Pell Tech Health Care Pvt. Ltd.

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WHO-GMP CERTIFIED

1. NAME OF THE MEDICINAL PRODUCT

1.1 Product Name: ATOTRIM V6 TABLETS (Clotrimazole Vaginal Tablets BP 100 mg).

1.2 Strength: 100 mg.

1.3 Pharmaceutical Dosage Form: Vaginal Tablets.

2. QUALITATIVE & QUANTITATIVE COMPOSITION

Qualitative & Quantitative Information

Batch size: Tablets

S. N.	R. M. CODE	INGREDIENTS	SPECIFICATION	QTY/ TAB		QTY. REQ.for 6.0 LAKH TABLETS (In kg)
				QTY./TAB.	UOM	
	GRANULATION					
	DRY MIXING					
1	RC046	Clotrimazole	BP	100.000	mg	
2	RL001	Lactose	BP	286.31	mg	
3	RS001	Maize Starch *	BP	351.7	mg	
4	RP004	P.V.P K-30	BP	6.030	mg	
5	RM001	Microcrystalline Cellulose	BP	50.55	mg	
TOTAL				794.59	mg	
	BINDER SOLUTION					
6	RS001	Maize Starch	BP	40.400	mg	
7	RP014	Purified Water	BP	q.s	ml	
TOTAL				834.990	mg	
	LUBRICATION					
8	RM004	Magnesium Stearate	BP	4.020	mg	
9	RT003	Talcum	BP	10.100	mg	
10	RS001	Maize Starch	BP	50.150	mg	
11	RC011	Colloidal Sillicon Dioxide (Cabosil)	BP	4.020	mg	
12	RC006	Crospovidone	BP	15.170	mg	
13	RM001	Microcrystalline Cellulose	BP	50.550	mg	
14	RP013	Polyethylene Glycol 6000(P.E.G-6000)	BP	6.000	mg	
TOTAL				975.000	mg	

Clotrimazole will be taken extra to compensate the loss due to moisture content.

* 10% Extra Maize Starch taken to compensate process loss during Drying

3. PHARMACEUTICAL FORMS.

White, bullet shaped tablet, flat on one end and curved on other end.

4. CLINICAL PARTICULARS.

4.1 Therapeutic indications.

ATOTRIM V6 are recommended for the treatment of candidal vaginitis.

4.2 Posology and Method of Administration.

Posology:

The tablets 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.

Adults:

Two vaginal tablets/pessaries should be inserted daily (preferably at night) for three consecutive days. Alternatively, one vaginal tablet may be inserted daily for six days, preferably at night. A second treatment may be carried out if necessary.

There is no separate dosage schedule for the elderly.

ATOTRIM V6 need moisture in the vagina in order to dissolve completely, otherwise undissolved pieces of the vaginal tablet might crumble out of the vagina. Pieces of undissolved vaginal tablet may be noticed by women who experience vaginal dryness. To help prevent this it is important that the vaginal tablet is inserted as high as possible into the vagina at bedtime.

Generally:

treatment during the menstrual period should not be performed due to the risk of the vaginal tablet being washed out by the menstrual flow. The treatment should be finished before the onset of menstruation.

Do not use tampons, intravaginal douches, spermicides or other vaginal products while using this product.

Vaginal intercourse should be avoided in case of vaginal infection and while using this product because the partner could become infected.

Children:

Not for use in children under 16.

Method of Administration:

ATOTRIM V6 tablets/ pessaries are for vaginal administration.

4.3 Contraindications:

Hypersensitivity to clotrimazole or any other ingredient in this medicine .

4.4 Special Warnings and Precautions for Use:

Medical advice should be sought if this is the first time the patient has experienced symptoms of candidal vaginitis.

Before using ATOTRIM V6 medical advice must be sought if any of the following are applicable:

- more than two infections of candidal vaginitis in the last six months.
- previous history of a sexually transmitted disease or exposure to partner with sexually transmitted disease.
- pregnancy or suspected pregnancy.
- aged under 16 or over 60 years.
- known hypersensitivity to imidazoles or other vaginal antifungal products.

ATOTRIM V6 should not be used if the patient has any of the following symptoms whereupon medical advice should be sought:

- irregular vaginal bleeding.
- abnormal vaginal bleeding or a blood-stained discharge.
- vulval or vaginal ulcers, blisters or sores.
- lower abdominal pain or dysuria.
- any adverse events such as redness, irritation or swelling associated with the treatment.
- fever or chills.
- nausea or vomiting.
- diarrhoea.
- foul smelling vaginal discharge.

Patients should be advised to consult their physician if the symptoms have not been relieved within one week of using ATOTRIM V6. The vaginal tablets/pessaries can be used again if the candidal infection returns after 7 days. However, if the candidal infection recurs more than twice within six months, patients should be advised to consult their physician.

4.5 Interaction with other Medicinal Products and other Forms of Interaction.

Laboratory tests have suggested that, when used together, this product may cause damage to latex contraceptives. Consequently the effectiveness of such contraceptives may be reduced. Patients should be advised to use alternative precautions for at least five days after using this product.

Concomitant medication with vaginal clotrimazole and oral tacrolimus (FK-506; immunosuppressant) might lead to increased tacrolimus plasma levels and similarly with sirolimus. Patients should thus be closely monitored for signs and symptoms of tacrolimus or sirolimus overdosage, if necessary by determination of the respective plasma levels.

4.6Pregnancy and Lactation .

Fertility:

No human studies of the effects of clotrimazole on fertility have been performed, however, animal studies have not demonstrated any effects of the drug on fertility.

Pregnancy:

There are limited amount of data from the use of clotrimazole in pregnant women. Animal studies with clotrimazole have shown reproductive toxicity at high oral doses. At the low systemic exposures of clotrimazole following vaginal treatment, harmful effects with respect to reproductive toxicity are not predicted.

Clotrimazole can be used during pregnancy, but only under the supervision of a physician or midwife.

During pregnancy the vaginal tablet should be inserted without using an applicator.

Lactation:

Available pharmacodynamic/toxicological data in animals have shown excretion of clotrimazole/metabolites in milk after intravenous administration. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from clotrimazole therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 Effects on Ability to Drive and use Machines.

The medication has no or negligible influence on the ability to drive or use machinery.

4.8 Undesirable Effects.

As the listed undesirable effects are based on spontaneous reports, assigning accurate frequency of occurrence for each is not possible.

Immune system disorders:

allergic reaction (syncope, hypotension, dyspnea, urticaria, pruritus).

Reproductive system and breast disorders:

genital peeling, pruritus, rash, oedema, erythema, discomfort, burning, irritation, pelvic pain, vaginal haemorrhage.

Gastrointestinal disorders:

abdominal pain.

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.

However, in the event of accidental oral ingestion, routine measures such as gastric lavage should be performed only if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). Gastric lavage should be carried out only if the airway can be protected adequately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group

Gynaecological antiinfectives and antiseptics – imidazole derivatives

Mechanism of Action

Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the fungal cytoplasmic membrane.

Clotrimazole has a broad antimycotic spectrum of action in vitro and in vivo, which includes dermatophytes, yeasts, moulds, etc.

Under appropriate test conditions, the MIC values for these types of fungi are in the region of less than 0.062-8.0 µg/ml substrate. The mode of action of clotrimazole is fungistatic or fungicidal depending on the concentration of clotrimazole at the site of infection. In-vitro activity is limited to proliferating fungal elements; fungal spores are only slightly sensitive.

Primarily resistant variants of sensitive fungal species are very rare; the development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.

5.2 Pharmacokinetic Properties

Pharmacokinetic investigations after vaginal application have shown that only a small amount of clotrimazole (3 – 10% of the dose) is absorbed. Due to the rapid hepatic metabolism of absorbed clotrimazole into pharmacologically inactive metabolites the resulting peak plasma concentrations of clotrimazole after vaginal application of a 500mg dose were less than 10 ng/ml, reflecting that clotrimazole applied intravaginally does not lead to measurable systemic effects or side effects.

5.3 Preclinical Safety Data

Non-clinical data reveal no special hazard for humans based on studies of repeated dose toxicity, genotoxicity and carcinogenicity.

Clotrimazole was not teratogenic in reproductive toxicity studies in mice, rats and rabbits. In rats high oral doses were associated with maternal toxicity, embryotoxicity, reduced fetal weights and decreased pup survival.

In rats clotrimazole and/or its metabolites were secreted into milk at levels higher than in plasma by a factor of 10 to 20 at 4 hrs after administration, followed by a decline to a factor of 0.4 by

24 hrs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

List of excipients

- Lactose
- Maize Starch
- P.V.P.K-30
- Microcrystalline Cellulose
- Magnesium Stearate
- Talcum
- Colloidal silicon dioxide
- Crospovidone
- P.E.G.6000

6.3 Incompabilities

None Known

6.3 Shelf Life

36 months

6.4 Special Precaution for Storage

Store below 25°C, dry & dark place. Protect from moisture .

6.5 Nature & Content of Container

6 tablets packed in Aluminium- Aluminium strip,

1 X 6 Aluminium-Aluminium strip packed in carton.

6.6 Special Precaution for disposal <and other handling>

The vaginal tablet is to be taken out of the aluminium package and inserted into the form of the disposable applicator.

The disposable applicator is to be inserted into the vagina as deep as possible. By carefully pushing the inner plunger as far as it will go, the vaginal tablet is placed in the vagina.

After usage the disposable applicator is to be removed from the vagina and safely disposed of out of the reach of children.

Use of the vaginal tablet in combination with the disposable applicator.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER

PELL TECH HEALTH CARE PVT. LTD.

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