NAME OF THE MEDICINALPRODUCT

1. Mycoten® -Plus Vaginal Tablets(Clotrimazole 200mg + Clindamycin 100mg)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200mg of clotrimazole and 100mg of clindamycin

For a full list of excipients, see section 6.1.

2. PHARMACEUTICAL FORM

Tablet

3. Clinical particulars

3.1 Therapeutic indications

Mycoten® -Plus Vaginal Tablets is indicated for treatment of infective leucorrhea (thick, whitish, vaginal discharge) mixed infection and non-specific vaginitis, vaginal candidiasis, bacterial vaginosis and trichomoniasis.

4.2 Posology and method of administration

Posology

Intravaginally – The capsule has to be introduced deeply into the vagina in lying position.
Treatment should not coincide with the period of menstruation.
Treatment of Bacterial Vaginosis and other gynecological infection: 1 Capsule a day for 7 days At bedtime.
Prophylaxis before gynecological procedures: 1 capsule a day for 3 days before the planned gynecological procedures and 4 days after the procedures.

4.3 Contraindications

Hypersensitivity to the components of the preparation.

Clindamycin Phosphate

Clindamycin is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin, a history of regional enteritis or ulcerative colitis, or a history of antibiotic-associated colitis.

Clotrimazole

Hypersensitivity to imidazole. First trimester of pregnancy Caution when used during pregnancy & lactation

4.4 Special warnings and precautions for use

It is not recommended to use Clindamycin and Clotrimazole Capsule during menstruation. If in process of use of Clindamycin and Clotrimazole Capsule the apparent or long term diarrhoea occurs, the treatment should be stopped, the appropriate diagnostical procedures are to be taken, and the treatment should be prescribed, if necessary. During treatment with vaginal capsule vaginal intercourse and use of other products with intravaginal route of introduction are not recommended

4.5 Interaction with other medicinal products and other forms of interaction

The antagonist effect is possible between Clindamycin and erythromycin; clotrimazole, if introduced intravaginally, depresses the activity of amphotericin B and other polyene antibacterial agents. If used at the same time with nystatin the effect of clotrimazole may be suppressed. Clindamycin Phosphate and Clotrimazole Capsule contain the components which may deteriorate reliability of the latex and rubber products, such as are the condoms or contraceptive vaginal diaphragms. That's why it is not recommended to use these products in process of treatment.

4.6 Pregnancy and Lactation

There are no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used only if clearly indicated during the first trimester of pregnancy. It is not known whether this drug passes into breast milk. Consult your doctor before breastfeeding.

Effects on ability to drive and use machines

None reported.

Undesirable effects

Clindamycin phosphate

Genital itching or burning; irritation not present before use of Clindamycin Suppositories; vaginal pain. Seek medical attention right away if any of these SEVERE side effects occur:

Severe allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue); blood/mucus in stools; diarrhea; new or worsening vaginal or vulvar itching; painful sex; severe stomach cramps; white vaginal discharge.

Clotrimazole

Pruritus; erythema, stinging, blistering, peeling, edema, urticaria, burning, general skin irritation, rash.

4.9 Overdose

Symptoms of overdose may include: severe headache, tiredness, dizziness, mental/mood changes (such as irritability, depression), vision changes (such as double vision, blurred vision), dry/peeling skin, bone/joint pain, loss of appetite, yellowing skin/eyes, dark urine, severe stomach/abdominal pain.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Clindamycin Phosphate
Clindamycin works primarily by binding to the 50s ribosomal subunit of bacteria. This agent disrupts protein synthesis by interfering with the transpeptidation reaction, which thereby inhibits early chain elongation. Clindamycin and the related drug lincomycin are often discussed along with the macrolides, but are not chemically related. Clindamycin may potentiate the opsonization and phagocytosis of bacteria even at subinhibitory concentrations. By disrupting bacterial protein synthesis, clindamycin causes changes in the cell wall surface which decreases adherence of bacteria to host cells and increases intracellular killing of organisms.

Clotrimazole
Clotrimazole is an antifungal medication commonly used in the treatment of fungal infections of both humans and animals such as vaginal yeast infections, oral thrush, and ringworm. It is also used to treat athlete's foot and jock itch. Clotrimazole is a broad-spectrum antifungal which binds to phospholipids in the cell membrane altering cell wall permeability causing a loss in essential intracellular elements.

5.2 Pharmacokinetic properties
Clindamycin Phosphate

Absorption: ~10% of topically applied drug is absorbed systemically.
No significant levels are seen in CSF, even with inflamed meninges; crosses the placenta; distributes into breast milk; high concentrations in bone and urine.
Metabolism: Hepatic
Elimination: Most of drug eliminated by hepatic metabolism

Clotrimazole

Absorption
Negligible through intact skin (topical); 3-10% (vaginal).
Metabolism
Hepatic; converted to inactive metabolites.
Excretion
Urine, faeces (as metabolites).

5.3 Preclinical safety data
Clindamycin phosphate
Transient neuromuscular blockade is a recognized side effect of clinical use of antibiotics, including clindamycin. Extensive analysis of the blockade has led to the conclusion that clindamycin exerts its main effect post-synaptically at the neuromuscular junction, with a minor component of the inhibition also occurring pre-synaptically. The basis for these effects has been determined to be the lipophilic nature of the structure of clindamycin, which allows the molecule to compete with calcium for entry into nerve terminals, resulting in interference with nerve transmission. The effect of clindamycin on neuromuscular transmission has potential relevance to gastrointestinal smooth muscle function and the development of enterocolitis. However, because systemic exposure following topical application of clindamycin is low, it is not anticipated that patients receiving treatment with Veltin Gel will be affected

Clotrimazole
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development. The local and systemic tolerance of clotrimazole in different dosage forms was assessed in intravaginal studies in dogs and monkeys and in subacute dermal studies in rabbits. There was no evidence of treatment-related local or systemic adverse effects

in any of these studies. The oral toxicity of clotrimazole has been well-studied. Following a single oral administration, clotrimazole was slight-to-moderately toxic in experimental animals, with LD50 values of 761 to 923 mg/kg bw for mice, 95 to 114 mg/kg bw for new born rats and 114 to 718 mg/kg bw for adult rats, > 1000 mg/kg bw for rabbits and > 2000 mg/kg bw for dogs and cats. In repeated dose oral studies conducted in rats and dogs, the liver was found to be the primary target organ for toxicity. This was evidenced by an increase in serum transaminase activities and the appearance of liver vacuolation and fatty deposits starting at 50 mg/kg in the chronic (78- week) rat study and at 100 mg/kg in the sub chronic (13-week) dog study. Clotrimazole has been extensively studied in in vitro and in vivo mutagencity assays, and no evidence of mutagenic potential was found. A 78-week oral dosing study of clotrimazole in rats did not show any carcinogenic effect

PHARMACEUTICAL PARTICULARS

5.2 List of excipients

Clotrimazole powder

Clindamycin Hydrochloride

Lactose Hydrous

Corn starch

Polyvinyl pyrollidone

FD and C Blue Lake

Tartrazine Yellow

Magnesium stearate

5.3 Incompatibilities

NA

5.4 Shelf life

48 months

5.5 Special precautions for storage

Store below 30^{o}C. Protect from light and moisture.

5.6 Nature and contents of container and special equipment for use, administration or implantation

Mycoten® -Plus Vaginal Tablets is presented as 2% Clotrimazole plus 1% Clindamycin in a blister of 1 x 7's per pack.

5.7 Special precautions for disposal and other handling

No special requirements.

6 APPLICANT/MANUFACTURER

Drugfield Pharmaceuticals Limited
Lynson Chemical Avenue Km38,
Lagos-Abeokuta Expressway
Sango-Otta, Ogun State, Nigeria
Tel: +2348033513989
Email:Info@drugfieldpharma.com