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INSTRUCTION
for medical use

BANBAKT®

Composition:
active substance: clindamycin;
each vaginal suppository contains clindamycin phosphate equivalent to 100 mg clindamycin;
excipients: hard fat.

Pharmaceutical form. Vaginal suppositories.
Basic physico-chemical properties: white to light yellow torpedo shaped suppositories.

Pharmacotherapeutic group. Gynecological antiinfectives and antiseptics, excluding combinations with corticosteroids. Antibiotics. Clindamycin. ATC code G01A A10.

Pharmacological properties.
Pharmacodynamics.
Mechanism of action. Clindamycin is a lincosamide antibiotic which inhibits bacterial protein synthesis by its action at the bacterial ribosome. The antibiotic binds preferentially to the 50S ribosomal subunit and affects the process of peptide chain initiation. Although clindamycin phosphate is inactive *in vitro*, rapid hydrolysis *in vivo* converts it 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.
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. 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.
Susceptibility *in vitro*. Clindamycin is active *in vitro* against the following registered strains of microorganisms associated with bacterial vaginosis: *Bacteroides spp., Gardnerella vaginalis*, *Mobiluncus spp., Mycoplasma hominis, Peptostreptococcus spp*.
Standard methodology for susceptibility testing of potential bacterial vaginosis pathogens, *Gardnerella vaginalis* and *Mobiluncus spp.* has not been specified. The borderline values for the sensitivity of gram-negative and gram-positive anaerobes to clindamycin have been published by EUCAST. For clinical isolates that have been shown to be sensitive to clindamycin and resistant to erythromycin, an analysis for induced resistance to clindamycin should also be performed using the D-test. However, the borderline values are intended more to determine the direction of systemic antibiotic treatment than topical treatment.
Pharmacokinetics.

Absorption. Systemic absorption of clindamycin was estimated following a once-a-day intravaginal dose of one clindamycin phosphate vaginal suppository (equivalent to 100 mg clindamycin) administered to 11 healthy female volunteers for 3 days. Approximately 30% (range 6% to 70%) of the administered dose was absorbed systemically on day 3 of dosing based on area under the concentration-time curve (AUC). Systemic absorption was estimated using a subtherapeutic 100 mg intravenous dose of clindamycin phosphate as a comparator in the same volunteers as well as a 100 mg dose of clindamycin phosphate vaginal cream. The mean area under the concentration-time curve (AUC) following day 3 of dosing with the suppository was 3.2 μg•hr/mL (range 0.42 to 11 μg•hr/mL). The maximum plasma concentration observed on day 3 of dosing with the suppository averaged 0.27 μg/mL (range 0.03 to 0.67 μg/mL) and was observed about 5 hours after dosing (range 1 to 10 hours). In contrast, the AUC and C_{max} after the single intravenous dose averaged 11 μg•hr/mL (range 5.1 to 26 μg•hr/mL) and 3.7 μg/mL (range 2.4 to 5.0 μg/mL), respectively. The mean apparent elimination half-life after dosing with the suppository was 11 hours (range 4 to 35 hours), and is considered to be limited by the absorption rate. The results from this study showed that systemic exposure to clindamycin (based on AUC) from the suppository was, on average, 3-fold lower than that from a single subtherapeutic 100 mg intravenous dose of clindamycin. Systemic absorption of clindamycin suppository was approximately 7-fold greater than that following dosing of the vaginal cream with average values of AUC and C_{max} of 0.4 μg.hr/mL (range 0.13 to 1.16 μg.hr/mL and 0.02μg/mL (range 0.01 to 0.07 μg/mL) respectively for the clindamycin vaginal cream. In addition, the recommended daily and total doses of intravaginal clindamycin suppository are far lower than those typically administered in oral or parenteral clindamycin therapy (100 mg of clindamycin per day for 3 days equivalent to about 30 mg absorbed per day from the suppository relative to 600 to 2700 mg/day for up to 10 days or more, orally or parenterally). The overall systemic exposure to clindamycin from clindamycin vaginal suppositories is substantially lower than the systemic exposure from therapeutic doses of oral clindamycin hydrochloride (2-fold to 20-fold lower) or parenteral clindamycin phosphate (40-fold to 50-fold lower).

Clinical characteristics.

Indications.

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

Contraindications.

Hypersensitivity to active ingredient, lincomycin or any excipient specified in the "Composition" section.

Banbakt® is also contraindicated to patients having colitis associated with the use of antibiotics in the history.

Interaction with other medicinal products and other forms of interaction.

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

When administered systemically, clindamycin phosphate 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 who take such medications (see "Overdose" and "Pharmacokinetics" sections).

It is not recommended to use latex condoms during treatment with clindamycin in the form of vaginal suppositories.

Special warnings and precautions for use.

Before or promptly after initiation of therapy with Banbakt®, other infections including *Trichomonas vaginalis*, *Candida albicans*, *Chlamydia trachomatis* and gonococcal infections may need to be investigated by adequate laboratory tests.

The use of Banbakt® may result in the overgrowth of nonsusceptible organisms, particularly yeasts.
Symptoms indicating pseudomembranous colitis may occur during or after antimicrobial use (see "Adverse reactions" section). Cases of pseudomembranous colitis have been reported with the use of almost all antibacterial agents, including clindamycin; the severity can range from mild to life-threatening. Therefore, it is important that this is considered in patients who present with diarrhea subsequent to the administration of antibacterial agents. Moderate cases may improve following withdrawal of the drug.
Clindamycin should be discontinued if pseudomembranous diarrhea occurs. Appropriate antibacterial treatment should be prescribed. Drugs that inhibit peristalsis are contraindicated in this case.
Caution is advised when prescribing Banbakt® for patients with inflammatory bowel disease, in particular Crohn's disease or nonspecific ulcerative colitis.
As with all vaginal infections, sexual intercourse during treatment with Banbakt® in the form of vaginal suppositories is not recommended. Latex condoms and diaphragms may be weakened if exposed to the suppository base used in vaginal suppositories (see "Interaction with other medicinal products and other forms of interaction" section). The use of such products within 72 hours following the treatment with the drug 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 Banbakt® in the form of vaginal suppositories is not recommended.
Acute renal impairment.
Rare cases of acute renal impairment, including acute renal failure, have been reported. Therefore, monitoring of renal function should be considered in patients receiving long-term clindamycin therapy with renal impairment or concomitant nephrotoxic drugs (see "Adverse reactions" section).
Special precautions for handling and disposing of the product.
Do not use this drug if the package containing vaginal suppositories is damaged, open or unhermetically packed.
Use during pregnancy or breastfeeding.
Pregnancy.
Animal studies have shown reproductive toxicity.
Use is not recommended during the first trimester of pregnancy, as there are no adequate and well-controlled studies in pregnant women over this period.
According to clinical studies, the use of clindamycin in a dosage form for vaginal use in women during the second trimester of pregnancy and systemic use of clindamycin phosphate during the second and third trimesters did not lead to the development of congenital anomalies.
Banbakt® can be used in the second and third trimesters of pregnancy only if clearly needed.
Lactation.
It is not known if clindamycin is excreted in breast milk following the use of vaginally administered clindamycin. Although used in much lower doses than clindamycin for systemic use, approximately 30% (range 6% to 70%) is absorbed into the systemic circulation. Following systemic administration, clindamycin has been reported in human breast milk at concentrations <0.5 to 3.8 μg/ml. In case of systematic use of clindamycin by breastfeeding women there is a risk of adverse effects on the microflora of the gastrointestinal tract of the breastfed infant, such as diarrhea or blood in the stool, or rash. The use of Banbakt® vaginal suppositories by breastfeeding women may be considered if the expected benefit to the mother outweighs the risk to the baby.
Fertility.
In animal studies the effect on fertility have not been shown.

Effects on ability to drive a car or use machines.
Banbakt® has no or negligible influence on the ability to drive or use machinery.

Administration and dosage.

Dosage.

Recommended dose is one suppository intravaginally at bedtime for three consecutive days.

Administration details.

Banbakt® is used intravaginally.

Method of administration.

- Remove the suppository from the contour packaging.
- Lie on the back with knees bent and tucked up to the chest.
- Insert a suppository into the vagina with the middle finger as deep as possible, but not to cause unpleasant sensations.

Use in elderly patients.

The use of Banbakt® in the form of vaginal suppositories has not been studied in patients over 65 years of age.

Use in patients with renal impairment.

The use of Banbakt® in the form of vaginal suppositories has not been studied in patients with impaired renal function.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Children.

Safety and efficacy of Banbakt® in the form of vaginal suppositories in children has not been established.

Overdose.

There are no reports of overdose with Banbakt® in the form of vaginal suppositories.

Clindamycin phosphate contained in the drug and used vaginally can be absorbed in an amount sufficient to develop systemic effects.

In the case of overdose, the use of general symptomatic and supportive treatment is indicated, if necessary.

Accidental oral intake can lead to effects similar to those that occur when therapeutic doses of clindamycin are administered orally.

Adverse reactions.

The safety of clindamycin in the form of vaginal suppositories has been evaluated in clinical trials in non-pregnant patients. The following frequency of adverse reactions has been reported: common (≥ 1/100 and < 1/10); uncommon (≥ 1/1000 and <1/100); unknown (frequency cannot be determined from the available data).

Infections and invasions: common – fungal infections, infections caused by *Candida*; unknown – clostridial colitis (caused by *Clostridioides difficile*).

Immune system disorders: unknown – hypersensitivity reactions*; drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).

Nervous system disorders: common – headache.

Gastrointestinal disorders: common – abdominal pain, diarrhea, nausea; uncommon – vomiting; unknown – pseudomembranous colitis**.

Skin and subcutaneous tissue disorders: common – pruritus (not at the application site); uncommon – rash.

Musculoskeletal and connective tissue disorders: uncommon – flank pain; unknown – polyarthritis.

Renal and urinary disorders: uncommon – pyelonephritis, dysuria: unknown – acute renal impairment, including acute renal failure (see “Special warnings and precautions for use” section).

Reproductive system and breast disorders: common – vulvovaginal candidiasis, vulvovaginal pain, vulvovaginal disorders; uncommon – vaginal infections, vaginal discharges, menstrual disorders.
General disorders at the application site: uncommon – application site pain, itching (at the application site), local edema, pain, fever (febrility).
* Maculopapular rash and urticaria have been observed during clindamycin therapy. Generalized mild to moderate skin rashes are the most frequently reported of all adverse reactions. Cases of acute generalized exanthematous pustulosis, erythema multiforme, some resembling Stevens-Johnson syndrome, have been associated with clindamycin. A few cases of anaphylactoid reactions have been reported. If a hypersensitivity reaction occurs, the drug should be discontinued.
** Pseudomembranous colitis is an event characteristic for the whole class of antibacterial agents.
Reporting of suspected adverse reactions.
Post-marketing reporting of adverse reactions is important. This makes it possible to monitor the benefit/risk ratio when using this medicinal product. Medical and pharmaceutical workers, as well as patients or their legal representatives should be notified of all cases of suspected adverse reactions and lack of effectiveness of the medicinal product through the Automated Pharmacovigilance Information System at the link: https://aisf.dec.gov.ua.

Shelf life.
2 years.

Storage conditions.
Store in the original package at the temperature not exceeding 25°C.
Keep out of reach of children.

Package.
3 suppositories in a strip. 1 strip in a carton package.

Condition of supply.
By prescription.

Manufacturer.
KUSUM HEALTHCARE PVT LTD.

Manufacturer's location and address of the place of business.
SP-289 (A), RIICO Industrial area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan), India.

Date of last revision.