



KAOFIN

REGISTRATION NUMBER Q- 7972-100

Anti-diarrheal and antibiotic with mucosal protectors.

FORMULA

Each 1 ml contains:

Gentamicin.....	12 mg
Sulfamethoxazole	100 mg
Trimethoprim	20 mg
Loperamide	0.5 mg
Vehicle c.b.p (Kaolin Pectina).....	1 mL



Presentations: 60 ml y 100 ml

INDICATIONS:

Antidiarrheal and antimicrobial broad spectrum useful in infections caused by Gram positive microorganisms, Gram negative as; *Escherichia coli*, *Pasteurella* spp, *Klebsiella* spp, *Pseudomonas* spp, *Proteus* spp, *Campylobacter* spp, *Vibrio* spp, *Treponema* spp and *Clostridium* spp, as well as in some protozoan infections: *Trichomonas*, *Isospora* and *Eimeria*, mycoplasmas and rickettsias sensitive to the action of the formula.

Used specifically as an adjuvant for the treatment of various diarrheas such as: viral and bacterial mechanics, acute and in cases where you want to reduce the intestinal motility of them.

KAOFIN ACTION SPECTRUM

The combination of two inhibitors of dihydro folic acid synthesis cause synergistic activity against different microorganisms. The combination of sulfamethoxazole-trimethoprim (SMX-TMP) and gentamicin have activity against gram-positive and gram-negative bacteria such as: *Bacillus anthracis*, *Clostridium welchii*, *Escherichia coli*, *Haemophilus ducreyi*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella pestis*, some *Proteus*, *Pseudomonas aeruginosa*, *Salmonella* spp, *Shigella* spp, some *Staphylococcus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Vibrio cholerae*. They have also manifested their effectiveness against protozoa such as *Coccidias* spp and *Toxoplasma gondii*.

Kaolin is an astringent used in the treatment of diarrhea, often in combination with pectin. It absorbs toxic substances and increases the volume of stool.

Pectin is a gelatinous substance found in fruit and some vegetables and is used as a solidifying agent in the preparation of jams and jellies and as an emulsifier and stabilizer of many foods. Its action is absorbent by preventing aqueous loss.

Kaolin and pectin are fine, inert protective powders that have great adhesion and coating power on the skin and mucous membranes, and therefore act mechanically without interfering with any digestive or metabolic process. They are able to remove bacteria and irritants that are a common cause of diarrhea.

MECHANISM OF ACTION:

Kaofin acts only at the level of the intestinal lumen by removing or destroying irritants and toxins, protecting the intestinal mucosa while reducing the inflammatory process.



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It fights infection by various mechanisms, first by the antibacterial action carried out by the action of sulfamethoxazole that inhibits the use of PABA (paraminobenzoic acid), which is necessary for normal bacterial metabolism. On the other hand, trimethoprim prevents the formation of hydrofolate to bacterial tetrahydrofolate reductase and antibiotic gentamicin from skin and mucosal contact.

Aminoglycosides such as gentamicin are not absorbed via the intestine because they are highly polarized cations of a basic nature, therefore little fat-soluble preventing their absorption.

Its mechanism of action is that it irreversibly joins the 30S subunit of the bacterial ribosome. This bond interferes with the elongation of the peptide chain. They also cause incorrect readings of the genetic code by forming abnormal proteins. Some of these are membrane proteins and the result is the formation of channels that allow more drugs to enter the cell.

Pectin is known to remove toxic products from developing bacteria. It can also destroy bacteria through the formation of galactourínico acid which produces a more favorable medium for the growth of diarrhea-causing microorganisms. In this way it can combine with toxic substances and render them inert.

Finally, the action of loperamide directly affects the intestinal smooth muscle, producing contractions of the circular muscle, it also acts centrally on the synapse to increase segmentation. Increases fluid absorption by blocking calcium channels or by inhibiting intrinsic calmodulin (calcium-binding protein). It also inhibits the activity of certain secretagogues, such as E. coli enterotoxin, bile acids, and prostaglandin **E2**. The net effect is to inhibit the flow of intestinal contents. Additional actions are delayed stomach emptying, increased tone of the ileocecal valve and anal sphincter. Although loperamide is chemically related to opioids, it has no analgesic effects even at high doses.

PHARMACOKINETICS AND PHARMACODYNAMICS:

The sulfamethoxazole/trimethoprim combination is rapidly absorbed by the gastrointestinal tract. After a single dose, peak plasma concentrations are reached within 1 to 4 hours. Oral absorption is greater than 85%. The half-life is 10-12 hours; it has a good distribution to all tissues and body fluids. The compound is mainly eliminated by urine.

Sulfamethoxazole is widely distributed in all tissues and fluids of the body including synovial, pleural, peritoneal and ocular fluids. It is also excreted in breast milk and crosses the placental barrier. Likewise, trimethoprim is rapidly distributed in tissues and fluids: high concentrations of TMP are found in bile, aqueous humor, bone marrow, prostate and vaginal fluid. In cerebrospinal fluid, concentrations are usually 30 to 50% of those in the blood. Similar to SMX, trimethoprim is excreted in breast milk and crosses the placental barrier.

Trimethoprim binds 44% to plasma proteins and 70% to sulfamethoxazole. Both drugs are preferentially eliminated by the kidney after having experienced a certain metabolism in the liver. Up to 80% of trimethoprim and 20% of sulfamethoxazole are eliminated in the urine unchanged. Both products are excreted by glomerular filtration with some tubular secretion. Some of the sulfamethoxazole is reabsorbed.

Sulfamethoxazole/trimethoprim is generally bactericidal by inhibiting sequential enzymes involved in the synthesis of bacterial folic acid. Sulfamethoxazole is structurally similar to p-aminobutyric acid (PABA) competitively inhibiting the formation of folic acid from PABA. For its part, trimethoprim is added to the enzyme dihydrofolate reductase, which prevents the formation of tetrahydrofolic acid from dihydrofolate. Tetrahydro folic acid (THF) is the active form of folic acid without which the bacterium cannot synthesize thymine, leading to interference in the synthesis of nucleic acids and proteins. By acting by these two different mechanisms, the trimethoprim-sulfamethoxazole combination is synergistic against a large number of bacteria.

After oral administration of gentamicin, being an aminoglycoside its absorption at the gastrointestinal level is almost zero, therefore it only acts only on the intestinal lumen but is able to eliminate within 12 hours the bacteria existing in the intestine and can last the effect up to 72 hours.



Gentamicin irreversibly joins the 30S subunit of ribosome, interfering with the correct reading of the genetic code with the consequent blocking of the protein synthesis of the bacteria, the antibiotic on its way to the ribosome requires various transport mechanisms dependent on oxygen and energy.

The action of kaolin is especially on the digestive tract, it forms a protective layer that covers the mucosa and the crater of an ulcer (when it exists) but is not absorbed. It is a chemically inert powder but does not neutralize hydrochloric acid.

Its protective action, by decreasing irritation of the mucosa, can decrease some acid secretion. At the level of intestine in healthy animals it has little action, but in case of diarrhea it offers mechanical protection preventing the irritating action of the intestinal contents and toxins of bacteria.

Loperamide is poorly absorbed in the gastrointestinal tract; less than 40% reach their peak concentration within 4-5 hours. Its half-life fluctuates between 7-14 hours its tissue distribution is not well understood. It is bound to plasma proteins by 97%, metabolises via hepatic and the duration of its effect around 24 hours. 30% of the dose is eliminated unmetabolized in the feces, and 2% is excreted in the urine.

Kaolin and Pectin are gastrointestinal protectors and adsorbents, which have astringent and demulcent properties necessary to increase the consistency of feces, reduce the number of bowel movements and the loss of fluids and electrolytes, in patients with diarrheal pictures.

Its adsorbent properties favor the elimination of toxins and other irritating substances that cause diarrhea.

WARNINGS

- All opioids such as loperamide should be used with caution in patients with hypothyroidism, renal failure, Addison syndrome, geriatric or weak, with glaucoma, or with secondary diarrhea caused by toxins and/or Salmonella sp., intestinal obstruction, or abdominal trauma.
- They should also not be used when there are liver problems especially when there are nervous signs or in hepatic encephalopathies.
- They are also contraindicated in cases where the patient is hypersensitive to narcotic analgesics or who are being treated with amino oxidase inhibitors.
- Because loperamide is potentially a neurotoxic substrate of P-glycoprotein, it should be used with caution in herding dogs (e.g. collies, Shetland, Australian Shepherds, etc.) that may have the genetic mutation that causes a non-functional protein.
- In dogs, constipation, inflammation and sedation are the most likely adverse reactions encountered when used for long treatments. It can also cause paralytic ileus, toxic megacolon, pancreatitis, and effects on the CNS. The use of antidiarrheal opioids in cats is controversial; this species may react with altered (excited) behavior.
- They are also contraindicated in cases where the patient is hypersensitive to narcotic analgesics or who are being treated with taminooxidase inhibitors. It should be used with caution in patients with head injuries or increased pressure, respiratory diseases and/or liver problems. This product is for veterinary use only. Keep in a cool, dry place away from children.
- Keep in a dry place, cool no more than 30°C and protected from direct sunlight. Do not leave it within reach of children, pets and disabled people. Product for exclusive use in Veterinary Medicine.

SPECIES:

Cattle, Sheep, Goats, Swine, Canines and Felines.

ROUTE OF ADMINISTRATION: Oral.



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DOSE:**Cattle, (milk and meat) Sheep, goats (milk and meat), pigs and canines:**

1 ml per 5 kg of body weight every 12 hours (equivalent to Gentamicin 2.4 mg/kg body weight, Sulfamethoxazole 20 mg/kg body weight, Trimethoprim 4 mg/kg body weight and Loperamide 0.1 mg/kg body weight).

Felines:

0.5 ml per 5kg of body weight every 12 hours (equivalent to Gentamicin 1.2 mg/kg body weight, Sulfamethoxazole 10 mg/kg body weight, Trimethoprim 2 mg/kg body weight and Loperamide 0.05 mg/kg body weight).

WITHDRAWAL PERIOD:

MEAT: Cattle, Sheep and Goats 10 days

Pigs and piglets 10 days

MILK: Cattle, Sheep and Goats 7 days

Consult the Veterinary Zootechnician

Exclusive literature for veterinarians.

Its sale requires a prescription.

Content Managers: Technical Department

Bibliography

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GLP

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