Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Taurolin 2% w/v solution for intraperitoneal lavage after dilution or solution for instillation

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: Taurolidine 2% w/v, 2.0 g/100 ml

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for intraperitoneal lavage after dilution or solution for instillation.
Clear, colourless to very faintly reddish solution with a pH of 7.0 to 7.6.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For use in the local treatment of peritonitis.

4.2 Posology and method of administration

Following standard supportive, surgical and peritoneal toilet procedures, Taurolin may be used as a supplementary peritoneal lavage for either single or repeated instillation depending upon the degree of severity of the presenting condition and the infecting agents.

Adult
Lavage. Up to 1 litre of 0.5% Taurolin pre-warmed to 37°C. Taurolin solution (2% w/v) should be diluted with recommended diluents (see 6.6) to a final concentration of 0.5% w/v.

Single instillation (eg, perforated appendix or local peritonitis). 200 ml Taurolin pre-warmed to 37°C should be instilled at the site of maximum contamination before closure. If a drain is left *in situ* it should be clamped for 2 hours to prevent drainage of Taurolin.

Repeated instillation (eg, generalised (diffuse or faecal) peritonitis). At laparotomy a subumbilical or suprapubic peritoneal dialysis catheter should be inserted through a stab wound in the upper abdomen to lie in relation to the right lobe of the liver. A tube drain down to the site of maximum contamination is brought through a stab wound in the lower abdomen. 300 ml Taurolin, pre-warmed to 37°C is instilled before closure. Thereafter, 100 ml Taurolin pre-warmed to 37°C is instilled daily through the catheter for up to 5 days postoperatively if indicated bacteriologically or clinically. The lower drain should be clamped for 2 hours after each instillation.

Elderly
Taurolin should be used with caution in patients with impaired renal function.

Children

There is limited clinical experience of use in young children, and Taurolin should not be administered to neonates, infants and children under 10 years of age.

Pre-, peri- and post-operative administration of antibiotics is possible.

4.3 Contraindications

Taurolin should not be used if an allergy against the active ingredient or the excipients is known or suspected.

Taurolin® should not be co-administered with oxidising agents such as Dakin's Solution, povidone iodine or hydrogen peroxide.

4.4 Special warnings and precautions for use

Long-term effects of use, particularly of repeated instillation beyond 5 days postoperatively have not yet been established.

During intra-operative application of Taurolin an increase or decrease in blood pressure or variation of the heart rate might be seen, particularly with light anaesthaesia.

Taurolin should not be co-administrated with oxidising agents, such as Dakin's Solution, povidone iodine or hydrogen peroxide. This can cause a metabolic acidosis.

As indicated in Section 4.2, Taurolin should be used with caution in patients with renal impairment.

4.5 Interaction with other medicinal products and other forms of interactions

When co-administered with systemic antibiotics, the product has an additive (or indifferent) antimicrobial interaction with cephalosporins, ureidopenicillins and metronidazole, and synergism with aminoglycosides, in addition to neutralizing their induced bacterial endotoxin release.

4.6 Fertility, pregnancy and lactation

Taurolidine has shown no evidence of teratogenicity in animal studies, but administration to pregnant or lactating women should only be undertaken if the clinician considers it essential.

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Taurolin is generally well-tolerated. Occasional local pain or irritation may occur in conscious, sensitive patient following the initial instillation, and can be abolished for subsequent Taurolin instillations by the pre-installation of 10 ml 0.1 % lignocaine.

Reporting of suspected adverse events
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 HPRA Pharmacovigilance, Earlesfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; Email: medsafety@hpra.ie

4.9 Overdose

There have been no reported cases of overdosage. Taurolin appears to be devoid of pharmacodynamic activity on major body systems, and has produced no adverse or toxic reactions on either local or systemic haematological, biochemical or metabolic parameters following intraperitoneal doses considerably in excess of those recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC-Code: B05CA05

Following administration of Taurolin, the bactericidal and antiendotoxin activity of the taurolidine molecule is by the release of three active methylol (hydroxymethyl) groups as taurolidine is rapidly metabolized by hydrolysis via taurultam and methyloltaurultam to methyloltaurinamide and taurine. These labile methylol groups react with the bacterial cell-wall resulting in lysis, and by inter- and intramolecular cross-linking of the lipopolysaccharide-protein complex, neutralization of the bacterial endotoxins which is enhanced by enzymatic activation. This mechanism of action is accelerated and maximised when Taurolin is pre-warmed to 37°C. Taurolin inhibits the formation of postoperative peritoneal adhesions, and *in vitro* has been shown to reduce the adherence of micro-organisms to mucosal epithelium. The chemical mode of action of tauroline via its reactive methylol groups confers greater potency *in vivo* than indicated by *in vitro* MIC (minimum inhibitory concentration) values, and also appears to preclude susceptibility to resistance mechanisms. Whilst taurolidine is highly active against the common infecting pathogens associated with peritonitis, this activity extends across a wide-spectrum of aerobic/anaerobic bacteria and fungi (with no diminution of effect in the presence of biological fluids, eg blood, serum, pus) including:

Gram positive bacteria (MIC/MBC 1– 2 mg/ml)
Staphylococci (including multiple-antibiotic resistant coagulase negative strains, Methicillin-resistant *Staph. aureus*), *Streptococci*, *Enterococci*, *Pneumococci*.

Gram negative bacteria (MIC/MBC 0.5 – 5 mg/ml)
Aerobacter species, *Citrobacter* species, *Enterobacter* species, *Escherichia coli, Proteus* species (in dole negative), *Proteusmirabilis, Pseudomonas* species (including *Ps. aeruginosa*). *Salmonella* species, *Serratia marcescens*, *Klebsiella* species.

Anaerobes (MIC/MBC 0.03–0.3 mg/ml)
Bacteroides species (including *Bact.fragilis*), *Fusobacteria*, *Clostridium* species, *Peptostreptococcus anaerobius*.

Fungi (MIC 0.3 – 5 mg/ml)
Candida albicans, Cryptococcus neoformans, Aspergillus species, *Trichophyton rubrum, Epidermophyton floccosum, Pityrosporum ovale.*

5.2 Pharmacokinetic properties

Taurolidine is metabolised with a short half-life to taurinamide, carbon dioxide and water. Absorption from the peritoneal cavity is rapid, with maximum concentrations of taurultam occurring between 10 and 15 minutes, and the half-life being less than one hour. Maximum plasma taurinamide concentration occurs between 0.5 and 2 hours, and the elimination half-life lies between 1.5 and 5.5 hours. The rate and extent of peritoneal absorption is not modified in the presence of peritonitis. Urinary estimations show excretion of taurinamide accounts for 25% of the Taurolin dose.

5.3 Preclinical safety data

Since taurolidine is well-established for its proposed use, additional preclinical safety data are not provided.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone
Sodium Hydroxide (pH adjuster)
Water for injections

6.2 Incompatibilities

Taurolin should not be co-administered with oxidising agents such as Dakin's Solution, povidone iodine or hydrogen peroxide. This can cause metabolic acidosis.

6.3 Shelf life

Three years if bottle unopened. Product should be used immediately after first opening/dilution

6.4 Special precautions for storage

Store at room temperature (15-25ºC).Do not refrigerate or freeze.

6.5 Nature and contents of container

Clear, Type II Ph.Eur. glass bottles (100ml and 250ml) with rubber closures and aluminium snap caps.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Preparation of dilute lavage solution. Taurolin 2% w/v should be diluted 1:3 with one of the following recommended diluents: Water for Injections BP; Sodium Chloride Intravenous Infusion BP, or Compound Sodium Chloride Injection BPC (Ringer's solution) to a concentration of 0.5% w/v. No other diluents should be used. Product is for single use only. Any remaining solution should be discarded. Product should be pre-warmed to 37ºC and inspected for visible particles before use.

7 MARKETING AUTHORISATION HOLDER

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Ballycoolin
Dublin
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8 MARKETING AUTHORISATION NUMBER

PA22637/005/001.

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10 DATE OF REVISION OF THE TEXT

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