**Summary of Product Characteristics for Pharmaceutical Products**

## 1. Name of the medicinal product:

VAGINORM (Clindamycin, Clotrimazole & Tinidazole Suppositories)

## 2. Qualitative and quantitative composition

Each suppository contains:
Clotrimazole 100 mg
Tinidazole 500 mg
Clindamycin Phosphate 123.2 mg Equivalent to Clindamycin 100 mg

For a full list of excipients, see section 6.1.

## 3. Pharmaceutical form

Suppository

A white colour, torpedo shaped Suppositories

## 4. Clinical particulars

### 4.1 Therapeutic indications

Vaginorm suppositories are recommended for the treatment of bacterial vaginosis and other gynecological infections caused by bacteria and fungi susceptible to the product.

Sanitation of genital tracts prior to gynecologic procedures.

### 4.2 Posology and method of administration

The suppositories should be inserted into the vagina, as high as possible, using the applicator provided. This is best achieved when lying back with legs bent up.
Treatment should not coincide with the period of menstruation. Treatment of Bacterial Vaginosis and other gynecological infection: 1 suppository a day for 7 days before sleep.

Prophylactic sanitation prior to gynecological procedures: 1 capsule a day for 3 days before the planned procedures and four 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.

*Tinidazole*
Tinidazole is contraindicated in patients with a history of blood dyscrasia although no persistent haematological abnormalities have been noted in clinical studies or animal studies.
Tinidazole should be avoided in patients with organic neurological disorders and people with known hypersensitivity to the drug and other 5-nitroimidazole derivatives.

## 4.4 Special warnings and precautions for use

Vaginorm is available in the form of a suppository. These formulations are meant for vaginal use only.
Common side effects of Vaginorm include burning sensation, irritation, and itching in the vaginal area.
However, these side effects are mild and temporary in nature and sometimes go off after applying to the affected area. Please inform your doctor if you use any prescription, non-prescription medicines, including vitamin and herbal supplements before using Vaginorm.
Do not use Vaginorm if you are allergic to Vaginorm or any of its components. Let your doctor know if have any liver, kidney and gastrointestinal diseases (diarrhoea and colitis, an inflammation of the colon), allergic conditions (asthma, hay fever, eczema), diabetes, and immune system problems (HIV-AIDS).
It is advised to use Vaginorm under your doctor's supervision if you use other azole antifungal medicines.
If in process of use of Vaginorm suppositories 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 the suppositories, vaginal intercourse and use of other products with intravaginal route of introduction are not recommended. Clotrimazole and mineral oil additive in Vaginorm may weaken rubber product's activity (such as latex condoms, diaphragms, cervical caps).

## 4.5 Interaction with other medicinal products and other forms of interaction

*Drug-Drug Interaction*:
Vaginorm may interact with anaesthetic agents/skeletal muscle relaxants (atracurium, cisatracurium, doxacurium, mivacurium, pancuronium, pipecuronium, rapacuronium, rocuronium, vecuronium, succinylcholine, tubocurarine, and metocurine) and respiratory drugs (budesonide, formoterol).

*Drug-Food Interaction:*

No interaction found/established.

*Drug-Disease Interaction*:
Before taking Vaginorm, let your doctor know if have any liver, kidney, and gastrointestinal diseases (diarrhoea and colitis, an inflammation of the colon), allergic conditions (asthma, hay fever, eczema), diabetes, and immune system problems (HIV-AIDS).

## 4.6 Fertility, pregnancy, and lactation

**Fertility:**
In animal studies, clindamycin had no effect on fertility or mating ability.

**Pregnancy:**
Vaginorm Suppository may be unsafe to use during pregnancy. Although there are limited studies in humans, animal studies have shown harmful effects on the developing baby. Your doctor will weigh the benefits and any potential risks before prescribing it to you. Please consult your doctor.

**Lactation:**
Vaginorm Suppository should be used with caution during breastfeeding. Breastfeeding should be held until the treatment of the mother is completed and the drug is eliminated from her body. If a single dose of Vaginorm Suppository is used, it is recommended to hold breastfeeding for 12-24 hours to allow the removal of the drug.

## 4.7 Effects on ability to drive and use machines.

No interaction found/established
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## 4.8 Undesirable effects

Most side effects do not require any medical attention and disappear as your body adjusts to the medicine.
Common side effects of Vaginorm:

- Vaginal burning sensation
- Itching
- General skin irritation

*Clindamycin:*
The table below lists the adverse reactions identified through clinical trial experience and post-marketing surveillance by system organ class and frequency. The frequency grouping is defined using the following convention: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very Rare (< 1/10,000); and Not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

| **System Organ Class** | **Common ≥ 1/100 to < 1/10** | **Uncommon ≥ 1/1 000 to <1/100** | **Not Known (cannot be estimated from available data)** |
|---|---|---|---|
| **Infections and Infestations** | pseudomembranous colitis*# | | *clostridium difficile* colitis*#, vaginal infection* |
| **Blood and Lymphatic System Disorders** | | | agranulocytosis*, neutropenia*, thrombocytopenia*, leukopenia*, eosinophilia |
| **Immune System Disorders** | | | anaphylactic shock*, anaphylactoid reaction*, anaphylactic reaction*, hypersensitivity* |
| **Nervous System Disorders** | | | dysgeusia |
| **Gastrointestinal Disorders** | diarrhoea, abdominal pain | vomiting, nausea | oesophageal ulcer*, oesophagitis* |
| **Hepatobiliary Disorders** | | | jaundice* |
| **Renal and urinary disorders** | | | acute kidney injury# |
| **Skin and Subcutaneous Tissue Disorders** | | rash maculopapular, urticaria | toxic epidermal necrolysis (TEN)*, Stevens Johnson syndrome (SJS)*, drug reaction with eosinophilia and systemic symptoms (DRESS)*, acute generalized exanthematous pustulosis (AGEP*, angioedema*, dermatitis exfoliative*, dermatitis bullous*, erythema multiforme*, pruritus, rash morbilliform* |
| **Investigations** | Liver function test abnormal | | |

*Clotrimazole:*
Immune system disorders: Anaphylactic reaction, angioedema, hypersensitivity.
Vascular disorder: syncope, hypotension.
Respiratory, thoracic and mediastinal disorders: dyspnea.
Gastrointestinal disorders: abdominal pain, nausea
Skin and Subcutaneous Tissue Disorders: Rash, urticaria, pruritus.
Reproductive system and breast disorders: Vaginal exfoliation, vaginal discharge, vaginal haemorrhage, vulvovaginal discomfort, vulvovaginal erythema, vulvovaginal burning sensation, vulvovaginal pruritus, vulvovaginal pain.
General disorders and administration site conditions: application site irritation, oedema, pain.

*Tinidazole:*

Autonomic Nervous System: flushing.
Body as a whole: fever, tiredness.
Central and Peripheral Nervous System: ataxia, convulsions (rarely), dizziness, headache, hypoesthesia, parathesia, peripheral neuropathy, sensory disturbances, and vertigo.
Gastrointestinal: abdominal pain, anorexia, diarrhoea, furry tongue, glossitis, nausea, stomatitis, vomiting. Haematopoietic: transient leukopenia.
Skin/Appendages: hypersensitivity reactions occasionally sever may occur in rare cases in the form of skin rash, pruritis, urticaria, and angioneurotic oedema.
Special senses: metallic taste.
Urinary system: dark urine.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions ND PQMPs to https://pv.pharmacyboardkenya.org

## 4.9 Overdose

No risk of acute intoxication is seen as it is unlikely to occur following a single vaginal or dermal application of an overdose (application over a large area under conditions favourable to absorption) or inadvertent oral ingestion. There is no specific antidote.
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 Pharmacodynamic 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.

*Tinidazole:*
Tinidazole is a prodrug and antiprotozoal agent. The nitro group of tinidazole is reduced in Trichomonas by a ferredoxin-medicated electron transport system. The free nitro radical generated as a result of this reduction is believed to be responsible for the antiprotozoal activity. It is suggested that the toxic free radicals covalently bind to DNA, causing DNA damage and leading to cell death. The mechanism by which tinidazole exhibits activity against Giardia and Entamoeba species is not known, though it is probably similar.

## 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; via oxidation and degradation of the imidazole cycle (desamination, O-desalkylation) and converted to inactive hydroxy metabolites.
Excretion: Urine, faeces (as metabolites). The elimination half-life for clotrimazole is 3.5 – 5 hours.

**Tinidazole**
Absorption**:** Rapidly and completely absorbed under fasting conditions. Administration with food results in a delay in Tmax of approximately 2 hours and a decline in Cmax of approximately 10%.
Metabolism: Hepatic, mainly via CYP34A.Tinidazole, like metronidazole, is significantly metabolized in humans prior to excretion. Tinidazole is partly metabolized by oxidation, hydroxylation and conjugation. Tinidazole is the major drug-related constituent in plasma after human treatment, along with a small amount of the 2-hydroxymethyl metabolite.
Elimination: Tinidazole is excreted by the liver and kidneys. Tinidazole is excreted in the urine mainly as unchanged drug.

## 5.3 Preclinical safety data
Not applicable

## 6. Pharmaceutical particulars

### 6.1 List of excipients
Suppository base
Polyethylene Glycol 6000
Paraffin
Titanium dioxide

### 6.2 Incompatibilities
Not applicable

### 6.3 Shelf life
36 months

### 6.4 Special precautions for storage:
Store below 30℃

### 6.5 Nature and contents of container
1 x 3 suppositories
Each strip has 3 suppositories.

### 6.6 Special precautions for disposal and other handling:
No special requirements

## 7. Marketing authorization holder and manufacturing site addresses

**Marketing authorization holder:**
Avetina Lifesciences Ltd.,
P.O. Box 3328-00506, Nairobi,
Kenya

**Manufacturing site address:**
Galen Pharmaceuticals Ltd.,
Plot No. 334/5 G.I.D.C. Estate Waghodia,
Vadodara, Gujarat 391760,
India.

## 8. Marketing authorization number
CTD10155

## 9. Date of first registration
07/07/2023

## 10. Date of revision of the text:
Sep-2023

## 11. Dosimetry:
Not Applicable

## 12. Instructions for Preparation of Radiopharmaceuticals:

Not Applicable