SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. Name of product:

Clindamycin and Clotrimazole soft gelatin vaginal suppositories (100mg + 100mg)

1.1. Name of drug product:

Clindamycin and Clotrimazole soft gelatin vaginal suppositories (100mg + 100mg)

1.2. Strength (composition):

Each soft gelatin vaginal suppository contains:

Clindamycin Phosphate BP

Equivalent to Clindamycin 100 mg

Clotrimazole BP 100 mg

1.3. Pharmaceutical dosage form:

Soft gelatin capsules.

2. QUALITATIVE AND QUANTITATIVE DECLARATION:

2.1 Qualitative Declaration:

S.No	Ingredients	Specification	Reason for Inclusion
1	Clindamycin Phosphate	BP	Antibacterial
2	Clotrimazole	BP	Antifungal
3	Polyethylene Glycol 400	USP	Diluent
4	Polyethylene Glycol 4000	USP	Thickening agent
5	Propylene glycol	BP	Humectants
6	Gelatin[3]	BP	Gelling agent
7	Glycerol	BP	Plasticizer
8	Titanium Dioxide	BP	Colouring agent
9	Ponceau 4R	IH	Colouring agent
10	Purified water	BP	Solublising agent

2.2 Quantitative Declaration:

Batch Size: 1,10,000 Capsules

S. No	Ingredients	Label claim mg/cap	Overage in %	Specifi[1] -cation	Added mg/cap	Added kg/batch	Reason for Inclusion
FILL MATERIALS							
1	Clindamycin Phosphate	100.00	-	BP	118.800	13.068	Antibacterial
2	Clotrimazole	100.00	-	BP	100.000	11.000	Antifungal
3	Polyethylene Glycol 400	-	-	USP	900.000	99.000	Diluent
4	Polyethylene Glycol 4000	-	-	USP	135.000	14.850	Thickening agent
5	Propylene glycol	-	-	BP	346.200	38.082	Humectants
SHELL MATERIALS[2]							
6	Gelatin[3]	-	-	BP	276.476	30.412	Gelling agent
7	Glycerol	-	-	BP	144.821	15.930	Plasticizer
8	Titanium Dioxide	-	-	BP	1.527	0.168	Colouring agent
9	Ponceau 4R	-	-	IH	0.176	0.019	Colouring agent
10	Purified water	-	-	BP	47.000	5.170	Solublising agent

Abbreviation:

BP: British Pharmacopoeia

USP: United States Pharmacopoeia

IH: In-House

1 Current pharmacopoeial monograph is implied.

2 In the batch formula excess material is added to compensate process loss. Process loss due to Cooking tank wastages, Placebo wastages, Service tank/spreader box retention, Net Wastage & Miscellaneous

3 Gelatin is derived from Bovine bones free from skulls, spinal cord and vertebrae. Country of origin - India.

3. PHARMACEUTICAL FORM:

Light pink coloured, oval shaped, opaque soft gelatin capsules containing white oily mass.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication:

Clindamycin and Clotrimazole Capsules is indicated in the treatment of bacterial vaginosis and other gynecologic infections caused by bacteria and fungi susceptible to the product. Sanitation of genital tracts prior gynecologic procedures.

Reference: http://en.wikipedia.org/wiki/Clindamycin

4.2 Posology and method of administration

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 before sleep.

Profilaxis 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

Reference:http://www.mims.com/USA/drug/info/Clindamycin%20Phosphate/Clindamycin%20Phosphate%20Gel?type=full

Clotrimazole:

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

Reference: http://medcatalog.net/tablets/clotrimazole.html

http://www.drugsupdate.com/generic/view/648

4.4 Special Warning & Precaution 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.

Reference: http://www.drugs.com/cdi/clindamycin-suppositories.html

If irritation or sensitivity develops with the use of Clotrimazole, treatment should be discontinued and appropriate therapy instituted.

Reference: http://www.drugsupdate.com/generic/view/648

4.5 Interaction with other medicinal products and other forms of Interactions:

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 breast-feeding.

Reference: http://www.drugs.com/cdi/clindamycin-suppositories.html

Although intravaginal application of clotrimazole has shown negligible absorption from both normal and inflamed human vaginal mucosa, clotrimazole vaginal preparations should not be

used in the first trimester of pregnancy unless the physician considers it essential to the welfare of the patient.

Reference:http://www.rxmed.com/b.main/b2.pharmaceutical/b2.1.monographs/CPS%20Monographs/CPS-%20(General%20Monographs-%20C)/CANESTEN_VAGINAL.html

4.7 Effects on ability to drive and use machine

None reported.

4.8 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.

Reference:http://www.drugs.com/cdi/clindamycin-suppositories.html

Clotrimazole:

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

Reference : http://www.drugs.com/ppa/clotrimazole.html

4.9 Over dose

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.

Reference: http://www.webmd.com/drugs/drug-10902-

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.

Reference: http://www.uptodate.com/contents/clindamycin-an-overview

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.

Reference: http://www.drugsupdate.com/generic/view/648

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

Reference:http://drugsarea.com/Dets-Drugs/Clindamycinpd.html#pharmacokinetics

Clotrimazole:

Absorption

Negligible through intact skin (topical); 3-10% (vaginal).

Metabolism

Hepatic; converted to inactive metabolites.

Excretion

Urine, faeces (as metabolites).

Reference: http://www.drugsupdate.com/generic/view/648

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.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients

S.No	Ingredients	Specification	Reason for Inclusion
1.	Polyethylene Glycol 400	USP	Diluent
2.	Polyethylene Glycol 4000	USP	Thickening agent
3.	Propylene glycol	BP	Humectants
4.	Gelatin	BP	Gelling agent
5.	Glycerol	BP	Plasticizer
6.	Titanium Dioxide	BP	Colouring agent
7.	Ponceau 4R	IH	Colouring agent
8.	Purified water	BP	Solublising agent

6.2 Incompabilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C.

Keep medicines out of reach of children. Read the product information leaflet carefully before use

6.5 Nature and contents of container

a) Type of package Blister pack

b) Nature and packaging material - 1X 7's blister pack

7. Marketing authorization holder and manufacturing site address

Manufacturing site address

SOFTGEL HEALTHCARE PRIVATE LIMITED

Survey no. 20/1, Vandalur- Kelambakkam Road,

Pudupakkam Village, Kancheepuram District– 603 103,

Tamilnadu, India.

8. Marketing authorization holder

9. Date of first registration/ renewal of the registration

10. Date of revision of the text – Nil