UNILAB

METRONIDAZOLE+MICONAZOLE NITRATE+LIDOCAINE

Trimic® Forte L
750 mg/ 200 mg/ 100 mg Vaginal Suppository
ANTI-PROTOZOAL / ANTI-FUNGAL / LOCAL ANESTHETIC

℞

FORMULATION
Each vaginal suppository contains:

Metronidazole BP	750 mg
Miconazole Nitrate BP	200 mg
Lidocaine BP	100 mg
Excipients	q.s.

PHARMACODYNAMIC PROPERTIES
TRIMIC® FORTE L contains miconazole nitrate for antifungal, metronidazole for antibacterial and antitrichomonal effects and lidocaine for local anaesthetic effect.

Miconazole nitrate which is a synthetic imidazole antifungal agent has a wide spectrum of activity and is particularly effective against pathogen fungi including Candida albicans and is effective against Gram positive bacteria. Metronidazole, a 5-nitroimidazole derivative is an antiprotozoal and an antibacterial agent and is effective against several infections caused by anaerobic bacteria and protozoa, such as Trichomonas vaginalis, Gardnerella vaginalis and anaerobic bacteria including anaerobic streptococci. Lidocaine stabilizes the neuronal membrane by inhibiting the conduction of impulses, thereby producing local anesthetic action.

PHARMACOKINETIC PROPERTIES
Absorption: Miconazole nitrate absorption by the intravaginal route is very low (approximately 1.4% of dose). Bioavailability of metronidazole by the intravaginal route is approximately 20% compared to oral administration. Lidocaine is absorbed from injured skin and mucous membranes in very low amounts.

Distribution: Miconazole nitrate has a problem binding ratio about 90-93%. It shows weak distribution to cerebrospinal fluid while it distributes widely to other tissues. Volume of distribution is 1,400 L. Metronidazole distributes to body tissues and fluids like gall bladder, bone, breast, milk, cerebral abscess, saliva, seminal and vaginal fluids widely and in nearly same concentrations as plasma. Plasma protein binding ratio is not more than 20%. Distribution volume is 0.25-0.85 L/kg. Lidocaine applied through oral or intravenous route is determined in bowels, urine and in low amounts in faeces. It is found in the urine as unchanged drug and its metabolites. Lidocaine binds with plasma proteins (primarily to α 1-acidglycoprotein, less to albumin) in a ratio 33%-80%. Distribution volume is 0.8-1.3 L/kg.

Biotransformation: Miconazole nitrate is metabolized in liver. Has two metabolites that are inactive. (2, 4-dichlorophenyl-1 H imidazole ethanol and 2, 4-dichloromandelic acid). Metronidazole is metabolized in the liver by oxidation. Its hydroxy metabolite is active. Major metabolites of metronidazole, hydroxy and acetic acid metabolites, are excreted in urine. The hydroxy metabolite has a 30% of biologic activity of metronidazole. Lidocaine is metabolized in the liver. Has active metabolites monoethylglycinexylidide (MEGX) and glycinexylidide (GX).

Elimination: Miconazole nitrate has half-life of 24 hours. Less than 1% of it is excreted by kidneys. 50% of it is excreted unchanged with faeces. By systemic or topical application 6-15% of metronidazole dose is excreted by faecal route, 60-80% unchanged and as metabolites in the urine. The ratio of the drug excreted unchanged in the urine is 20%. Lidocaine is excreted in urine as metabolites and unchanged form (10% of the applied dose).

INDICATIONS
TRIMIC® FORTE L vaginal suppositories are used in the treatment of candidal vulvovaginitis due to Candida albicans, in bacterial vaginitis due to anaerobic bacteria and Gardnerella vaginalis, in trichomonal vaginitis due to Trichomonas vaginalis and in mixed vaginal infections.

DOSAGE AND ADMINISTRATION
Usual dose: Insert one vaginal suppository into the vagina for 7 nights.

In recurrent cases, or when the vaginitis has been resistant to other treatments use one vaginal suppository for 14 nights.

CONTRAINDICATIONS
TRIMIC® FORTE L is contraindicated in patients hypersensitive to miconazole, metronidazole or lidocaine or their derivatives, during the first trimester of pregnancy, in cases of porphyria, epilepsy and severe liver function disorders.

WARNINGS AND PRECAUTIONS
TRIMIC® FORTE L vaginal suppositories should not be used in young people (girls) who are not sexually mature. Sexual partners of patients with Trichomonas vaginalis should be treated at the same time. Patients should be warned not to take alcohol during the therapy and for 3 days after the end of a course of treatment, because of the possibility of disulfram-like reactions.

Pregnancy and Lactation
The active ingredients can have a compromised action on fetus and newborn growth, hence people who need to administer the drug should avoid pregnancy with a proper birth control method.

There is no sufficient data on the use of miconazole, metronidazole and lidocaine in pregnant women during the first trimester. Therefore it should not be used in the first trimester of pregnancy. If the product is used during pregnancy it should be under medical supervision only if benefits outweigh the risk. Breastfeeding should be discontinued during therapy, since metronidazole appears in milk. Breastfeeding can be started again 24-48 hours after the end of treatment.

INTERACTIONS
Caution should be taken while administering TRIMIC® FORTE L vaginal suppository concomitantly with alcohol and other drugs such as amiodarone, astemizole, terfenadine, disulfiram, phenytoin, phenobarbital, fluorouracil, carbamazepine, lithium, oral anticoagulants, cyclosporine, cimetidine, acenocoumarol, anisindione, dicoumarol, phenindione, phenprocoumon, warfarin, cisapride, fosphenytoin, fentanyl, glimepiride, oxybutynin, oxycodone, pimozide, tolterodine, trimetrexate and propranolol.

ADVERSE EFFECTS
The incidence of systemic side effects is very rare since after intravaginal administration of Metronidazole is very low. Miconazole nitrate can cause vaginal irritation (burning, itching). These symptoms may be prevented with the local anesthetic action of lidocaine.

In vaginitis, since the vaginal mucosa may be inflamed, vaginal burning, itching and vaginal irritation symptoms may occur when the first vaginal suppository is administered or towards the third day of the therapy. These symptoms decrease very fast and disappear when the therapy is continued. If there is severe irritation, then consult physician or discontinue the treatment.

In case of systemic absorption which is very rare in nature, of active ingredients adverse reactions such as leukopenia, methemoglobinemia, hypersensitivity reactions, allergic reactions, depression, mental changes, vertigo, headache, fatigue, weakness, malaise, tingling, loss of sensation, paraesthesia, peripheral neuropathy, numbness, disorientation, agitation, psychosis, seizure, speech impairment, hyperesthesia, lethargy, hallucination, sensation of heat, ataxia, convulsion, nervousness, uneasiness, euphory, confusion, ringing in the ears, somnolence, fuzzy or double vision, cold, tremor, loss of consciousness, coma (rare), anxiety, insomnia, arrhythmia, bradycardia, arteriospasm, decrease in blood pressure, cardiovascular collapse, increase in defibrillator threshold, edema, flushing, heart block, hypotension, sinus node suppression, taste changes, metallic taste in mouth, vomiting, nausea, constipation, dry mouth, diarrhea, lack of appetite, abdominal pain or cramp, vaginal discharge, vaginitis, vulvovaginal irritation, pelvic inconvenience, thirst, vaginal burning, itching and irritation, abdominal pain, skin rash, local irritation, abdominal pain, skin rash, local irritation, sensitivity, contact dermatitis may be observed.

OVERDOSE
In case of large quantities of the vaginal suppository are used, systemic effects due to metronidazole may occur; however, no life-critical indications are expected due to metronidazole applied through vaginal route.

Symptomatic and supporting treatment is applied on overdose. There is no specific antidote to metronidazole. Symptoms due to metronidazole overdose are nausea, vomiting, abdominal pain, diarrhea, itching, metallic taste, ataxia, vertigo, paresthesia, convulsion, leukopenia, darkening of urine; symptoms due to miconazole nitrate overdosage are sore throat and mouth, anorexia, nausea, vomiting, headache, diarrhea. Lidocaine may cause cardiac rhythm disorders, shortness of breath, coma and even death, especially if applied to extensive skin surfaces and especially in very high doses.

STORAGE
Store in a dry place, below 30ºC.
Protect from light.
Keep out of the reach and sight of children.

ADVERSE DRUG REACTION REPORTING STATEMENT
*For suspected adverse drug reactions, seek medical attention immediately and report to the FDA at www.fda.gov.ph AND Unilab at +632-8-**UNILAB**-1 (+632-8-**864522**-1) for Metro Manila or toll-free +1-800-10-UNILAB-1 for provinces, or e-mail productsafety@unilab.com.ph.*

By reporting undesirable effects, you can help provide more information on the safety of this medicine.

CAUTION
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY
TRIMIC® FORTE L 750mg/ 200mg/ 100 mg Vaginal Suppository, in PVC Coated Polyethylene Foil x 7's (Box of 7's)

Manufactured by: **Bliss GVS Pharma Ltd.**
Plot No. 11, Dewan Udyog Nagar, Aliyali,
Palghar 401404 Maharashtra State, India

Imported and Distributed by: **UNILAB, Inc.**
No. 66 United Street, Mandaluyong City,Metro Manila, Philippines

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HOW TO USE VAGINAL SUPPOSITORY

1. Wash your hands.
2. Do not open vaginal suppository if it seems soft, hold the foil wrapper under cold water or place it in refrigerator for few minutes to harden it before removing the wrapper.
3. Remove one vaginal suppository from the strip and hold it in fingertips.
4. Remove any foil or plastic wrapping stuck to the pessary.
5. Sit or lie down with your knees bent and legs apart.
6. Gently insert the suppository into the vagina as far as comfortably possible using your fingers.
7. Wash your hands again.