 6 healthy men after intravenous injection was 12.2 L or 0.17 L/kg. Plasma protein binding is very low.
Oxytocin may be found in small quantities in mother's breast milk.

Biotransformation:
A glycoprotein aminopeptidase, oxytocinase, is produced during pregnancy and appears in the plasma. It is capable of degrading oxytocin. Enzyme activity increases gradually until term approaches; at which time it rises steeply to high levels. Enzyme activity then declines after delivery. Enzyme activity in the placenta and in the uterine tissue is also high during this period. There is little or no degradation of oxytocin by plasma in men, nonpregnant women or cord blood.

Elimination:
The relative ease with which the rate and force of uterine contractions can be regulated by the intravenous infusion of Oxytocin is due to the short half-life of oxytocin. Values reported by various investigators range from 3 to 20 minutes. Removal of oxytocin from plasma is accomplished mainly by the liver and the kidneys. The metabolic clearance rate amounts to about 20 mL/kg/min in men as well as in pregnant women. Less than 1% of a given dose is excreted unchanged in the urine.

Renal impairment:
No studies have been performed in renally impaired patients. However, considering the excretion of oxytocin and its reduced urinary excretion because of anti-diuretic properties, the possible accumulation of oxytocin can result in prolonged action.

Hepatic impairment:
No studies have been performed in hepatically impaired patients. Pharmacokinetic alteration in patients with impaired hepatic function is unlikely since metabolising enzyme, oxytocinase, is not confined to liver alone and the oxytocinase levels in placenta during the term has significantly increased. Therefore, biotransformation of oxytocin in impaired hepatic function may not result in substantial changes in metabolic clearance of oxytocin.

5.3 Pre-clinical Safety Data:
There are no pre-clinical data of relevance to the prescriber which are additional to those already included in other sections of the Summary of Product Characteristics

6. Pharmaceutical particulars:

6.1 List of Excipients:

Chlorobutanol Hemihydrate B.P.
Sodium Acetate (Trihydrate) B.P.
Glacial Acetic Acid B.P.
Water for Injections B.P. (Bulk)

6.2 Incompatibilities:

Oxytocin should not be infused via the same apparatus as blood or plasma, because the peptide linkages are rapidly inactivated by oxytocin-inactivating enzymes. Oxytocin is incompatible with solutions containing sodium metabisulphite as a stabiliser.

6.3 Shelf – life:

24 Months

6.4 Special precautions for storage:

Store at a temperature between 2°C & 8° C. Do not freeze.

6.5 Nature and contents of container:

1ml Flint ampoule red double band snap-off. Such 5 ampoules are packed in a blister. Such 2 blister packed in inner printed carton along with package insert.

6.6 Special Precautions for Handling and Disposal:

Compatibility of oxytocin has been demonstrated with 0.9 % saline and 5 % dextrose solutions. Oxytocin is not compatible with solutions containing bisulphites and metabisulphites as preservatives. Due attention should be paid to the choice of infusion fluid in individual patients. Generally, Oxytocin should be administered in a combination of dextrose and an electrolyte solution (such as 4 % dextrose in N/5 saline), or in an isotonic electrolyte solution. The use of 5% dextrose in water is not recommended. Due to the absence of compatibility studies, Oxytocin must not be mixed with other medicinal products.

7. Marketing authorization holder:

NEON LABORATORIES LIMITED
140, Damji Shamji Industrial Complex,
28, Mahal Indl. Estate, Mahakali
Caves Road, Andheri (East),
Mumbai - 400 093

8. Marketing authorization number:

752

9. Date of first authorization / Renewal of the authorisation:

18/12/2014

10. Date of revision of the text:

28/02/2026