FUNGICIDE

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory

Abbreviated Prescribing information for FUNGICIDE TAB (Ketoconazole 200mg Tablets)

[Please refer the complete prescribing information available at www.torrentpharma.com]

MECHANISM OF ACTION: Ketoconazole is a steroidogenesis inhibitor. Ketoconazole is an imidazole derivative that is a potent inhibitor of cortisol synthesis resulting from its ability to inhibit several cytochrome P450 enzymes in the adrenal glands. Ketoconazole inhibits primarily the activity of 17α-hydroxylase, but it also inhibits 11-hydroxylation steps, and at higher doses the cholesterol side-chain cleavage enzyme. Therefore, ketoconazole is an inhibitor of cortisol and aldosterone synthesis. Ketoconazole is also a potent inhibitor of androgens synthesis, inhibiting the activity of C17-20 lyase in the adrenals and also in Leydig cells. Apart from adrenal blocking effect, ketoconazole may also have direct effects on corticotropic tumour cells in patients with Cushing's disease

DOSAGE AND ADMINISTRATION: 200 mg Uncoated Tablet. For oral administration.

CONTRAINDICATION: Coadministration of a number of CYP3A4 substrates is contraindicated with Ketoconazole Tablets. Contraindicated in patients with Pregnancy, Breastfeeding, ergot alkaloids (eg dihydroergotamine, ergometrine (ergonovine), ergotamine and methylergometrine (methylergonovine) due to an increased risk of ergotism and other serious vasospastic adverse reactions acute or chronic liver disease, hyperkalemia and hypotension, dabigatran due to an increased bleeding risk; eplerenone due to an increased risk of hyperkalemia, telithromycin and clarithromycin in patients with severe renal impairment due to an increased risk of hepatotoxicity, quetiapine due to an increased risk of toxicity and QT interval prolongation and hypotension and to the patients having hypersensitivity to the drug, vardenafil in men older than 75-years due to increased risk of adverse reactions, fesoterodine and solifenacin in patients with renal impairment and tolvaptan used for a specific disease called “syndrome of inappropriate antidiuretic hormone secretion.

WARNINGS & PRECAUTIONS: Monitoring of liver function , Monitoring of adrenal function, Block and replace regimen, Monitoring of the QTc interval, Contraception, Decreased gastric acidity , Potential interaction with medicinal products, Use with hepatotoxic medicinal products , Use with hepatotoxic medicinal products , Co-administration of ketoconazole and other medicinal products known to have potentially hepatotoxic effect (eg paracetamol) is not recommended since the combination may lead to increased risk of liver damage, Use with pasireotide, Coexisting inflammatory/autoimmune disorders , Patients should be advised against alcohol consumption while on treatment and Warning regarding excipients : This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucosegalactose malabsorption should not take this medicine.

DRUG INTERACTION: Concomitant therapy with medicinal products that are contraindicated during treatment with ketoconazole and resulting in potentially life-threatening adverse reactions : CYP3A4 metabolised HMG-CoA reductase inhibitors (e.g. simvastatin, atorvastatin and lovastatin) due to an increased risk of skeletal muscle toxicity including rhabdomyolysis; eplerenone due to an increased risk of hyperkalemia and hypotension; substances that may have their plasma concentrations increased and have QT prolonging potential : methadone, disopyramide, quinidine, dronedarone, pimozide, sertindole, saquinavir (saquinavir/ritonavir 1000/100 mg bid), ranolazine, mizolastine, halofantrine, dabigatran due to an increased bleeding risk, triazolam, oral midazolam and alprazolam due to potential for prolonged or increased sedation and respiratory depression, ergot alkaloids (eg dihydroergotamine, ergometrine (ergonovine), ergotamine and methylergometrine (methylergonovine) due to an increased risk of ergotism and other serious vasospastic adverse reactions events, lurasidone, quetiapine due to an increased risk of toxicity, telithromycin and clarithromycin in patients with severe renal impairment due to an increased risk of hepatotoxicity and QT interval prolongation, felodipine,

nisoldipine due to an increased risk of oedema and congestive heart failure, colchicine in patients with renal impairment due to an increased risk of severe adverse reactions, irinotecan due to an alteration of the metabolism of this medicinal product, everolimus, sirolimus (also known as rapamycin) due to an increase of the plasma concentrations of these medicinal products, vardenafil in men older than 75-years due to increased risk of adverse reactions, paritaprevir/ombitasvir (ritonavir) due to increased risk of adverse reactions, fesoterodine and solifenacin in patients with renal impairment, tolvaptan used for a specific disease called "syndrome of inappropriate antidiuretic hormone secretion". Interactions and recommendations for co-administration: Analgesic opioid, Antiarrhythmics, Anticoagulants and antiplatelet drugs, Anticonvulsants, Antidiabetics, Anti-infectives, Antipsychotics, Anxiolytics and Hypnotics, Antivirals products, Phosphodiesterase(PDE5) inhibitors, Respiratory Drugs, Lipid Lowering Drugs, Gastrointestinal Drugs, Cardiovascular Drugs, Miscellaneous, Calcium Channel Blockers, Beta Blockers. Other interactions

Exceptional cases of a disulfiram-like reaction have been reported when ketoconazole was co-administered with alcohol, characterised by flushing, rash, peripheral oedema, nausea and headache, have been reported. All symptoms resolved completely within a few hours.

Co-administration of ketoconazole and pasireotide is not recommended since the combination can lead to a QT prolongation in patients with known cardiac rhythm disorders.

There is no evidence to suggest that there is an interaction between ketoconazole and other steroidogenesis inhibitors (i.e. metyrapone).

ADVERSE REACTIONS: Anaphylactoid reaction, Gynecomastia, Alcohol intolerance, Hyperlipidemia, Insomnia, Nervousness, Headache, Dizziness, Paresthesia, Somnolence, Photophobia, Orthostatic hypotension, Epistaxis, Vomiting, Diarrhea, Nausea, Constipation, Abdominal pain, Dry mouth, Dysgeusia, Dyspepsia, Flatulence, Tongue discoloration, Hepatic function abnormal, Erythema multiforme, Rash, Dermatitis, Erythema, Urticaria, Pruritus, Alopecia, Xeroderma, Myalgia, Menstrual disorder, Asthenia, Fatigue, Hot flush, Malaise, Edema peripheral, Pyrexia, Chills, Platelet count decreased, reversible intracranial pressure increased, serious hepatotoxicity, acute generalized exanthematous pustulosis, arthralgia and erectile dysfunction.

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.
Torrent house, Off Ashram road,
Ahmedabad - 380009, INDIA

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(Additional information is available on request)