SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Oxytocin 10IU Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 10IU oxytocin, equivalent to 17 micrograms of oxytocin EP in solution.

Each 1ml ampoule also contains 2.9 mg (0.13 mmol) of sodium.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

A clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Induction of labour for medical reasons; stimulation of labour in hypotonic uterine inertia; during caesarean section, following delivery of the child; prevention and treatment of postpartum uterine atony and haemorrhage.

Early stages of pregnancy as a adjunctive therapy for the management of incomplete, inevitable, or missed abortion.

4.2 Posology and method of administration

Induction or enhancement of labour*:* Oxytocin should not be started for 6 hours following administration of vaginal prostaglandins. Oxytocin should be administered as an iv drip infusion or, preferably, by means of a variable-speed infusion pump. For drip infusion it is recommended that 5 IU of oxytocin be added to 500ml of a physiological electrolyte solution. For patients in whom infusion of sodium chloride must be avoided, 5% dextrose solution may be used as the diluent (see Section 4.4 "Special warnings and precautions for use"). To ensure even mixing, the bottle or bag must be turned upside down several times before use.

The initial infusion rate should be set at 1 to 4mU/min (2 to 8 drops/min). It may be gradually increased at intervals not shorter than 20 min, until a contraction pattern similar to that of normal labour is established. In pregnancy near term this can often be achieved with an infusion of less than 10mU/min (20 drops/min), and the recommended maximum rate is 20mU/min (40 drops/min). In the unusual event that higher rates are required, as may occur in the management of foetal death *in utero* or for induction of labour at an earlier stage of pregnancy, when the uterus is less sensitive to oxytocin, it is advisable to use a more concentrated oxytocin solution, e.g., 10 IU in 500ml.

When using a motor-driven infusion pump which delivers smaller volumes than those given by drip infusion, the concentration suitable for infusion within the recommended dosage range must be calculated according to the specifications of the pump. The frequency, strength, and duration of contractions as well as the foetal heart rate must be carefully monitored throughout the infusion. Once an adequate level of uterine activity is attained, aiming for 3 to 4 contractions every 10 minutes, the infusion rate can often be reduced. In the event of uterine hyperactivity and/or foetal distress, the infusion must be discontinued immediately.

If, in women who are at term or near term, regular contractions are not established after the infusion of a total amount of 5 IU, it is recommended that the attempt to induce labour be ceased; it may be repeated on the following day, starting again from a rate of 1 to 4mU/min (see Section 4.3 "Contra-indications").

Caesarean section*:* 5 IU by slow iv injection immediately after delivery.

Prevention of postpartum uterine haemorrhage*:* The usual dose is 5 IU slowly iv after delivery of the placenta. In women given oxytocin for induction or enhancement of labour, the infusion should be continued at an increased rate during the third stage of labour and for the next few hours thereafter.

Treatment of postpartum uterine haemorrhage*:* 5 IU slowly iv, followed in severe cases by iv infusion of a solution containing 5 to 20 IU of oxytocin in 500ml of a non-hydrating diluent, run at the rate necessary to control uterine atony.

Incomplete, inevitable, or missed abortion*:* 5 IU slowly iv, if necessary followed by iv infusion at a rate of 20 to 40mU/min or higher.

Children: Not applicable.

Elderly: Not applicable.

Route of administration: Intravenous infusion or intravenous injection.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients;
- Dystocia;
- Fragility or overdistension of the uterus;
- Hypertonic uterine contractions or foetal distress, when delivery is not imminent;
- Pre-eclamptic toxaemia and severe cardiovascular disorders;
- Predisposition to amniotic fluid embolism (foetal death in utero, retroplacentar hematoma);
- Placenta praevia.

4.4 Special warnings and precautions for use

Warnings

Administration of oxytocin at excessive doses results in uterine overstimulation with hypertonicity of the uterus and may cause reversible foetal distress.

QT interval prolongation has been observed after oxytocin administration. Therefore it should be administered with caution in patients with potentially pro-arrhythmic conditions such as congenital or documented acquired QT prolongation.

Precautions for use

For the induction of labour, administration of oxytocin by direct IM or IV injection is formally avoided. Administration by IV infusion should only be under qualified medical supervision.

Careful monitoring of foetal heart rate and uterine motility is essential from the beginning to the end of delivery to prevent foetal distress or hypertonicity of the uterus reversible after oxytocin withdrawal.

In case of postpartum haemorrhage and postpartum atony, it remains essential to ensure of uterine vacuity before administration of oxytocin.

It has been found that prostaglandins potentiate the effect of oxytocin. Therefore, if used in sequence, the patient's uterine activity should be carefully monitored.

In rare circumstances, the pharmacological induction of labour using uteronic agents increases the risk of postpartum disseminated intravascular coagulation (DIC). The pharmacological induction itself and not a particular agent is linked to such a risk. This risk is increased in particular if the woman has additional risk factors for DIC such as being 35 years of age or over, complications during pregnancy and gestational age more than 40 weeks. In these women, oxytocin or any other alternative drug

should be used with care, and the practitioner should be alerted by signs of DIC (fibrinolysis).

Because oxytocin possesses slight antidiuretic activity, its prolonged iv administration at high doses in conjunction with large volumes of fluid, as may be the case in the treatment of inevitable or missed abortion or in the management of postpartum haemorrhage, may cause water intoxication associated with hyponatraemia. To avoid this rare complication, the following precautions must be observed whenever high doses of oxytocin are administered over a long time: an electrolyte-containing diluent must be used (not dextrose); the volume of infused fluid should be kept low (by infusing oxytocin at a higher concentration than recommended for the induction or enhancement of labour at term); fluid intake by mouth must be restricted; a fluid balance chart should be kept, and serum electrolytes should be measured when electrolyte imbalance is suspected.

Anaphylaxis in women with latex allergy
There have been reports of anaphylaxis following administration of oxytocin in women with a known latex allergy. Due to the existing structural homology between oxytocin and latex, latex allergy/intolerance may be an important predisposing risk factor for anaphylaxis following oxytocin administration.

4.5 Interaction with other medicinal products and other forms of interaction

Some inhalation anaesthetics, e.g., cyclopropane or halothane, may enhance the hypotensive effect of oxytocin and reduce its oxytocic action. Their concurrent use with oxytocin has also been reported to cause cardiac rhythm disturbances.

When given during or after epidural anaesthesia, oxytocin may potentiate the pressor effect of sympathomimetic vasoconstrictor agents.
Prostaglandins :
Since it has been found that prostaglandins potentiate the effect of oxytocin and are risk factors of uterine rupture, it is not recommended that these drugs are used together. If used in sequence, the patient's uterine activity should be carefully monitored.

4.6 Fertility, Pregnancy and lactation

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 is not expected to present a risk of foetal abnormalities when used as indicated.

Lactation:
Oxytocin may be found in small quantities in mothers' 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 use machines

Not Applicable.

4.8 Undesirable effects

- Rarely, oxytocin may cause nausea, vomiting, cardiac arrhythmias (such as QT interval prolongation, see section 4.4 Special warnings and special precautions for use) and postpartum disseminated intravascular coagulation (see section 4.4 Special warnings and special precautions for use).

- Very rarely, water intoxication associated with maternal and neonatal hyponatraemia has been reported in cases where high doses of oxytocin have been administered over a prolonged period of time (see Section 4.4 "Special warnings and precautions for use"). Symptoms of water intoxication include headache, nausea, vomiting and seizures.

  Rapid IV bolus injection of oxytocin may result in acute short-lasting hypotension accompanied with flushing and reflex tachycardia.

  Exceptionally, skin rashes and anaphylactoid reactions or anaphylactic shock have been reported.

Immune system disorders	
Exceptionally	Anaphylactoid reaction or anaphylactic shock.
Nervous system disorders	
Very rarely	Headache, seizures
Cardiac disorders	
Common:	Tachycardia, bradycardia
Rarely	Arrhythmia
Gastrointestinal disorders	
Rarely	Nausea, vomiting
Skin and subcutaneous tissue disorders	
Exceptionally	Rash

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

When oxytocin is used by IV infusion, administration at too high doses results in:

- Foetal distress (decrease of cardiac rhythm, hypoxia and presence of meconium in amniotic fluid);

- Uterine overstimulation which may cause, or may lead to hypertonicity, tetanic contractions, soft tissue damage or rupture of the uterus, and exceptionally placental abruption and/or amniotic fluid embolism.

When signs or symptoms of overdose occur during continuous IV administration of oxytocin, the infusion must be discontinued at once and oxygen should be given to the mother.

In cases of water intoxication it is essential to restrict fluid intake, correct electrolyte imbalance, and control convulsions that may eventually occur, by judicious use of diazepam.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Systemic hormonal preparations excl sex hormones and insulins

ATC code: H01B B02

The active principle of oxytocin is a synthetic nonapeptide identical with oxytocin, a hormone released by the posterior lobe of the pituitary. It exerts a stimulatory effect on the smooth musculature of the uterus, particularly towards the end of pregnancy, during labour, after delivery, and in the puerperium, i.e., at times when the number of specific oxytocin receptors in the myometrium is increased.

When given by low-dose iv infusion, oxytocin elicits rhythmic uterine contractions that are indistinguishable in frequency, force, and duration from those observed during spontaneous labour. At higher infusion dosages, or when given by single injection, the drug is capable of causing sustained uterine contractions.

Being synthetic, oxytocin does not contain vasopressin, but even in its pure form oxytocin possesses some weak intrinsic vasopressin-like antidiuretic activity.

Another pharmacological effect observed with high doses of oxytocin, particularly when administered by rapid iv bolus injection, consists of a transient direct relaxing effect on vascular smooth muscle, resulting in brief hypotension, flushing and reflex tachycardia.

5.2 Pharmacokinetic properties

The plasma half-life of oxytocin is of the order of five minutes, hence the need for continuous iv infusion. Elimination is via the liver, kidney, functional mammary gland and oxytocinase.

5.3 Preclinical 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

Sodium chloride

Sodium acetate tri-hydrate,

Acetic acid, glacial

Water for injections.

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

Three years

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). May be stored below 25°C for 6 months, but then discarded.

6.5 Nature and contents of container

Colourless glass (Type I) 1ml ampoules. Boxes containing 5, 10, 50 and 100 ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Oxytocin is compatible with the following infusion fluids, but due attention should be paid to the advisability of using electrolyte fluids in individual patients: sodium/potassium chloride (103mmol Na^+ and 51mmol K^+), sodium bicarbonate 1.39%, sodium chloride 0.9%, sodium lactate 1.72%, dextrose 5%, laevulose 20%, macrodex 6%, rheomacrodex 10%, Ringer's solution.

7 MARKETING AUTHORISATION HOLDER

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A-4866 Unterach

Austria

8 MARKETING AUTHORISATION NUMBER(S)

PL 40369/0006

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/10/2024

10 DATE OF REVISION OF THE TEXT

23/10/2024