Dalacin*

Clindamycin Phosphate

100 mg/ 5 ml Vaginal Cream

Reference market:

Belgium

AFME Markets using same as LPD:

Egypt

SUMMARY OF PRODUCT CHARACTERISTICS

Egypt, August 2023

1. NAME OF THE MEDICINAL PRODUCT

Dalacin 2% Vaginal cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

White Semi solid cream.

The active ingredient is clindamycin phosphate in a concentration of 2.38% equivalent to 2% clindamycin base.

Dalacin Vaginal cream is packed in a 16.5 gram tube, accompanied by 3 (HDPE) disposable applicators and an inner leaflet

Excipients with known effect:
Dalacin Vaginal contains 250 mg of propylene glycol per 5 grams of cream in one applicator, which is equivalent to 50 mg/g of propylene glycol.
Dalacin Vaginal contains 160.5 mg cetylstearyl alcohol per 5 grams of cream in one applicator, which is equivalent to 32.1 mg/g of cetylstearyl alcohol.
Dalacin Vaginal contains 50 mg of benzyl alcohol per 5 grams of cream in one applicator, which is equivalent to 10 mg/g of benzyl alcohol.
See section 4.4.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Vaginal cream.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of bacterial vaginosis (formerly referred to as Haemophilus vaginitis, Gardnerella vaginitis, nonspecific vaginitis, Corynebacterium vaginitis, or anaerobic vaginitis).

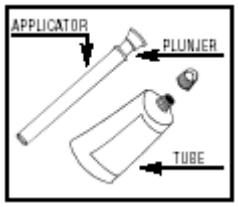
Other pathogens commonly associated with vulvovaginitis, *Trichomonas vaginalis* and *Candida albicans*, infections with *Chlamydia trachomatis* and gonococcal infections should be ruled out beforehand by appropriate laboratory methods.

Like other antibiotics, information regarding the prevention of local resistance as well as the official recommendations regarding prescription of antibiotics must be reviewed before prescribing clindamycin.

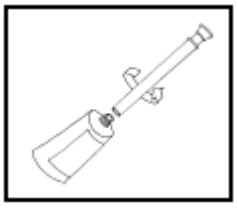
4.2 Posology and method of administration

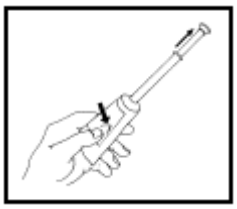
Posology

Inject into the vagina one applicator full (approximately 5 grams) of cream per day for 7 consecutive days at bedtime.



Open the tube.


Screw a plastic applicator on the tube.


Push softly at the bottom of the tube in order to fill the applicator with cream until you experience resistance; the plunger is now pushed out of the applicator for the greater part; unscrew the applicator; close the tube.

Method of administration

While the patient is lying on her back, insert the applicator deeply into the vagina and inject the cream. Dispose of the applicator after use.

4.3 Contraindications

- Hypersensitivity to the active substance clindamycin, to lincomycin, to any other related substance or to any of the excipients listed in section 6.1.
- Clindamycin is also contraindicated in individuals with a history of antibiotic-associated colitis.

4.4 Special warnings and precautions for use

- Before or after initiation of therapy with clindamycin, other infections including *Trichomonas vaginalis*, *Candida albicans*, *Chlamydia trachomatis* and gonococcal infections may need to be investigated by adequate laboratory tests.
- The use of clindamycin may result in the overgrowth of non-susceptible organisms, particularly yeasts.
- Onset of symptoms suggestive of pseudomembranous colitis may occur during or after antimicrobial treatment (see section 4.8). Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clindamycin, and may range in severity from mild to life-threatening. Therefore, it is important that this is considered in patients who present with diarrhoea subsequent to the administration of antibacterial agents. Moderate cases may improve following withdrawal of the drug. Clindamycin treatment must be stopped if pseudomembranous diarrhoea occurs. An adequate antibacterial therapy should be prescribed. Drugs inhibiting peristalsis are contra-indicated in this situation.
- Caution is advised in patients when prescribing clindamycin to individuals with inflammatory bowel disease such as Crohn's disease or ulcerative colitis.
- As with all vaginal infections, it is not recommended to have sexual intercourse during the infection and consequently also during the treatment with clindamycin vaginal cream. If the

patient does want to have sexual intercourse, it is preferable to wait minimum 2 hours after applying the cream. Latex condoms and diaphragms may be weakened if exposed to the suppository base used in clindamycin vaginal cream. The use of such products within 72 hours following treatment with Dalacin Vaginal is not recommended as such use could be associated with diminished contraceptive efficacy or protection against sexually transmitted disease.

– The use of other vaginal products (such as tampons and douches) during the treatment with clindamycin vaginal cream is not recommended.

Propylene glycol and cetylstearyl alcohol present in Dalacin Vaginal Cream may cause local skin reactions or irritations. Benzyl alcohol may cause allergic reactions.

Excipients information

Dalacin Vaginal cream contains propylene glycol, cetylstearyl alcohol and benzyl alcohol (see section 2).

Cetylstearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

Benzyl alcohol may cause allergic reactions and mild local irritation.

Paediatric population

Safety and efficacy in paediatric patients under 16 years of age have not been established.

4.5 Interaction with other medicinal products and other forms of interaction

No information is available on the concomitant use of other vaginal medications with clindamycin.

Cross resistance has been demonstrated between clindamycin and lincomycin. (see section 5.1.) Systemic 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 as vecuronium, rocuronium, gentamicin, rapacuronium (with magnesium), pancuronium. Synergistic effects of other antibiotics together with clindamycin on neuromuscular blocking agents have been described. Careful attention is therefore needed when using antibiotics together with muscle relaxants, because the synergy effect triggered by the combination could cause deeper muscle relaxation and delay recovery (see section 4.9).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data on the use of clindamycin in pregnant women during the first trimester of pregnancy. In clinical trials, the use of Dalacin Vaginal in pregnant women and systemic administration of clindamycin during the second and third trimester have not been associated with an increased incidence of congenital abnormalities. Animal studies did not reveal any direct or indirect deleterious effects on reproduction (see section 5.3).

As a precaution, it is best to avoid using Dalacin Vaginal during the first trimester of pregnancy. Dalacin Vaginal may be used during the second and third trimester of pregnancy following appropriate diagnosis by a physician.

Breastfeeding

It is not known if clindamycin is excreted in human breast milk following the use of vaginally administered clindamycin vaginal cream. Clindamycin has been reported to appear in human breast milk in ranges from <0.5 to 3.8 μg/mL following systemic use. It should be noted however that following vaginal administration of Dalacin Vaginal, serum levels are about 200 times lower than following oral or parenteral administration.

Clindamycin has the potential to cause adverse effects on the breastfed infant's gastrointestinal flora such as diarrhoea or blood in the stool, or rash. Given the low systemic absorption for vaginally applied clindamycin cream (0.6-11% resulting in 3- 93 ng/ml serum concentrations in the mother), the risk for the infant is unlikely. Dalacin Vaginal can be used during breast-feeding. The infant should be

monitored for adverse drug reactions. If these occur, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Dalacin Vaginal therapy taking into account the developmental and health benefits of breastfeeding for the child along with the mother's clinical need for clindamycin and any potential adverse effects on the breastfed child from clindamycin or from the underlying maternal condition.

Fertility

Fertility studies conducted in rats with clindamycin administered orally or subcutaneously did not show any deleterious effects on fertility or mating ability (see section 5.3). There are no data on fertility in humans. No animal fertility studies have been performed using the vaginal route of administration.

4.7 Effects on ability to drive and use machines

Clindamycin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The table below lists the adverse reactions identified through clinical trial experience and post-marketing surveillance by system organ class and frequency. Adverse reactions identified from post-marketing experience are included in *italics*. 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.

The safety of clindamycin vaginal cream was evaluated in both non-pregnant patients and pregnant patients during their second and third trimesters. The majority of undesirable adverse effects were of mild or moderate severity. The most commonly reported adverse reaction is vulvovaginal candidiasis.

System Organ Class	Very Common ≥ 1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Frequency not known (cannot be estimated from available data)
Infections and infestations		Fungal infection, Candida infection	Bacterial infection	Skin candida
Immune system disorders			Hypersensitivity	
Endocrine disorders				Hyperthyroidism
Nervous system disorders		Headache, Dizziness, Dysgeusia		
Ear and labyrinth disorders			Vertigo	
Respiratory, thoracic and mediastinal disorders		Upper respiratory tract infection	Epistaxis	
Gastrointestinal disorders		Abdominal pain, Constipation, Diarrhoea, Nausea, Vomiting	Abdominal distension, Flatulence, Halitosis	*Pseudomembranous colitis* (see section 4.4), Gastrointestinal disorder, Dyspepsia

System Organ Class	Very Common ≥ 1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Frequency not known (cannot be estimated from available data)
Skin and subcutaneous tissue disorders		Pruritus (non-applicable site), Rash	Urticaria Erythema	Rash maculopapular
Musculoskeletal and connective tissue disorders		Back pain		
Renal and urinary disorders		Urinary tract infection, Glycosuria*, Proteinuria	Dysuria	
Pregnancy, puerperium and perinatal conditions		Abnormal labour*		
Reproductive system and breast disorders	Vulvovaginal candidiasis	Vulvovaginitis, Vulvovaginal disorder, Menstrual disorder, Vulvovaginal pain, Metrorrhagia, Vaginal discharge	Vulvaginitis trichomonal, Vaginal infection, Pelvic pain	Endometriosis
General disorders and administration site conditions				Inflammation, Pain
Investigations			Microbiology test abnormal	

* The undesirable effects of "abnormal labour" and "glycosuria" only apply to pregnant women.

Pseudomembranous colitis may occur during treatment (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after marketing authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions according to their local country requirements.

To report any side effect (s):

Pharmacovigilance center, Pfizer Pharmaceutical Company: EGY.AEReporting@pfizer.com
Egyptian Pharmacovigilance center (EPVC), EDA: pv.followup@edaegypt.gov.eg

4.9 Overdose

There are no reports of overdose with clindamycin. Vaginally applied clindamycin phosphate contained in Dalacin Vaginal can be absorbed in sufficient amounts to produce systemic effects.

In the event of overdosage, general symptomatic and supportive measures are indicated as required.

Accidental oral intake can lead to effects comparable with those of therapeutic concentrations of orally administered clindamycin.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibiotics and antiseptics for vaginal use
ATC code: G01AA10

Mechanism of action
Clindamycin is a lincosamide antibiotic that inhibits bacterial protein synthesis at the level of the bacterial ribosome. The antibiotic binds preferentially to the 50S ribosomal subunit and affects the translation process. Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.

Clindamycin, like most protein synthesis inhibitors, is predominantly bacteriostatic and efficacy is associated with the length of time the concentration of active ingredient remains above the minimum inhibitory concentration (MIC) of the infecting organism. Mechanism of resistance
Resistance to clindamycin is most often due to modification of the target site on the ribosome, usually by chemical modification of RNA bases or by point mutations in RNA or occasionally in proteins. Clinical isolates that test susceptible to clindamycin and resistant to erythromycin should also be tested for inducible clindamycin resistance using the D-test. Cross resistance has been demonstrated *in vitro* between lincosamides, macrolides and streptogramins B in some organisms. Cross resistance has been demonstrated between clindamycin and lincomycin.

Antimicrobial activity
Clindamycin has been shown to be effective in the treatment of infections caused by susceptible anaerobic bacteria or susceptible strains of Gram positive aerobic bacteria. Clindamycin has been shown to have *in vitro* activity against the following organisms which are associated with bacterial vaginosis:
- *Gardnerella vaginalis*
- *Mobiluncus* spp.
- *Bacteroides* spp.
- *Mycoplasma hominis*
- *Peptostreptococcus* spp.

Antagonism has been demonstrated between clindamycin and erythromycin *in vitro*.

5.2 Pharmacokinetic properties

Absorption

Following once a day dosing of 100 mg of vaginally administered clindamycin phosphate, peak serum clindamycin levels average 20 ng/ml (level range, 3 to 93 ng/ml) in healthy volunteers. Approximately 4% (level range, 0.6 to 11%) of the administered dose is absorbed systemically. In women with bacterial vaginosis, the amount of clindamycin absorbed following vaginal administration of 5 grams of Dalacin Vaginal is 5% (range, 2 to 8%), which is nearly the same as in healthy volunteers.

5.3 Preclinical safety data

Fertility studies conducted in rats treated with oral clindamycin with a dose of maximum 300 mg/kg/day (about 1.1 times the highest recommended adult human dose based on mg/m^2) did not show any effects on fertility or mating ability.

Embryo and foetus development studies in rats following oral administration and in rats and rabbits following subcutaneous administration did not show any developmental toxicity, except in doses causing maternal toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitan monostearate, polysorbate 60, propylene glycol (E1520), stearic acid, Cetostearyl alcohol, cetyl palmitate, Mineral oil, benzyl alcohol (E1519), purified water.

6.2 Incompatibilities

Dalacin Vaginal contains oil-based ingredients. Some of these ingredients may affect the quality of the rubber of condoms and diaphragms, thereby reducing their contraceptive efficacy and protection against sexually transmitted diseases, including AIDS. The use of this type of products during treatment with Dalacin Vaginal is therefore not recommended.

6.3 Shelf life

Do not use Dalacin Vaginal cream after the expiry date which is stated on the carton /label after EXP:. The expiry date refers to the last day of that month.

6.4 Special precautions for storage

Store at room temperature not exceeding 25°C. don't freeze.

6.5 Nature and contents of container

Carton box containing one aluminium tube containing 16.5 g cream + white HDPE plastic screw cap + 3 plastic HDPE applicators + inner leaflet.

6.6 Special precautions for disposal

Keep out of the sight and reach of children.

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

7. FURTHER INFORMATION

MARKETING AUTHORISATION HOLDER
Pfizer Limited- United Kingdom

MANUFACTURED BY
Viatris Egypt

PACKED & RELEASED BY
Viatris Egypt

8. DATE OF REVISION OF THE TEXT

June 2023

THIS IS A MEDICAMENT

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the Pharmacist who sold the medicament.
- The doctor and the Pharmacist are experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
-

Keep all medicaments out of reach and sight of children

Council of Arab Health Ministers
Union of Arabic Pharmacists