

KiroPred 20

REGISTRATION NUMBER Q-0790-035

FORMULA:

Each tablet contains:

Prednisolone 20 mg.

Excipient q.s. 1 tablet

DOSAGE SIZE AND FORM: Bottle with 20 oral tablets
ORAL TABLETS



Prednisolone

Glucocorticoid

DESCRIPTION:

KiroPred 20 contains Prednisolone, an active metabolite of Prednisone that is an intermediate-acting glucocorticoid anti-inflammatory, predominantly glucocorticoid and with low mineralocorticoid activity. Glucocorticoids are natural or synthetic adrenal steroids that are rapidly absorbed from the gastrointestinal tract.

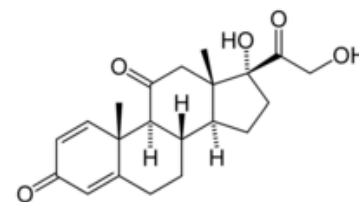
INDICATIONS:

They are used as replacement therapy in cases of adrenal deficiency states. Synthetic analogues such as prednisolone are mainly used for their potent anti-inflammatory effects. In dogs and cats, it is useful for treating a wide range of endocrine, musculoskeletal, and inflammatory diseases, and conditions of autoimmune diseases, such as skin, ear, eye, respiratory, hematologic, and neoplastic diseases, allergies, arthritis, ulcerative colitis, eosinophilic enteritis, systemic lupus erythematosus and disease with known response to corticosteroid treatment.

MECHANISM OF ACTION:

Prednisone and prednisolone are bioequivalent. In most species, prednisone is converted in the liver into prednisolone; however, cats and patients with liver failure do not seem to convert it efficiently.

It acts on almost all animal cells; with an anti-inflammatory potency 3 to 5 times greater than hydrocortisone, it easily crosses the cell membrane and binds with high affinity to cytoplasmic receptors. Activation of these receptors induces transcription and synthesis of specific proteins. This action is exerted directly on the tissues protecting them from inflammatory chemicals, preventing their reaction to them; inhibits edema, fibrin deposits, capillary dilation, and migration of macrophages to the site of inflammation, as well as capillary and fibroblast proliferation, collagen deposits and the formation of scars associated with inflammation. Prednisolone also has antiallergic action by blocking the action of histidine-decarboxylase, decreasing the synthesis of prostaglandins, and slowing epithelial regeneration.



PHARMACOKINETICS

Prednisolone is absorbed by all routes and is effective when administered orally.

90% of glucocorticoids or more are reversibly bound to proteins (albumin-corticosteroid-binding globulin). Almost all reduced metabolites are enzymatically coupled through the 3-hydroxyl with sulfate or glucuronic acid to form sulfate esters or water-soluble glucuronides, which are excreted as such. Its biotransformation occurs mainly by hepatic, renal and tissue routes, for the most part in inactive metabolites. Its elimination is mainly carried out by renal excretion of inactive metabolites.

EFFECTS OF PREDNISOLONE ON DIFFERENT TISSUES, ORGANS, AND SYSTEMS.

This can be taken as part of the treatment or as side effects, especially in long-term treatments.

In the **cardio-vascular system**, it reduces permeability and increases vasoconstriction. After its application it has a slight positive inotropic effect and increases blood pressure by being a vasoconstrictor.

At a **cellular level**, it inhibits the proliferation of fibroblasts, the response to macrophage migration and in general the response to chemical mediators of inflammation.

In the **Nervous system**, it lowers the pain threshold in wounds, alters mood and behavior, decreases the response to pyrogens and stimulates appetite.

Endocrine system: When dosed for a long time or at very high doses, the release of ACTH from the anterior pituitary is suppressed, reducing, or avoiding the emission of endogenous corticosteroids. Stress factors such as: kidney disease, liver disease and diabetes, can sometimes cancel the suppression of the effects of exogenously administered steroids. The release of thyrotropin (TSH), follicle stimulating hormone (FSH), prolactin and luteinizing hormone (LH) can be reduced when prednisolone is administered at pharmacological doses. The conversion of thyroxine (T₄) into triiodothyronine (T₃) can be decreased by prednisolone and increase plasma levels of parathyroid hormone. Prednisolone can inhibit osteoblastic and vasopressin (ADH) function by reducing the activity on the renal tubules, diuresis may occur.

Hematopoietic system: The number of circulating platelets, neutrophils and red blood cells can be observed increasing, but inhibiting platelet aggregation. It also inhibits the response of bone marrow and spleen (decreasing lymphocytes, monocytes, and eosinophils). Elimination of old red blood cells is slowed down. It can also provoke the involution of lymphoid tissue.

Gastrointestinal system: It increases the secretion of gastric acid, pepsin, and trypsin. The structure of mucin is modified; it reduces the proliferation of mucous cells and the absorption of calcium and iron.

At the **hepatic** level, there is an increase in fat and glycogen deposits in hepatocytes, serum levels of alanine-aminotransferase (ALT) and gamma-glutamyl transpeptidase (GGT) are increased. There may also be a significant increase in serum alkaline phosphatase.

Immune system: Prednisolone can decrease circulating levels of T lymphocytes; inhibit lymphokines; neutrophils, macrophages, and monocyte migration; it reduces interferon production; it inhibits chemotaxis and phagocytosis, antigen processing, and lowers the rate of intracellular death.

The acquired specific immunity is affected to a lesser extent than the nonspecific immune response. The complement cascade system is inhibited, and the clinical signs of infection are masked. Histamine synthesis is suppressed. Therefore, it is used in the treatment of autoimmune diseases such as Lupus, as an immunosuppressant.

Metabolic effects: Stimulates gluconeogenesis and increases the mobilization of fatty acids from tissues and their oxidation, as well as plasma levels of triglycerides, cholesterol, and glycerol.



Musculoskeletal disorders: Excess or deficiency of prednisolone can cause muscle weakness, atrophy, and osteoporosis. Bone growth can be stopped by inhibition of somatotropin, increased calcium excretion and inhibition of vitamin D activation.

In the reproductive system: Generally, has no effect, but excess doses at the beginning of pregnancy can have teratogenic effects. In ruminants and equines, its administration can induce labor when administered in the last stages of gestation. At high doses and/or prolonged administration to mothers can inhibit the growth of the newborn.

Kidney, fluids, and electrolytes: Prednisolone can increase potassium; excretion of calcium, sodium, and chlorine in urine, reabsorption of extracellular fluid and increase excretion. Hypokalemia and/or hypocalcemia rarely occur. Diuresis can also be induced.

Skin: Thinning of the dermal tissue, distension of hair follicles, which can lead to alopecia.

The aforementioned effects are generally not considered adverse reactions and many of these effects only occur at high doses and in long-term treatments, so it is recommended to monitor the patient under treatment.

Customer information: Customers should carefully follow the dosage instructions and **not** abruptly discontinue the drug without consulting with the veterinary doctor first. Customers should be informed about the possible adverse effects that can be seen with this type of drugs.

SPECIES: Canines and felines

DOSE KIROPRED 20

ANTI-INFLAMMATORY DOSE: 0.5 to 1 mg/kg of weight every 12 hours (equivalent to 1 tablet for every 20 - 40 kilos of weight)

IMMUNOSUPPRESSIVE DOSE: 2 mg/kg of weight every 12 hours (equivalent to one tablet per 10 kg of weight)

ROUTE OF ADMINISTRATION: Oral

SUGGESTED DOSES

0.2 - 2.2 mg/kg per day. The dose is variable and should be individualized based on the specific disease, severity, and response of the patient. The initial dose should be maintained or adjusted until a satisfactory response is observed, and it should be gradually decreased after the problem has been resolved. The decrease in the dose will also depend on the time of dosing, when dosed in short periods (3 to 7 days) it can be carried out in a staggered manner during the two or three final days of treatment, so a short treatment could last from 6 to 10 days.

In the case of treatments that last for more than a week, the dose should be reduced little by little, which could take an average of 7 to 15 days to achieve proper handling of the product.

In tumors as an adjuvant:

In tumors of the **central nervous system** 0.5 - 1 mg/kg orally once a day, then decrease the dose over the next week or month, depending on the patient's needs. In **canine lymphomas**: various protocols 25 mg/m², orally. In **multiple myeloma**: 0.5 mg/kg. In the case of **macroglobulinemia** dosage: 0.5 mg/kg once a day orally.

Adjuvant for the treatment of respiratory disorders:

- Chronic or allergic, eosinophilic bronchitis: 0.5 - 1 mg/kg orally every 24 hours.
- Trachea collapse: Initially 0.5 mg/kg orally, once, or twice a day.

For therapy of gastrointestinal tract disorders:

- For eosinophilic colitis or gastritis: 0.5 - 2 mg/kg orally for 7 to 10 days. In eosinophilic enteritis: 0.5 mg/kg once a day (7 to 10 days). For lymphocytic or plasmocytic enteritis: 2.2 mg/kg/day divided into two oral doses for 5 to 10 days. For superficial chronic gastritis: 0.5 - 1.0 mg/kg.
- In the case of food allergy or intolerance: 0.5 mg/kg once a day orally;
- For exocrine pancreatic: 1 - 2 mg/kg every 12 hours orally for 7 to 14 days,

For diseases of the adrenal gland:

In subacute or chronic adrenal insufficiency as an adjunct to treatment: 0.2 - 0.4 mg/kg/day orally. In azotemia, when the results with other drugs are not enough: 0.1 - 0.3 mg/kg/day orally.

For joint therapy in intoxications:

1 - 2 mg/kg, 2 to 3 times a day

For reproductive disorders therapy:

In female dogs prone to relapses after initial treatment of eclampsia 0.25 mg/kg

For CNS disorders:

For granulomatous meningoencephalitis, non-bacterial meningitis, reticulosis, hydrocephalus: prednisone 1 - 2 mg/kg per day orally twice a day for life, gradually reducing the dose.

For adjuvant therapy in intervertebral disc disease (IVD):

For cervical, thoraco-lumbar injuries: 0.5 mg/kg orally for 3 days, then 0.5 mg/kg once a day for 3 to 5 days.

For dermatological or other immuno-mediated disorders

- For adjuvant treatment of urticaria and angioedema: 2 mg/kg orally, to be reduced slowly if the treatment is longer than one week.
- In the case of canine atopy: 0.5 mg/kg orally initially for 5 to 10 days, then gradually decrease the dose until the minimum effect dose is reached.
- For hypersensitivity type II (cytotoxic): 2 mg/kg twice a day
- In the case of surface therapy pyoderma: 1 mg/kg/day for 5 to 7 days.
- For immune-mediated arthritis: 2 - 4 mg/kg/day is the initial treatment. After an induction period of 2 to 3 weeks, the dose is decreased to 1 - 2 mg/kg/day if the synovial fluid is not inflammatory. After 3 to 4 weeks of interval, the dose should be brought to 1 mg/kg every other day and if there is remission of signs, discontinue after 2 or 3 months.

*As anti-inflammatory drugs in the adjuvant treatment of **internal otitis**:*

0.25 mg/kg/day for the first 5 to 7 days of treatment.

For **adjuvant** therapy of *myasthenia gravis*: to 0.5 mg/kg/day orally, increase by 0.5 mg/kg/day every 2 to 4 days until the total dose is 2 mg/kg/day.

**Cats:**

As an immunosuppressive agent:

Initially 2 - 4 mg/kg daily in split doses. Reduce the dose every other day to a low dose as allowed by the patient.

Adjuvant for the treatment of respiratory disorders:

- In the case of feline asthma therapy: 1 - 2 mg/kg/day (Papich 1986)
- For emergency events: 5 mg of prednisone orally three times a day initially, and then rapidly decrease to once a day. (Nobody 1986)

For therapy of gastrointestinal tract disorders:

- For plasmocytic and lymphocytic enteritis: 2 mg/kg split into two oral doses daily for 5 to 10 days, then 1 mg/kg/day for 5 to 10 days, then reduce the dose.
- In inflammatory bowel disease: 1 - 2 mg/kg/day split into 2 doses. Treatment can last up to 3 months

Warning

- Corticosteroids may mask some signs of infection and it may be necessary to suspend treatment until the diagnosis is reassessed.
- Corticosteroid overdosage can result in sodium retention, fluid retention, potassium loss, weight gain, and thin skin.
- Prolonged use and without proper supervision can lead to endocrine disruptions such as Cushing's disease (ACTH suppression). It can also cause anorexia, nausea, vomiting, fever, pain, behavior change, osteoporosis.
- Do not suddenly suspend its application if it was used for prolonged periods.
- Store in a cool, dry place.
- Keep out of reach of children.

Drug-Drug interactions:

Simultaneous administration with phenobarbital, phenytoin, ephedrine decreases the therapeutic effect of prednisolone by increasing its metabolism.

The application of a corticosteroid and diuretic can produce potassium depletion that favors hypokalemia.

A corticosteroid with glycosides can raise the possibility of arrhythmias or digitalis poisoning.

The combination of glucocorticoids with non-corticosteroid anti-inflammatory drugs can lead to gastrointestinal ulcers.

Vaccines based on dead or inactivated microorganisms do not pose any danger to patients treated with corticosteroids, although the immune response is not as good as that achieved in normal animals, booster doses may be necessary. Live virus vaccines should not be administered to patients treated with corticosteroids, who are immunocompromised, due to the possibility of virus replication and adverse reactions.

The risk of gastrointestinal adverse reactions caused by non-steroidal anti-inflammatory drugs increases if a corticosteroid is administered concomitantly.

Contraindications

- Traditionally, it has been said that corticosteroids are contraindicated in patients with systemic fungal infections. However, many clinicians have the opinion that corticosteroids can be administered to these patients as long as adequate antifungal treatment has been established. Secondary infections are frequent during treatment with corticosteroids, due to their immunosuppressive effect.



- Corticosteroids should be used with caution in patients with gastrointestinal diseases due to the possibility of intestinal perforation and in patients with liver diseases that cause albuminemia such as cirrhosis. Although corticosteroids are used for the treatment of acute exacerbations of some gastrointestinal diseases, such as ulcerative colitis, their long-term use is not recommended. Corticosteroids should not be used in patients with peptic ulcer unless there are extreme cases that make their use inevitable.
- Therapeutic doses of corticosteroids administered for long periods of time suppress hypothalamic-pituitary-adrenal function and, if abruptly discontinued, can cause acute adrenal insufficiency. It is therefore necessary to discontinue corticosteroids gradually considering that hypothalamic-pituitary-adrenal suppression can last for months.
- In general, patients treated with corticosteroids should not be immunized with live virus-based vaccines, in particular when used in immunosuppressive doses. It is recommended that vaccinations be carried out at least 2 weeks before starting the administration of the corticosteroid.

Precautions and relation with effects of carcinogenic, mutagenic, teratogenesis and on fertility:

Not reported to date.

WARNINGS AND/OR RESTRICTIONS:

It can provoke Na retention, edema, hypotension, acne, hirsute hair, thin skin, round face, capillary fragility. ACTH suppression, adenocortical insufficiency, anorexia, nausea, vomiting, lethargy, fever, pain, behavior change. Osteoporosis. Do not suddenly suspend its application if it was used for prolonged periods. Keep in a cool, dry place, in a range within 15-30 °C and protected from direct sunlight. Keep out of reach of children and pets. Product for exclusive use in Veterinary Medicine.

**AVAILABLE BY PRESCRIPTION ONLY
CONSULT A VETERINARY DOCTOR**