

KETOCONAZOLE

BRAND NAME: NIZORAL

AVAILABLE IN
200 mg
TABLETS

BACKGROUND

Fungal infections are generally resistant to therapy. Treatment is prolonged, often requiring months depending on how deep the infection is and how strong the patient's immune system is. Fungal infections can be limited to the skin such as with "Ringworm" or Malassezia dermatitis, or they can involve more crucial organs such as the lung, bone, even the nervous system. The superficial infections can generally be eradicated in a matter of weeks while the deeper infections may take over a year.

In the past, the only treatment for life-threatening fungal infections was a medication called Amphotericin B. This medication could only be given intravenously in a fluid drip and was associated with a high incidence of kidney failure (some sources say up to 50%). Obviously, an innovation in treatment was needed. Ketoconazole represents this innovation. Ketoconazole not only is free from renal side effects, but is also given orally as a tablet sparing patients expensive hospitalization time.

Since ketoconazole's introduction, related anti-fungals have been released to improve upon its activity. For example, itraconazole was introduced to reduce the incidence of nausea side effects. Fluconazole was developed to improve penetration of the central nervous system and treat fungal infections there. With the introduction of generic forms ketoconazole and its relatives, treatment of fungal disease can be affordable, safer, and more effective.

HOW THIS MEDICATION WORKS

Ketoconazole works by interfering with the structure of the fungal cell wall. Depending on the fungus and depending on the dose used, ketoconazole may kill the fungus or just inhibit its ability to reproduce. Fungal infections for which ketoconazole is commonly used include:

- Malassezia Dermatitis
- Aspergillosis
- Cryptococcosis
- Coccidiomycosis (Valley Fever)
- Histoplasmosis
- Blastomycosis
- Dermatophytosis (Ringworm), though other medications are preferred

There is another effect of ketoconazole that is generally thought of as a side effect but can be used as therapeutic goal. Ketoconazole can also be used to slow the body's removal of the immunomodulating drug, cyclosporine. Cyclosporine is presently a very expensive medication so using ketoconazole to spare its use may reduce the dose requirement to make treatment affordable.

Ketoconazole also blocks the synthesis of cortisone in the adrenal gland. This means that ketoconazole can be used in the treatment of Cushing's disease, where an excess amount of adrenal hormone is produced. That said, other medications are more effective and are preferred.

SIDE EFFECTS

- The most common side effects are nausea, vomiting, and diarrhea. These may be reduced by giving ketoconazole with food or by dividing the dose into several smaller doses. If nausea is severe, it should resolve with discontinuation of the medication.
- At higher doses or in certain individuals, liver disease can result from administration but this should resolve with discontinuation of the medication. This is usually a problem for cats rather than dogs and can be dose-dependent or independent and consists of cholangiohepatitis-type inflammation.

- The liver enzymes routinely measured on a blood panel commonly increase with ketoconazole use and does not necessarily indicate the development of the liver reaction mentioned above. When ketoconazole use is long term, liver enzymes should be monitored.
- Some individuals will show a lightening of the hair coat while taking ketoconazole. This effect reverses with discontinuation of the medication.
- Ketoconazole interferes with testicular secretion of testosterone and may produce a feminizing effect in males.
- Ketoconazole also interferes with the adrenal gland's production of cortisone and can thus be used in the treatment of Cushing's Disease. For more information on this subject, click here.
- Ketoconazole is not safe for use during pregnancy and should not be handled by pregnant women.

The lethal dose of this medication is at least 50 times the usual recommended dose, thus serious side effects are unusual (despite the fact that nausea and upset stomach are not unusual).

INTERACTIONS WITH OTHER DRUGS

- Ketoconazole is better absorbed in the presence of acid thus it is better not to give ketoconazole in the presence of antacids. Sucralfate, another medication used for stomach ulceration, may also interfere with absorption of ketoconazole. Stagger ketoconazole and antacids by a couple of hours if possible.
- Cyclosporine, an immune suppressive agents used in transplant patients as well as in certain immune mediated conditions, will have increased blood levels when it is given in the presence of ketoconazole. As mentioned, this pharmacological "trick" can be exploited to reduce the dose of cyclosporine.
- Other drugs that may have higher blood levels or stronger effects than normal include: methylprednisolone (a corticosteroid), glipizide (an oral medication for diabetes mellitus), cyclophosphamide (an agent of chemotherapy), ivermectin (in higher doses), vincristine (used in cancer chemotherapy), tramadol (a pain management drug), cannabinoids, opioids, antianxiety medications (clomipramine, buspirone, trazodone, benzodiazepines such as alprazolam, or amitriptyline) and warfarin (an anticoagulant).
- Another medication that can potentially be pushed into a toxic range by concurrent ketoconazole is colchicine. This bears special mention because Shar pei with fever syndrome might require treatment for fungal skin disease, which is common in this breed.
- Macrolide antibiotics such as azithromycin and erythromycin can increase ketoconazole concentrations and increase the likelihood of ketoconazole side effects.
- When ketoconazole and cisapride are used concurrently, dangerous heart rhythm disturbances can result; these medications should not be used together.
- Theophylline, an airway dilator, may be less effective with concurrent use of ketoconazole.

CONCERNS AND CAUTIONS

- Ketoconazole is best not used in breeding male animals due to its feminization effect. It is also best avoided in patients with pre-existing liver disease or with decreased platelet (blood clotting cell) levels.
- Ketoconazole has potential to cause birth defects.
- When ketoconazole therapy will continue for months at a time, many veterinarians will monitor liver enzymes and complete blood counts. This is not necessary when medication is used for only a few weeks.
- Ketoconazole is absorbed into the body best when it is given with food.
- Normal liver function is required for the body to properly process ketoconazole. If a patient has pre-existing liver disease or is harboring a diseased liver that had not yet declared symptoms, the use of a medication that processed by the liver may over-tax the liver and clinical disease can develop. Symptoms could mimic the nausea side effect that is relatively common and benign with ketoconazole. Since it may be difficult to interpret the significance of nausea symptoms, it is important to report any such symptoms to your veterinarian so he or she can determine the best course.
- STORE AT ROOM TEMPERATURE PROTECTED FROM LIGHT.
- IF A DOSE IS SKIPPED, DO NOT DOUBLE UP ON THE NEXT DOSE.



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