SHALMET
(Metronidazole Injection USP 0.5 % w/v)

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SHALMET (Metronidazole Injection USP 0.5% w/v)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Name of ingredients	Quantity per 100 ml in mg	Function (reason for inclusion)
Metronidazole USP	500.0	Active Ingredient
Sodium Chloride USP	800.0	Alkalinizing Agent
Hydrochloric Acid USP	If required	pH adjustment
L.D.P.E Granules IH	27.14 gm	Stabilizers
Water for Injection USP	q.s. to 100 ml	Solvent

Definitions: United States Pharmacopoeia

3. PHARMACEUTICAL FORM

Solution for infusion.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

1. Treatment of infections caused by Bacteriodes fragilis and other species of bacteroides like Fusobacteria, Eubacteria and Anaerobic cocci such as: a Intra-abdominal infections- appendicitis, cholecystitis, peritonitis, liver abscess and post-operative wound infection. b. Gynacological and obstetrical infection-puerperal sepsis, pelvis cellulitis, pelvic peritonitis. c. Respiratory infections-nacrotising pneumonia, empyema, lung abscess. d. Central nervous system infections meningitis, brain abscess.e. Miscellaneous infection-septicemia, gas gangrene, osteomyelitis.

2. Prevention of post operative infections due to anaerobic bacteria.

3. Treatment of amoebic abscess of the liver and in moribund or toxic cases of fulminating intestinal amebiasis.

In a mixed aerobic and anaerobic infection, antibiotics appropriate for the treatment of the aerobic infection should be used in addition to SHALMET injection.

4.2 Posology and method of administration

Adult and Children over 12 years of age: 500 mg (100 ml) infused over a period of 20 minutes at a rate of 5 ml minutes repeated 8 hourly. Children below 12 years of age: Depending upon clinical and bacteriological assessment, the physician may decide the duration of treatment .Depending on the weight of the child the volume of fluid to be infused should be determined on the basis of 7.5 mg/kg. The rate of infusion as well as the frequency remains the same as in adults. 20 mins at the rate of 5 ml/min repeated 8 hourly. Oral medication should be substituted as soon as this becomes feasible (200-400 mg three daily).

Direction for Use: 1.The overwrap is a moisture barrier. The inner container maintains the sterility of the product.2. After removing overwrap check for minute leaks by squeezing the container .Do no use if leaks are found and return for replacement.3 Bring the injection bottle to room temperature or preferably

to 37^0C just before use.4. Clean the spout of injection bottle with surgical spirit.5.Keep the bottle on a table or on a hard surface and insert the cannula of the sterile infusion set into the spout of injection bottle (Please note that the cannula of the infusion set should be inserted fully and not half way into the spout of the SHALMET IV bottle to avoid leakage.6 For administration hold the bottle upside down. 7. Inject intravenously slowly at a rate of about 5 ml/minute. 8. To admit air, insert a sterile injection cannula on the top of the inverted bottle anywhere above the level of the liquid.

Caution: Even invisible damage to bottle caused during storage or transit may result in contamination. Do not use it leak found on squeezing, or contents not clear.

Caution: Admixture al 10.0% Dextrose. Penicillin G. Potassium and Ringer Lactate Solution of SHALMET I.V, Infusion is contraindicated because of chemical incompatibility.

Route of Administration: Intravenous

4.3 Contraindications

SHALMET is contraindicated in patients with a prior history of hypersensitivity to metronidazole or other nitroimidazole derivatives. Metronidazole is also contraindicated in patients with trichomoniasis is during the first trimester of pregnancy.

4.4 Special warnings and precautions for use

WARNINGS: Central and Peripheral Nervous System Effects. Convulsive seizures, encephalopathy, aseptic meningitis, optic and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity, have been reported in patients treated with metronidazole. The appearance of abnormal neurologic signs demands the prompt discontinuation of metronidazole therapy. Metronidazole should be administered with caution to patients with central nervous system diseases,

PRECAUTIONS: General: Patients with severe hepatic disease metabolize metro idazole slowly, with resultant accumulation of metronidazole and its metabolites in the plasma, accordingly for such patients, doses below those usually recent' ended should be administered cautiously. Known or previously unrecognized candidiasis may present more prominent symptoms during therapy with rnetronidezole and requires treatment with a candidacidal agent.

Geriatric use: Decreased renal function does not alter the single-dose pharmacokinetics of metronidazole. However, plasma clearance of metronidazole is decreased in patients with decreased liver function. Therefore, in elderly Patients monitoring of serum levels may be necessary to adjust the rnetronidezole dosage accordingly.

Pediatric use: Safety and effectiveness in pediatric patients have not been established, except in the treatment of amebiasis.

4.5 Interaction with other medicinal products and other forms of interaction

1. Clinically significant interaction between metronidazole and Warfarin has been reported. Metronidazole has been found to increase prothrombin time. It is preferable to discontinue oral anticoagulants 24 hours prior to administration of SHALMET Injection. 2. Simultaneous administration of Metronidazole and disulfiram has been reported to cause acute psychosis and confusional state 3. It is advisable to avoid mixing IV infusions of different drugs in keeping with this rule, SHALMET Injection should not be mixed with any other drug.

4.6 Pregnancy and lactation

Since SHALMET crosses the placental barrier and enters the fetal circulation rapidly, it should not be administered to pregnant patents during the first trimester. In second and third trimester of pregnancy the drug should he used only if clearly needed.

Use in nursing mothers: Since SHALMET is secreted in human milk in concentrations similar to those found in plasma, and since tumors were increased in rats and mice treated with the drug, a decision should be made whether to discontinue nursing or to continue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Not Applicable.

4.8 Undesirable effects

Side effects have seldom been reported in patients treated with intravenous metronidazole. Further studies are needed to determine the frequency and nature of adverse effects likely to be encountered with higher dosage and greater duration of metronidazole treatment. Sometimes necessary for the treatment of severe anaerobic infections. Adverse effects which occur commonly with dosages of metronidazole used to treat trichomoniasis and a amebiasis have included anorexia, nausea, abdominal pain, vomiting. Vertigo, tiredness and dark coloration of the urine. Less commonly reported side effects have included ataxia, headache, transient and reversible neutropenia, metallic taste, vaginal and urethral burning, gastric irritation, diarrhoea, furred tongue. Peripheral neuropathy has also occurred in a patient treated with I.V. metronidazole for anaerobic infection, Transient epileptiform seizures have been reported in a few patients undergoing intensive high d dosage metronidazole treatment for radio sensitization.

4.9 Overdose

Symptoms reported include nausea, vomiting, and ataxia, Oral metronidazole has been studied as a radiation sensitizer in the treatment of malignant tumors. Neurotoxic effects, including seizures and peripheral neuropathy, have been reported after; 5 to 7 days of doses 6 to 10.4 g every other day. There is no specific antidote for metronidazole overdose; therefore, management of the patient should consist of symptomatic and supportive therapy.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: SHALMET is a synthetic antiprotozoal and antibacterial agent.
ATC Code: J01X D01

5.1 Pharmacodynamic properties

SHALMET is active against a wide range of pathogenic organisms, such as: Bacteroides, Fusobacteria, Eubacteria, Anaerobic cocci and Trichomonas vaginalis. Its mechanism of action is thought to involve interference with DNA by a metabolite in which the nitro group of metronidazole has been reduced. SHALMET exerts an antimicrobial effect in an anaerobic environment by the following possibly mechanism: once it enters into the organism, the drug is reduced by intracellular electron transport proteins. Because of this alteration to the Metronidazole molecule, a concentration gradient is maintained which promotes the drug intracellular transport. Presumably, free radicals are formed which in turn react with cellular components resulting in death of the microorganism.

5.2 Pharmacokinetic properties

Following an intravenous infusion (over 20 minutes) of 500 mg Metronidazole, in patients with anaerobic infections serum concentrations achieved were 35.2mcg/ml at 1 hr. 339 mcg/ml at 4 hours and 25.7mcg/ml at 8 hrs, The half-life followings single intravenous dose is 6 - 7 hours. Metronidazole is only slightly bound to plasma proteins, it readily penetrates tissues and has a large apparent volume of distribution over 70 -95 of body weight. It attains bactericidal concentrations in most tissues and body

fluids including brain, CSF, abscess cavities, saliva, bile, vaginal secretions, amniotic fluid and breast milk.

Metabolism: Metronidazole is eliminated in man largely by metabolism resulting from side chain oxidation, hydroxylation or conjugation of the parent compound. The major metabolic product is 1-(2-hydroxyethy) 2- hydroymethyl-5-nitroimidazole which along with its glucuronide accounts for 40% to 50% of recovered urinary material, The acid and alcohol metabolites of metronidazole are 50% and 30% as active respectively as metronidazole,

Excretion: Over a period of 24 hours urine y recovery of total nitro derivatives accounts for 35 to 65% Renal clearance is 10.2m1 per min,/ 1.75 sq.m. After intravenous administration of a low dose, 63% of the total radio activity is excreted in the urine and 6.2% he the faeces, over a 3-day period. In patients with a normal biliary tract, the concentration of Metronidazole in gall bladder bile after an intravenous dose of 500mg is significantly higher than in serum.

Influence of Disease on Kinetics: Accumulation of metronidazole has been demonstrated in serum after continual doses in patient with impaired renal function. Therefore, dosage frequency can be reduced in patients with severe renal insufficiency.

5.3 Preclinical safety data

None.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride, Hydrochloric acid, Water for injections.

6.2 Incompatibilities

Not None

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 30°C. Protect from sunlight. Keep out of reach of children

6.5 Nature and contents of container

SHALMET Injection is available in a 100 ml container (FFS Polyethylene) packed in BOPP bag, then packed in a monocarton with package insert.

6.6 Special precautions for disposal and other handling

Use within 7 days after removing infusion bag from the carton. Keep the infusion bag in the overwrap until time of use.

7. MARKETING AUTHORISATION HOLDER

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30th Floor, Almas Towers,
Jumeirah Lakes Towers Dubai-UAE.
Telephone: +971 4 4309111
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8. MANUFACTURER

SHALINA LABORATORIES PVT. LTD.
Manufacturing Site Address:
FRESENIUS KABI INDIA PVT. LTD.
Plot No. A/3, MIDC, Ranjangaon Ganpati, Taluka: Shirur, District: Pune, Maharashtra, India

9. DATE OF REVISION OF TEXT

Every two years.

10. LEGAL CATERGORY

POM (Prescription Only Medicines)