Racona Capsule

(Itraconazole Capsules USP)

ریکونا کیپسولز

(اٹراکونازول یو ایس پی)

COMPOSITION: Each capsule contains:
Itraconazole immediate Release Coated Pellets Eq. to Itraconazole ... 100mg.
[USP Specs.]

BOXED WARNING

Congestive Heart Failure, Cardiac Effects and Drug Interactions: Itraconazole Capsules should not be administered for the treatment of onychomycosis in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or a history of CHF. If signs or symptoms of congestive heart failure occur during administration of Itraconazole Capsules, discontinue administration. **Drug Interactions:** Coadministration of cisapride, pimozide, quinidine, defetilide, or levacitilemethadol (levomethadyl) with itraconazole capsule is contraindicated. Itraconazole a potent cytochrome P450 3A4 isoenzyme system (CYP3A4) inhibitor may increased plasma concentrations of drugs metabolized by this pathway. Serious cardiovascular events, including QT prolongation, torsade de pointes, ventricular tachycardia, cardiac arrest and/or sudden death have been occurred in patients using cisapride, pimozide, levacetylmethadole, (levomathadyl) or quinidine, concomitantly with itaconazole and/or other CYP 3A4 inhibitors.

DESCRIPTION: Itraconazole is Antimycotics for systemic use, triazole derivatives.
When administered orally, it has shown fungistatic activity against superficial dermatophytes and Candida species including C. albicans and C. glabrata. Itraconazole has shown *in vitro* antifungal activity against a variety of fungi and yeasts.

CLINICAL PHARMACOLOGY:
Mechanism of Action: Itraconazole inhibits fungal 14α-demethylase, resulting in a depletion of ergosterol and disruption of membrane synthesis by fungi.
Pharmacokinetics: General pharmacokinetic characteristics: The pharmacokinetics of Itraconazole has been investigated in healthy subjects, special populations and patients after single and multiple dosing.
Absorption: Itraconazole is rapidly absorbed after oral administration. Peak plasma concentrations of the unchanged drug are reached within 2 to 5 hours following an oral dose. The observed absolute bioavailability of Itraconazole is about 55%. Oral bioavailability is maximal when the capsules are taken immediately after a full meal.
Distribution: Most of the Itraconazole in plasma is bound to protein (99.8%) with albumin being the main binding component (99.6% for the hydroxy- metabolite). It has also a marked affinity for lipids. Only 0.2% of the Itraconazole in plasma is present as free drug. Itraconazole is distributed in a large apparent volume in the body (> 700 L), suggesting its extensive distribution into tissues: Concentrations in lung, kidney, liver, bone, stomach, spleen and muscle were found to be two to three times higher than corresponding concentrations in plasma. Brain to plasma ratios were about 1 as measured in beagle dogs. The uptake into keratinous tissues, skin in particular, is up to four times higher than in plasma.
Biotransformation: Itraconazole is extensively metabolised by the liver into a large number of metabolites. One of the main metabolites is hydroxy-itraconazole, which has *in vitro* antifungal activity comparable to Itraconazole. Plasma concentrations of the hydroxy-itraconazole are about twice those of itraconazole. As shown in *in vitro* studies, CYP 3A4 is the major enzyme that is involved in the metabolism of Itraconazole.
Elimination: Itraconazole is excreted as inactive metabolites to about 35% in urine within one week and to about 54% with feces. Renal excretion of the parent drug accounts for less than 0.03% of the dose, whereas fecal excretion of unchanged drug varies between 3-18% of the dose. Itraconazole clearance decreases at higher doses due to saturable hepatic metabolism.

INDICATIONS: Itraconazole is indicated for the treatment of the following fungal infections when thought likely to be susceptible:
- Vulvovaginal candidiasis.
- Pityriasis versicolor.
- Dermatophytoses caused by organisms susceptible to Itraconazole (Trichophyton spp. Microsporum spp. Epidermophyton floccosum) e.g. tinea pedis, tinea cruris, tinea corporis, tinea manuum.
- Oral candidiasis.
- Onychomycosis caused by dermatophytes and/or yeasts.

DOSAGE AND ADMINISTRATION:
Treatment schedules in adults for each indication are as follows:

Indication	Dose
Vulvovaginal candidiasis	200 (Two capsules of 100mg) mg twice daily for 1 day
Pityriasis versicolor	200mg (Two capsules of 100mg) once daily for 7 days
Tinea corporis, tinea cruris	100mg once daily for 15 days
Tinea pedis, tinea manuum	100mg once daily for 30 days
Oral candidiasis	100mg once daily for 14 days
Onychomycosis	200mg (Two capsules of 100mg) once daily for 3 months

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For skin infections, optimal clinical and mycological effects are reached at 1-4 weeks after cessation of treatment and for nail infections at 6-9 months after the cessation of treatment. This is because elimination of Itraconazole from skin and nails is slower than from plasma.
In Acquired Immune Deficiency Syndrome and neutropenic patients: for the treatment of oral candidiasis 200mg (Two capsules of 100mg) mg once daily for 14 days is recommended due to the impaired absorption of Itraconazole in these patient groups. The length of treatment for systemic fungal infections should be dictated by the mycological and clinical response to therapy.
Paediatric population: Since clinical data on the use of Itraconazole in paediatric patients is limited, its use in children is not recommended, unless the potential benefit outweighs the potential risks.
Elderly: There are inadequate data on Itraconazole in elderly for its use to be recommended, unless the potential benefits outweigh the risks.
Hepatic impairment: Itraconazole is predominantly metabolised by the liver. A slight decrease in oral bioavailability in cirrhotic patients has been observed, although this was not of statistical significance. The terminal half-life was significantly increased. The dose should be adapted if necessary. Monitoring of plasma levels may be necessary.
Renal impairment: The oral bioavailability of Itraconazole may be lower in patients with renal insufficiency. Dose adjustment may be considered. Monitoring of plasma levels may be necessary. Itraconazole cannot be removed by dialysis.
Decreased gastric acidity: Absorption of itraconazole is impaired when gastric acidity is decreased.

CONTRAINDICATIONS: Itraconazole is contraindicated in patients with known hypersensitivity to the active substance or to any of the excipients.

WARNINGS AND PRECAUTIONS: Itraconazole capsule should not be administered for the treatment of onychomycosis in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or a history of CHF, If signs and symptoms of congestive heart failure occur during administration of Itraconazole capsules discontinue administration.

PREGNANCY AND LACTATION: Itraconazole must not be used during pregnancy except for life-threatening cases where the potential benefit to the mother outweighs the potential harm to the fetus.
A very small amount of Itraconazole is excreted in human milk. The expected benefits of Itraconazole capsules therapy should therefore be weighed against the potential risk of breast-feeding. In case of doubt, the patient should not breast-feed.

SIDE EFFECTS: Racona Capsules appears to be a relatively safe drug. Side effects, usually minor, are more likely during a prolonged course of treatment. Cases of nausea and vomiting, constipation, headache and dizziness are observed. Abnormal liver function tests are also observed in patients with long-term therapy, urticarial, endocrine effects including enlarged breast (In males) and adrenal suppression, tingling in the fingers and toes (Very rare) and congestive heart failure were also observed rarely.

DRUG INTERACTIONS: As **Racona** need acid for its absorption, antacid, H_2 receptor antagonists (Cimetidine, Famotidine, Ranitidine) and Omeprazole should not be taken for 2 hours after **Racona. Racona** increases the concentration of some drugs.
Those on Racona should not take these drugs:
• Cispride • HMG-CoA reductase inhibitors (Atorvastatin, Lovastatin, Simvastatin); Fluvastatin and Prevastatin) are acceptable alternatives. • Midazolam and Trizolam. • The antihistamines, Astemizole and Terfenadine.
The dose of these drugs should be reduced:
• Warfarin • Digoxin • Methyl prednisolone • Cyclosporin • Tacrolimus • Vinca alkaloids.
The dose of these drugs may need reducing if side effects arise:
• Quinidine • Calcium channel blockers • Antidiabetic sulphonylurea medication (Tolbutamide, Glibenclamide, Gliclazide, Glipizide)
The following drugs decreases the concentration of Racona (Itraconazole):
• Rifampicin • Isoniazid • Phenytoin and Carbamazepine **Racona** is not thought to inactive with the oral contraceptive pill.

OVERDOSE: No data are available. In the event of an overdose, supportive measures should be employed. Within the first hour after ingestion, gastric lavage may be performed. Activated charcoal may be given if considered appropriate.
Itraconazole cannot be removed by haemodialysis. No specific antidote is available.

INSTRUCTIONS: Store below 30°C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION: Racona 100mg Capsules are available in pack size of 4's.

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
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