西亚试剂® Xiya Reagent 说明书

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化 学 品 安 全 技 术 说 明 书

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MSDS标题

KETOCONAZOLE MSDS报告

产品标题

酮康唑

CAS号

65277-42-1

化学品及企业标识

PRODUCT NAME

KETOCONAZOLE

NFPA

Flammability	1
Toxicity	3
Body Contact	0
Reactivity	1
Chronic	2

SCALE: Min/Nil=0 Low=1 Moderate=2 High=3 Extreme=4

PRODUCT USE

Lipoxygenase (LOX) inhibitor; LOXs belong to a heterogenous family of lipid- peroxidising enzymes and are involved in the biosynthesis of mediators of inflammation. Orally active, broad spectrum anti- fungal agent with activity similar to that of miconazole. It has been given by mouth in the treatment of systemic mycotic infections in a dose of 200 mg once or twice daily with meals. A maximum of 400 mg once daily has been used when necessary.

Available as scored tablets of 200 mg. Also used dermally (2%) in an aqueous cream base. The material exerts a fungistatic effect at plasma levels (mean approx. 3.5 ug/ml) achieved following an oral dose of 200 mg.

SYNONYMS

C26-H28-Cl2-N4-O4, "cis-1-acetyl-4-[(2-(2, 4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1, 3-", "cis-1-acetyl-4-[(2-(2, 4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1, 3-", dioxolan-4-yl]-methoxy]phenyl]piperazine, dioxolan-4-yl]-methoxy]phenyl]piperazine, Fungarest, Fungoral, Ketoconazol, Ketoderm, Ketoisdin, R-41400, R-41400, Elubiol, Nizoral, "Orifungal M", Panfungol, "imidazole anti-fungal antimycotic azole agent"

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW

RISK

Toxic if swallowed.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

Toxic effects may result from the accidental ingestion of the material; animal experiments indicate that ingestion of less than 40 gram may be fatal or may produce serious damage to the health of the individual. Aromatase inhibitors produce several side effects including mood swing, depression, weight gain, hot flushes, vaginal dryness, bloating, early onset of menopause. Long-term use may result in bone weakness, increased risk of blood clots, gastrointestinal disturbance,and sweats. Aromatase inhibitors lower the level of oestrogen in post-menopausal women who have hormone-receptor-positive breast cancers. Prior to menopause oestrogen is mostly produced in the ovaries. Post-menopausal women produce oestrogen from another hormone, androgen. Aromatase inhibitors prevent the enzyme, aromatase from catalysing this reaction. Breast cancer cell growth in post-menopausal women is stimulated by oestrogen. At sufficiently high doses the material may be hepatotoxic(i.e. poisonous to the liver).

EYE

Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn). Slight abrasive damage may also result. The material may produce foreign body irritation in certain individuals.

SKIN

Skin contact is not thought to produce harmful health effects (as classified using animal models). Systemic harm, however, has been identified following exposure of animals by at least one other route and the material may still produce health damage following entry through wounds, lesions or abrasions. Good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting. Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

The material is not thought to produce respiratory irritation (as classified using animal models). Nevertheless inhalation of dusts, or fume, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress. Inhalation of dusts, generated by the material during the course of normal handling, may be damaging to the health of the individual.

CHRONIC HEALTH EFFECTS

Exposure to the material may cause concerns for human fertility, on the basis that similar materials provide some evidence of impaired fertility in the absence of toxic effects, or evidence of impaired fertility occurring at around the same dose levels as other toxic effects, but which are not a secondary non-specific consequence of other toxic effects.. Based on experience with animal studies, there is a possibility that exposure to the material may result in toxic effects to the development of the fetus, at levels which do not cause significant toxic effects to the mother. Imidazole is structurally related to histamine and has been used as an antagonist to counteract the effects of excess histamine found in certain induced physiological conditions (it therefore acts as an antihistamine). Imidazoles have been reported to disrupt male fertility through disruption of testicular function. 2-Methylimidazole decreased luteinising hormone secretion and tissue interstitial fluid testosterone concentration two hours after injection into Sprague Dawley rats. Imidazoles bind to cytochrome P450 haeme, resulting in inhibition of catalysis. However, 2-substituted imidazoles are considered to be poor inhibitors. Imidazole is probably an inducer of cytochrome P4502E1. In general, inducers of this isozyme stabilise the enzyme by preventing phosporylation of a serine which leads to haeme loss. Several drugs containing an imidazole moiety were retained and bound in connective tissue when administered to laboratory animals. The bound material was primarily recovered from elastin (70%) and the collagen. It is postulated that reaction with aldehydes gives an aldol condensation product. Azole fungicides show a broad antifungal activity and are used either to prevent fungal infections or to cure an infection. Therefore, they are important tools in integrated agricultural production. According to their chemical structure, azole compounds are classified into triazoles and

imidazoles; however, their antifungal activity is due to the same molecular mechanism. The cell membrane assembly of fungi and yeast is disturbed by blocking the synthesis of the essential membrane component ergosterol. This fundamental biochemical mechanism is the basis for the use of azole fungicides in agriculture and in human and veterinary antimycotic therapies. The enzyme involved is sterol 14[alpha]-demethylase, which is found in several phyla. In mammals, it converts lanosterol into the meiosis-activating sterols (MAS) which regulate or modify cell division. These precursors of cholesterol have been discovered to moderate the development of male and female germ (sexual) cells. Several metabolites of lanosterol have been regarded only as precursors of cholesterol without any biological function in animals. This view dramatically changed recently with the observation that FF-MAS isolated from human follicle fluid and T-MAS isolated from bull testis as well as the MAS- 412 and MAS-414 induced resumption of meiosis in cultivated mouse oocytes (Byskov et al. 1995). Aromatase is another target enzyme of azole compounds. In steroidogenesis, it converts androgens into the corresponding estrogens. The importance of androgens and estrogens for the development of reproductive organs, for fertility, and in certain sex steroid- dependent diseases is well known. Therefore, azole compounds can be directed against aromatase to treat estrogen-responsive diseases. Based on the inhibitory activity of azoles on key enzymes involved in sex steroid hormone synthesis, it is likely that effects on fertility, sexual behavior, and reproductive organ development will occur depending on dose level and duration of treatment of laboratory animals. Several azole compounds were shown to inhibit the aromatase and to disturb the balance of androgens and estrogens in vivo. In fact, the clinical use of azole compounds in estrogen-dependent diseases is based on this effect. Additionally, azole antifungals developed to inhibit the sterol 14[alpha]-demethylase of fungi and yeast in agriculture and medicine are also inhibiting aromatase. Therefore, these antifungals may unintentionally disturb the balance of androgens and estrogens. Until now, it is not clear whether this effect is compensated by an increased expression of aromatase or by other unknown mechanisms. The broad use of biologically active compounds in human therapy as well as in nonhuman applications may involve some risks, as exemplified by emerging antibiotic resistance. In agriculture, fungi and yeast are well known to develop resistance to azoles, and some molecular mechanisms of resistance development have been described. The significance of the agricultural azole resistance for human clinical antimycotic therapies has been discussed in Europe, but is not clarified yet. The actual target enzyme of azole antifungals, the fungal sterol 14[alpha]-demethylase, is expressed in many species including humans, and it is highly conserved through evolution. Hence, it seems reasonable to assume that most of the azole antifungals used in agriculture and medicine as well as azoles used in management of breast cancer also act as inhibitors on human sterol 14[alpha]-demethylase to an unknown extent. The toxicologic profiles of individual azole fungicides provide evidence for endocrine effects. In fact, many of these fungicides have effects on prostate, testis, uterus, and ovaries as well as on fertility, development, and sexual behavior. The current database does not allow us to establish causal relationships of these effects with inhibition of sterol 14[alpha]-demethylase and/or aromatase, but the overall view strongly suggests a connection with disturbed steroidogenesis. Zam et al;

Environmental Health Perspectives - 3/1/2003 . In rats increased fragility of long bones, leading in some cases to fractures, was observed after 3-6 months of treatment. A variety of other hormonally related disturbances were also noted in the rat. Similar adverse effects have so far not been reported in humans. Tablets containing ketoconazole are contra-indicated in pregnant women, patients with hepatic failure or those recovering from hepatitis. For a similar product: The substance can be absorbed in the body by inhalation and ingestion. Upon oral intake the substance causes in animal experiments: abnormal position, muscle twitches of the paws, sedation (500-2000 mg/kg), muscle vibrations (250-2000 mg/kg), muscle weakening (250-1000 mg/kg). lowered body temperature (250-500 mg/kg), protruding eyeballs (500 and 2000 mg/kg). [Janssen Pharamaceutica]