METRONIDAZOLE + MICONAZOLE NITRATE

NEO-PENOTRAN®
Vaginal Suppository

FORMULATION
Each vaginal suppository contains Metronidazole 500mg and Miconazole nitrate 100mg

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMICS
Metronidazole + Miconazole nitrate (Neo-Penotran® Vaginal Suppository) contains miconazole for antifungal and metronidazole for antibacterial and antitrichomonal effects. Miconazole nitrate which is an antifungal has a wide spectrum of activity and is particularly effective against pathogen fungi including Candida albicans. In addition, miconazole nitrate is effective against Gram (+) bacteria. Metronidazole is an antibacterial and antiprotozoal agent that is effective against Gardnerella vaginalis and against anaerobic bacterial including anaerobic streptococci and Trichomonas vaginalis.

PHARMACOKINETICS
Absorption of miconazole nitrate through the intravaginal route is very low (approximately 1.4% of dose). Bioavailability of metronidazole by this route is 20% compared to the oral route. Miconazole nitrate cannot be detected in plasma after vaginal application of Neo-Penotran®. Steady state level of metronidazole in plasma reaches 1.6 – 7.2 µg/mL. Metronidazole is metabolized in the liver. The hydroxyl-metabolite is effective. The half-life of metronidazole is 6-11 hours. Approximately 20% of the dose is excreted unchanged in urine.

INDICATIONS
Metronidazole + Miconazole nitrate (Neo-Penotran®) vaginal suppository is used for local treatment of vaginalis infection with the involvement of certain fungi (eg Candida albicans), some bacteria and other pathogenic organisms (Trichomonas vaginalis). Your doctor needs to decide whether Metronidazole + Miconazole nitrate (Neo-Penotran®) is suitable for the treatment of your condition.

CONTRAINdications
You should not use Metronidazole + Miconazole nitrate (Neo-Penotran®) if:
- You suffer from hypersensitivity to any of the ingredients of the suppository
- You are pregnant (particularly in the first 3 months)

Your doctor needs to carefully evaluate whether you may use Metronidazole + Miconazole nitrate (Neo-Penotran®) if you suffer from:
- Severe problems with your liver (liver function disorders including metabolic disease called “porphyria”)
- Diseases of the nervous system
- Disturbances in the production of blood (hematopoiesis)

WARNINGS / PRECAUTIONS
You must not take alcohol during the therapy and for at least 24-48 hours after the end of course of treatment because of the possibility of increased alcohol incompatibility. You must not
use the suppository together with the contraceptive diaphragms and condoms since the ovule base may affect the rubber, which may possibly break.

**Pregnancy and Lactation**
After the first three months of pregnancy, Metronidazole + Miconazole nitrate (Neo-Penotran®) suppository can be used when considered essential by your doctor, but must be used under observation. You must not breastfeed your baby while using Metronidazole + Miconazole nitrate (Neo-Penotran®), since active ingredients pass into the milk. You may start breast feeding again after 24-48 hours after the treatment is finished.

**SIDE EFFECTS / ADVERSE REACTIONS**
There were no deaths or serious adverse events in clinical trials. Medical events judged to be common, uncommon and rare are listed below. Unless the percentages are otherwise stipulated, the occurrence of individual adverse reactions was less than 1%.

**Vaginal disorders**
Vaginal irritation (burning, itching) 2-6%. Owing to inflammation of vaginal mucosa in vaginitis, vaginal irritation can be seen after the administration of the first ovule or towards the third day of treatment. These complaints disappear quickly when the treatment continues. If there is severe irritation, contact your doctor because it may be necessary to stop the treatment.

**Stomach and intestinal disorders**
Abdominal or cramp (3%), Metallic taste (1.7%), constipation, dry mouth, seldom diarrhea, lack of appetite, vomiting and nausea.

**Nervous system disorders**
Headache, movement disorders (ataxia), dizziness, mental changes, disorders of the nerves (peripheral neuropathy) after overdose or long period of usage, cramps.

**Skin disorders**
Rash

**Blood disorders**
Decrease of white blood cells

**INFORM YOUR PHYSICIAN WHENEVER AN UNEXPECTED EFFECT IS OBSERVED.**

**DRUG INTERACTIONS**
Due to absorption of active ingredients of Metronidazole + Miconazole nitrate (Neo-Penotran®), interactions may occur if you used the preparation with alcohol (Metronidazole + Miconazole nitrate (Neo-Penotran®) may lead to an increased alcohol incompatibility) or with any of the following drugs (inform your doctor if you take them):
- Drugs that make your blood thinner (oral anti-coagulants)
- Anti-epileptics (phenytoin, phenobarbital)
- A drug reducing the acid in your stomach (cimetidine)
- A drug for the treatment of alcoholism (disulfiram)
- A drug against psychosis and depression (lithium)
- Anti-allergic medicines (astemizole and tertenadine)

Laboratory tests may change while you use Metronidazole + Miconazole (Neo-Penotran®): interference with blood levels of liver enzymes, glucose (hexokinase method), theophylline, and
procainamide have been observed. If blood tests are made, remind your doctor that you use Neo-Penotran®.

**DOSAGE AND ADMINISTRATION**

Do not use without consulting a physician. Unless your doctor advises otherwise, insert 1 vaginal ovule at night and 1 vaginal ovule in the morning for 7 days. In recurrent cases, or when vaginitis has resisted other treatments. 1 vaginal ovule should be inserted high into the vagina at night and in the morning for 14 days. The ovule should be inserted high into the vagina with the help of the disposable fingerstalls enclosed in the package.

Elderly (over 65 years): Dosage as for younger adults
Children: Not recommended for children.
Not recommended for virgins.
Not to be swallowed or applied by other routes.

**OVERDOSAGE AND TREATMENT**

There is no human experience with overdose of Metronidazole + Miconazole nitrate (Neo-Penotran®) suppository. Metronidazole could be absorbed in sufficient amounts to produce effects in your body. If large quantities of the product are accidentally taken, an appropriate method of emptying your stomach may be considered necessary. Symptoms of Metronidazole overdose are nausea, vomiting, abdominal pain, diarrhea, itching, metallic taste, movement disorders (ataxia), vertigo, unusual sensations on the skin (paresthesia), cramps, decrease of white blood cells, and darkening of urine. Symptoms of Miconazole nitrate overdose are nausea, vomiting, sore throat and mouth, decrease appetite, headache and diarrhea.

**CAUTION**

Food, Drugs, Devices and Cosmetic Act prohibits dispensing without prescription.

**STORAGE CONDITIONS**

Store below 25°C, do not freeze.
Keep out of the reach of children and keep the product in its original package.
Do not use after the expiration date indicated on the package.

**AVAILABILITY**

A package contains 14 vaginal suppositories with 14 disposable fingerstalls.

Registration No.: DR-XY32313

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