FORMULATION:
Each vaginal suppository contains 100mg Tioconazole and 150mg Tinidazole.

PHARMACOLOGICAL PROPERTIES:

Pharmacodynamics:
Tioconazole is a synthetic antifungal agent with a high in-vitro efficacy to yeast and fungi (including dermatophytes). Also, it is effective against Trichomonas vaginalis, Gardnerella vaginalis, Bacteroides spp., and some Gram (+) bacteria (including Staphylococcus and Streptococcus spp.). In clinical studies, tioconazole is found to be effective in the treatment of Candida albicans and other Candida species (Torulopsis glabrate) and to vaginal infections caused by Trichomonas vaginalis.

Tioconazole shows its effect by altering permeability of the fungal cell membrane. Ergosterol is an essential component of the fungal cell membrane. Tioconazole inhibits the ergosterol synthesis by interacting with 14 α-demethylase, a P-450 cytochrome enzyme that converts lanosterol to ergosterol. Inhibition of ergosterol synthesis leads to increase of cellular permeability and therefore to leakage of intracellular phosphorus compounds and potassium across the cell membrane.

Tinidazole is effective against protozoans and anaerobic bacteria. Its antiprotozoal activity includes Trichomonas vaginalis, Entamoeba histolytica and Giardia lamblia. Tinidazole is effective against Gardnerella vaginalis and the majority of anaerobic bacteria (Bacteroides fragilis, Bacteroides melaninogenicus, Bacteroides spp., Clostridium spp., Eubacterium spp., Peptostreptococcus spp., and Veillonella spp.).

The complete mechanism of action of tinidazole has not been fully clarified. The reduction of the nitro group is mediated by a ferrodoxin system and a low oxidation reduction potential which is only generated by anaerobic bacteria. This may be the reason for anaerobes having a higher tinidazole uptake than aerobes, although tinidazole can penetrate cell membranes of both types of microorganisms. The reduction process creates reactive intermediates and a diffusion gradient, which enhances tinidazole uptake. Although cross-resistance is common for 5-nitroimidazoles, 65% to 70% of Trichomonas vaginalis strains highly resistant to Metronidazole have shown increased susceptibility to tinidazole.

Pharmacokinetics:
Individually applied, tioconazole and tinidazole are absorbed in low levels from the vaginal mucous. Therefore, when applied in combination systemic absorption is expected to be in low levels.

INDICATIONS:
Tioconazole + Tinidazole (Gynomax®) vaginal suppository is indicated in the treatment of vaginitis caused by Candida, Trichomonas, and Gardnerella and vaginitis due to mixed infections.

CONTRAINDICATIONS:
Tioconazole + Tinidazole (Gynomax®) vaginal suppository is contraindicated in patients who have shown hypersensitivity to the active ingredients or their derivatives, during the first trimester of
pregnancy, lactation, and in patients with current picture or history of organic neurologic disorders and blood dyscrasia.

**SPECIAL WARNINGS AND PRECAUTIONS FOR USE:**
The pregnancy category of Tioconazole and Tinidazole is C.

Tinidazole crosses the placental barrier and appears in the breast milk of mice. Since the effects of components in this composition on fetal development and new born are not known, Tioconazole + Tinidazole (Gynomax®) vaginal suppository should not be used in the first trimester of pregnancy and during breastfeeding.

Usage of tioconazole / tinidazole combination during the last months of pregnancy must be evaluated according to the potential benefits / possible risks ratio to the mother and the baby.

As other drugs of similar structure, tinidazole must not be used in patients with current picture or history of blood dyscrasia. In the animal and clinical studies, no persistent hematologic abnormalities were observed.

The vaginal suppositories must not be used with contraceptive diaphragms and condoms since the suppository base may react with the rubber. Patients should be warned not to take alcohol during the therapy and for at least 2 days after the end of the course of treatment.

**SIDE EFFECTS / ADVERSE EVENTS:**
Tioconazole + Tinidazole (Gynomax®) vaginal suppository is well tolerated in the application site. Allergic reactions and local burning sensations are most common adverse effects. Urinary burning, edema and signs of local irritation can be seen rarely.

Although it is not reported in the vaginal application of tioconazole / tinidazole combination, some gastrointestinal and neurologic adverse events with transient leucopenia related to the systemic usage of tinidazole are reported.

Other rarely observed adverse events are hypersensitivity reactions like chronic headache, fatigue, darkening of urine, cutaneous eruption, itching, urticaria and angioneurotic edema.

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

**DRUG INTERACTIONS:**
Due to systemic management of tinidazole with alcohol, colic, redness and vomiting can occur. Although systemic absorption rate after vaginal application is low, this possibility must be taken into consideration.

**POSOLOGY AND METHOD OF ADMINISTRATION:**
Do not use without consulting a physician. If it is advised otherwise by a physician, 1 suppository should be inserted high into the vagina at night for 7 days. Alternatively, it is advised to use suppository in the morning and 1 suppository at night for 3 days. Suppositories should be inserted high into the vagina by the help of disposable fingerstalls included in the package.

Elderly (over 65 years): As for younger adults
Children: Not recommended for children
Not recommended for virgins
Not to be swallowed nor applied by other routes.
OVERDOSAGE AND TREATMENT:
If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used. There exist no specific antidote; symptomatic treatment is applied.

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

STORAGE CONDITIONS:
Store at temperatures not exceeding 25°C. Do not store in refrigerator.

Keep out of reach of children and keep in its original package.

AVAILABILITY:
A package contains 7 vaginal suppositories with 7 disposable fingerstalls.

Registration No.: DR-XY37056

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