SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product
CLINDAREX (Clindamycin and Clotrimazole Soft Gelatin Capsules for Vaginal Use)

2. Qualitative and Quantitative composition
Product Name: CLINDAREX (Clindamycin and Clotrimazole Soft Gelatin Capsules for Vaginal Use)

Composition:
Each soft gelatin capsule for vaginal use contains:
Clindamycin Phosphate USP
Eq. to Clindamycin ……..100 mg
Clotrimazole BP……200 mg

For full list of excipients, see section 6.1

3. Pharmaceutical form
Soft Gelatin Capsule
Description: Pink colored oval shaped soft gelatin capsules filled with white paste.

4. Clinical Particulars

4.1 Therapeutic Indication:
CLINDAREX is mainly indicated for the following conditions:
- Bacterial vaginosis
- Candidal vaginitis,
- Trichomonas vaginitis
- Nonspecific vaginitis.

4.2 Posology and method of administration:
1 capsule should be inserted in to the vagina, for 7 consecutive nights preferably before retiring to bed. Treatment should be avoided during the menstrual period.

Direction for Use:
1. Wash hands thoroughly before and after insertion of CLINDAREX in the vagina.
2. The capsule should be inserted as deep as into the vagina as possible. This is best achieved when lying on the back with legs pulled in a little towards body.
3. After insertion of CLINDAREX, no activity should be done such as standing, walking, running etc. Hence CLINDAREX should be inserted while retiring to bed.
4. For best results take the complete therapy for 7 days. Do not discontinue in the middle.
5. Discontinue only if severe irritation is experienced, only after consulting the doctor.
6. If a particular dose is missed, administer immediately when recalled.

4.3 Contraindication:
CLINDAREX is contraindicated in patients with a known history of hypersensitivity to Clindamycin, Clotrimazole, Metronidazole, or any other ingredient in this medicine.

4.4 Special warnings and precautions for use
The patient should be instructed not to engage in vaginal intercourse or use of other vaginal products (such as tampons or douches) during treatment with CLINDAREX. CLINDAREX is to be administered intravaginally and is not to be taken orally.
CLINDAREX 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.

4.5 Interaction with other medicinal products and other forms of interaction
Cross resistance has been demonstrated between clindamycin and lincomycin, and erythromycin and clindamycin. Antagonism has been demonstrated between clindamycin and erythromycin *in vitro.*

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, it should be used with caution in patients receiving such agents.

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.

4.6 Fertility, Pregnancy and lactation
There has no adequate and well-controlled study for the use of CLINDAREX in pregnant women. Hence CLINDAREX should be used in pregnancy and lactation only if clearly needed or under physician's advice.

4.7 Effects on ability to drive and use machines
No data available

4.8 Undesirable effects
CLINDAREX vaginal Capsules are well tolerated locally i.e. intravaginally. Adverse effects may be associated with local irritation and contact dermatitis; sufficient clindamycin may be absorbed to produce systemic effects. Cervicitis, vaginitis, or vulvovaginal irritation has been reported with intravaginal use; a small amount of systemic absorption also occurs.

Other adverse effects are skin rashes, urticaria, and pruritus occur occasionally and erythema multiforme, angioedema, and anaphylaxis.

4.9 Overdose and Treatment
There is no risk of acute intoxication is seen as it is unlikely to occur following a single intravaginal application of an overdose (because of low absorption).

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 and general symptomatic and supportive measures are indicated as required. There is no specific antidote.

5. Pharmacological Properties
5.1 Pharmacodynamic properties
Clindamycin binds to the 50'S subunit of the bacterial ribosome and inhibit the early stages of protein synthesis. The action of clindamycin is mainly bacteriostatic, although high concentrations may be slowly bactericidal against sensitive strains. Synergistic activity has been reported between clindamycin and ceftazidime or metronidazole, and also with ciprofloxacin against some anaerobes.

Clindamycin is an antimicrobial agent against most strains of the organisms that have been reported to be associated with bacterial vaginosis as *Bacteroides* spp., *Gardnerella vaginalis, Mobiluncus* spp., *Mycoplasma hominis, Peptostreptococcus* spp.

Clotrimazole acts against fungi by inhibiting with ergosterol synthesis and therefore alters the permeability of the cell membrane of sensitive fungi. Clotrimazole has a broad antimycotic spectrum of action which includes dermatophytes, yeasts, moulds, etc.

5.2 Pharmacokinetic properties
Clindamycin is available about 30% of a dose systemically from vaginal pessaries. It is widely distributed in body fluids and tissues. It diffuses across the placenta into the fetal circulation and has been reported to appear in breast milk. It accumulates in leucocytes and macrophages. Over 90% of clindamycin in the circulation is bound to plasma proteins.

Clindamycin undergoes metabolised hepatically to the active *N*-demethyl and sulfoxide metabolites, and also to some inactive metabolites. About 10% of a dose is excreted in the urine as active drug or metabolites and about 4% in the faeces; the remainder is excreted as inactive metabolites. Excretion is slow, and takes place over several days.

Clotrimazole has absorption of 3 to 10% of a dose after vaginal use. It is metabolised in the liver to inactive compounds and excreted in the faeces and urine.

5.3 Preclinical Safety Data:
No data available

Pregnancy: There was no evidence of teratogenicity when vancomycin was administered IV to rats in dosages up to 200 mg/kg daily (1180 mg/m2 or equivalent to the recommended maximum human dosage based on mg/m2) or to rabbits in dosage up to 120 mg/kg daily (1320 mg/m2 or 1.1 times the recommended maximum human dosage based on mg/m2). There were no effects on fetal weight or development in rats at the highest dosage tested or in rabbits given 80 mg/kg daily (880 mg/m2 or 0.74 times the maximum recommended human dosage based on mg/m2).

6. Pharmaceutical Particulars
6.1 List of excipients:
Light Liquid Paraffin BP,
White Soft Paraffin BP,
Yellow Bees wax BP,
Gelatin BP,
Glycerol BP,
Methyl Hydroxybenzoate BP,
Propyl Hydroxybenzoate BP,
Colour Titanium Dioxide BP,
Ponceau 4 R,
Purified Water BP
6.2 Incompatibilities:
Not Applicable

6.3 Shelf Life:
24 Months

6.4 Special precautions for storage:
Store below 30◦C. Protect from light

6.5 Nature and contents of container:

PVC blister pack of 1 x 7's

6.6 Special precautions for Disposal:
None

7. Marketing Authorization Holder and Manufacturing Site Addresses:
Gelnova Laboratories (India) Pvt. Limited
C-125, T.T.C. Industrial Area, Mahape,
Navi Mumbai- 400 705,
Dist. Thane, **India.**

8. Marketing Authorization Number:
TAN 22 HM 0082

9. Date of first Registration/ Renewal of the registration:
11/04/2022

10. Date of Revision of the text: