

MATERIAL SAFETY DATA SHEET

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION






Product name	fluconazole
Chemical Name	"alpha-(2, 4-difluorophenyl)-"
Synonyms	"alpha-(1H-1, 2, 4-triazol-1-ylmethyl)-1H-1, 2, 4-triazole-1-ethanol", "2-(2, 4-difluorophenyl)-1, 3-bis(1H-1, 2, 4-triazol-1-yl)-2-propanol", Diflucan, UK-49858, "bistriazole/azole/antimycotic antifungal agent", "Dizole one"
Molecular Formula	C ₁₃ H ₁₂ F ₂ N ₆ O
Usage	Oral antifungal in the treatment of candidiasis. Fluconazole is a highly selective inhibitor of fungal cytochrome P-450 sterol C-14-alpha demethylation. Mammalian cell demethylation is much less sensitive to fluconazole inhibition..

Manufacture/supplier identification :

Company	Ipca Laboratories Limited, 48, Kandivli Industrial Estate, Kandivli (West), Mumbai - 400 067 Telephone : 66474747:Telefax 2868 2875
Contact for information:	Ipca Laboratories Limited, Post Box No. 33, P.O. Sejavta, Dist. Ratlam (M.P.) 457 002
Emergency telephone No.:	Telephone:(07412)278000,279080-81,Telefax (07412)279083
E Mail	ipcartm@ipca.co.in

Section 2 – HAZARD IDENTIFICATION

HAZARD RATINGS

	Min	Max	
Flammability:	1		
Toxicity:	2		Min/Nil=0
Body Contact:	0		Low=1
Reactivity:	1		Moderate=2
Chronic:	2		High=3 Extreme=4

GHS Classification

Acute Toxicity (Oral) Category 4
Chronic Aquatic Hazard Category 2
Reproductive Toxicity Category 2

**EMERGENCY OVERVIEW**
HAZARD**WARNING**

Determined by Chemwatch using GHS criteria:

H411 H302 H361 H361

Toxic to aquatic life with long lasting effects

Harmful if swallowed

Suspected of damaging fertility

Suspected of damaging the unborn child

PRECAUTIONARY STATEMENTS**Prevention**

P-201 Obtain special instructions before use.

P-202 Do not handle until all safety precautions have been read and understood.

P264: Wash thoroughly after handling.

P270: Do not eat, drink or smoke when using this product

P273: Avoid release to the environment

P-281 Use personal protective equipment as required.

Response

P301+312: IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell.

P308+313: IF exposed or concerned: Get medical advice/ attention.

P330: Rinse mouth.

P391: Collect spillage.

Storage

P-405 Store locked up.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
fluconazole	86386-73-4	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.
 - For advice, contact a Poisons Information Centre or a doctor.
 - Urgent hospital treatment is likely to be needed.
 - In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition.
 - If the services of a medical officer or medical doctor are readily available, the patient should be placed in his/her care and a copy of the MSDS should be provided. Further action will be the responsibility of the medical specialist.
 - If medical attention is not available on the worksite or surroundings send the patient to a hospital together with a copy of the MSDS.
 - Where medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:
 - INDUCE vomiting with fingers down the back of the throat, ONLY IF CONSCIOUS. Lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.
- NOTE: Wear a protective glove when inducing vomiting by mechanical means.

EYE

- If this product comes in contact with the eyes:
- Wash out immediately with fresh running water.
- Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.
- Seek medical attention without delay; if pain persists or recurs seek medical attention.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN

- If skin contact occurs:
 - Immediately remove all contaminated clothing, including footwear.
 - Flush skin and hair with running water (and soap if available).
 - Seek medical attention in event of irritation.

INHALED

- If dust is inhaled, remove from contaminated area.
- Encourage patient to blow nose to ensure clear passage of breathing.
- If irritation or discomfort persists seek medical attention.

NOTES TO PHYSICIAN

- for poisons (where specific treatment regime is absent):

BASIC TREATMENT

- Establish a patent airway with suction where necessary.
- Watch for signs of respiratory insufficiency and assist ventilation as necessary.
- Administer oxygen by non-rebreather mask at 10 to 15 L/min.
- Monitor and treat, where necessary, for pulmonary oedema .
- Monitor and treat, where necessary, for shock.
- Anticipate seizures .
- DO NOT use emetics. Where ingestion is suspected rinse mouth and give up to 200 ml water (5 ml/kg recommended) for dilution where patient is able to swallow, has a strong gag reflex and does not drool.

ADVANCED TREATMENT

- Consider orotracheal or nasotracheal intubation for airway control in unconscious patient or where respiratory arrest has occurred.
 - Positive-pressure ventilation using a bag-valve mask might be of use.
 - Monitor and treat, where necessary, for arrhythmias.
 - Start an IV D5W TKO. If signs of hypovolaemia are present use lactated Ringers solution. Fluid overload might create complications.
 - Drug therapy should be considered for pulmonary oedema.
 - Hypotension with signs of hypovolaemia requires the cautious administration of fluids. Fluid overload might create complications.
 - Treat seizures with diazepam.
 - Proparacaine hydrochloride should be used to assist eye irrigation.
- BRONSTEIN, A.C. and CURRANCE, P.L.
EMERGENCY CARE FOR HAZARDOUS MATERIALS EXPOSURE: 2nd Ed. 1994.
Treat symptomatically.

Fluconazole is largely excreted in the urine; forced volume diuresis would probably increase the elimination rate. A three-hour haemodialysis session decreases plasma levels by approximately 50%.

Section 5 - FIRE FIGHTING MEASURES

EXTINGUISHING MEDIA

- Water spray or fog.
- Foam.
- Dry chemical powder.
- BCF (where regulations permit).
- Carbon dioxide

FIRE FIGHTING

- Alert Fire Brigade and tell them location and nature of hazard.
- Wear full body protective clothing with breathing apparatus.
- Prevent, by any means available, spillage from entering drains or water course.
- Use fire fighting procedures suitable for surrounding area.
- Do not approach containers suspected to be hot.
- Cool fire exposed containers with water spray from a protected location.
- If safe to do so, remove containers from path of fire.
- Equipment should be thoroughly decontaminated after use.

FIRE/EXPLOSION HAZARD

- Combustible solid which burns but propagates flame with difficulty; it is estimated that most organic dusts are combustible (circa 70%) - according to the circumstances under which the combustion process occurs, such materials may cause fires and / or dust explosions.
- Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion.

Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust (420 micron or less) may burn rapidly and fiercely if ignited - particles exceeding this limit will generally not form flammable dust clouds.; once initiated, however, larger particles up to 1400 microns diameter will contribute to the propagation of an explosion.

- In the same way as gases and vapours, dusts in the form of a cloud are only ignitable over a range of concentrations; in principle, the concepts of lower explosive limit (LEL) and upper explosive limit (UEL).are applicable to dust clouds but only the LEL is of practical use; - this is because of the inherent difficulty of achieving homogeneous dust clouds at high temperatures (for dusts the LEL is often called the "Minimum Explosible Concentration", MEC)
- A dust explosion may release of large quantities of gaseous products; this in turn creates a subsequent pressure rise of explosive force capable of damaging plant and buildings and injuring people.

- Usually the initial or primary explosion takes place in a confined space such as plant or machinery, and can be of sufficient force to damage or rupture the plant. If the shock wave from the primary explosion enters the surrounding area, it will disturb any settled dust layers, forming a second dust cloud, and often initiate a much larger secondary explosion. All large scale explosions have resulted from chain reactions of this type.
 - Dry dust can be charged electrostatically by turbulence, pneumatic transport, pouring, in exhaust ducts and during transport.
 - Build-up of electrostatic charge may be prevented by bonding and grounding.
 - Powder handling equipment such as dust collectors, dryers and mills may require additional protection measures such as explosion venting.
 - All movable parts coming in contact with this material should have a speed of less than 1-meter/sec
 - A sudden release of statically charged materials from storage or process equipment, particularly at elevated temperatures and/ or pressure, may result in ignition especially in the absence of an apparent ignition source
 - One important effect of the particulate nature of powders is that the surface area and surface structure (and often moisture content) can vary widely from sample to sample, depending of how the powder was manufactured and handled; this means that it is virtually impossible to use flammability data published in the literature for dusts (in contrast to that published for gases and vapours).
 - Autoignition temperatures are often quoted for dust clouds (minimum ignition temperature (MIT)) and dust layers (layer ignition temperature (LIT)); LIT generally falls as the thickness of the layer increases.
- Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), hydrogen fluoride, nitrogen oxides (NO_x), other pyrolysis products typical of burning organic material.

FIRE INCOMPATIBILITY

- Avoid contamination with oxidising agents i.e. nitrates, oxidising acids, chlorine bleaches, pool chlorine etc. as ignition may result.

Personal Protective Equipment

Breathing apparatus.
Gas tight chemical resistant suit.
Limit exposure duration to 1 BA set 30 mins.

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- Remove all ignition sources.

- Clean up all spills immediately.
- Avoid contact with skin and eyes.
- Control personal contact by using protective equipment.
- Use dry clean up procedures and avoid generating dust.
- Place in a suitable, labelled container for waste disposal.

Environmental hazard - contain spillage.

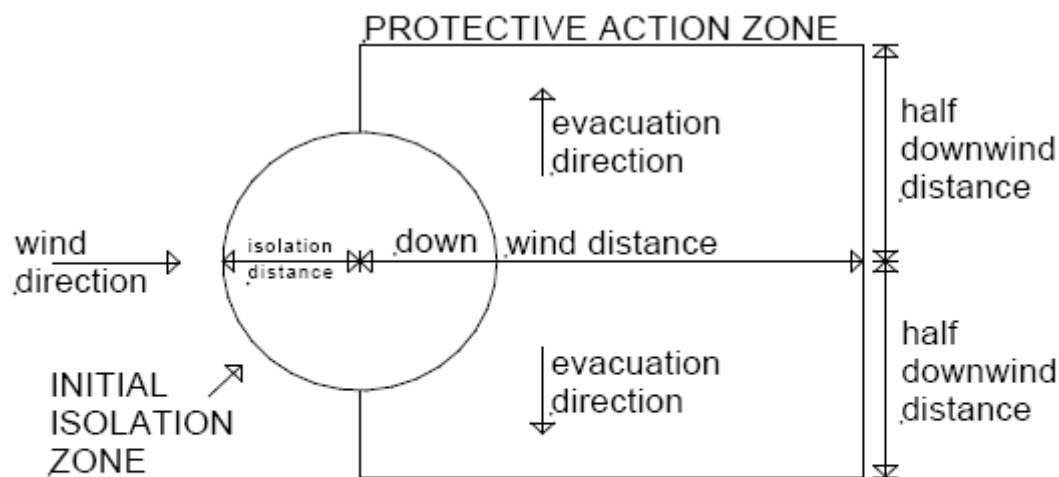
MAJOR SPILLS

- Environmental hazard - contain spillage.

Moderate hazard.

- CAUTION: Advise personnel in area.
- Alert Emergency Services and tell them location and nature of hazard.
- Control personal contact by wearing protective clothing.
- Prevent, by any means available, spillage from entering drains or water courses.
- Recover product wherever possible.
- IF DRY: Use dry clean up procedures and avoid generating dust. Collect residues and place in sealed plastic bags or other containers for disposal. IF WET: Vacuum/shovel up and place in labelled containers for disposal.
- ALWAYS: Wash area down with large amounts of water and prevent runoff into drains.
- If contamination of drains or waterways occurs, advise Emergency Services.

PROTECTIVE ACTIONS FOR SPILL



From IERG (Canada/Australia)

Isolation Distance	-
Downwind Protection Distance	10 metres
IERG Number	47

FOOTNOTES

1 PROTECTIVE ACTION ZONE is defined as the area in which people are at risk of harmful exposure. This zone assumes that random changes in wind direction confines the vapour plume to an area within 30 degrees on either side of the predominant wind direction, resulting in a crosswind protective action distance equal to the downwind protective action distance.

2 PROTECTIVE ACTIONS should be initiated to the extent possible, beginning with those closest to the spill and working away from the site in the downwind direction. Within the protective action zone a level of vapour concentration may exist resulting in nearly all unprotected persons becoming incapacitated and unable to take protective action and/or incurring serious or irreversible health effects.

3 INITIAL ISOLATION ZONE is determined as an area, including upwind of the incident, within which a high probability of localised wind reversal may expose nearly all persons without appropriate protection to lifethreatening concentrations of the material.

4 SMALL SPILLS involve a leaking package of 200 litres (55 US gallons) or less, such as a drum (jerrican or box with inner containers). Larger packages leaking less than 200 litres and compressed gas leaking from a small cylinder are also considered "small spills".

LARGE SPILLS involve many small leaking packages or a leaking package of greater than 200 litres, such as a cargo tank, portable tank or a "one-tonne" compressed gas cylinder.

5 Guide 151 is taken from the US DOT emergency response guide book.

6 IERG information is derived from CANUTEC - Transport Canada.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- Prevent concentration in hollows and sumps.
- DO NOT enter confined spaces until atmosphere has been checked.
- DO NOT allow material to contact humans, exposed food or food utensils.
- Avoid contact with incompatible materials.
- When handling, DO NOT eat, drink or smoke.
- Keep containers securely sealed when not in use.
- Avoid physical damage to containers.
- Always wash hands with soap and water after handling.
- Work clothes should be laundered separately. Launder contaminated clothing before re-use.
- Use good occupational work practice.
- Observe manufacturer's storing and handling recommendations.
- Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.

- Do NOT cut, drill, grind or weld such containers.
- In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

SUITABLE CONTAINER

- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE INCOMPATIBILITY

- Avoid reaction with oxidising agents

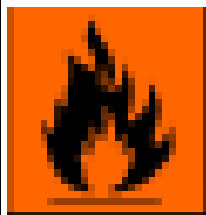
STORAGE REQUIREMENTS

- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry, well-ventilated area.
- Store away from incompatible materials and foodstuff containers.
- Protect containers against physical damage and check regularly for leaks.
- Observe manufacturer's storing and handling recommendations.

For major quantities:

- Consider storage in bunded areas - ensure storage areas are isolated from sources of community water (including stormwater, ground water, lakes and streams).
- Ensure that accidental discharge to air or water is the subject of a contingency disaster management plan; this may require consultation with local authorities.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS



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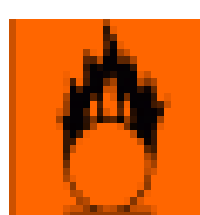
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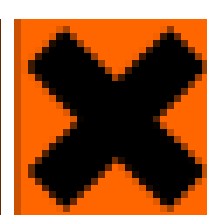
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X



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+: May be stored together

O: May be stored together with specific preventions

X: Must not be stored together

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION**EXPOSURE CONTROLS**

The following materials had no OELs on our records

• fluconazole:

CAS:86386- 73- 4

MATERIAL DATA**FLUCONAZOLE:**

■ It is the goal of the ACGIH (and other Agencies) to recommend TLVs (or their equivalent) for all substances for which there is evidence of health effects at airborne concentrations encountered in the workplace.

At this time no TLV has been established, even though this material may produce adverse health effects (as evidenced in animal experiments or clinical experience). Airborne concentrations must be maintained as low as is practically possible and occupational exposure must be kept to a minimum.

NOTE: The ACGIH occupational exposure standard for Particles Not Otherwise Specified (P.N.O.S) does NOT apply.

CEL TWA: 0.5 mg/m³

PERSONAL PROTECTION**EYE**

- Safety glasses with side shields
- Chemical goggles.
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or

irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59].

HANDS/FEET

■ Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly.

Application of a non-perfumed moisturiser is recommended.

Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.

- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocautchouc
- polyvinyl chloride

Gloves should be examined for wear and/ or degradation constantly

OTHER

- Overalls.
- P.V.C. apron.
- Barrier cream.
- Skin cleansing cream.
- Eye wash unit.

RESPIRATOR

- Respirators may be necessary when engineering and administrative controls do not adequately prevent exposures.
- The decision to use respiratory protection should be based on professional judgment that takes into account toxicity information, exposure measurement data, and frequency and likelihood of the worker's exposure - ensure users are not subject to high thermal loads which may result in heat stress or distress due to personal protective equipment (powered, positive

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flow, full face apparatus may be an option).

- Published occupational exposure limits, where they exist, will assist in determining the adequacy of the selected respiratory. These may be government mandated or vendor recommended.
- Certified respirators will be useful for protecting workers from inhalation of particulates when properly selected and fit tested as part of a complete respiratory protection program.
- Use approved positive flow mask if significant quantities of dust becomes airborne.
- Try to avoid creating dust conditions.

RESPIRATOR

Protection Factor	Half- Face Respirator	Full- Face Respirator	Powered Air Respirator
10 xES	P1 Air- line*	- -	PAPR- P1 -
50 xES	Air- line**	P2	PAPR- P2
100 xES	-	P3	-
		Air- line*	-
100+ xES	-	Air- line**	PAPR- P3

* - Negative pressure demand

** - Continuous flow.

The local concentration of material, quantity and conditions of use determine the type of personal protective equipment required. For further information consult site specific CHEMWATCH data (if available), or your Occupational Health and Safety Advisor.

ENGINEERING CONTROLS

- Local exhaust ventilation is required where solids are handled as powders or crystals; even when particulates are relatively large, a certain proportion will be powdered by mutual friction.
- Exhaust ventilation should be designed to prevent accumulation and recirculation of particulates in the workplace.
- If in spite of local exhaust an adverse concentration of the substance in air could occur, respiratory protection should be considered. Such protection might consist of:
 - (a): particle dust respirators, if necessary, combined with an absorption cartridge;
 - (b): filter respirators with absorption cartridge or canister of the right type;
 - (c): fresh-air hoods or masks
- Build-up of electrostatic charge on the dust particle, may be prevented by bonding and grounding.
- Powder handling equipment such as dust collectors, dryers and mills may require additional protection measures such as explosion venting. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to efficiently remove the contaminant.

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Type of Contaminant:

direct spray, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)

grinding, abrasive blasting, tumbling, high speed wheel generated dusts (released at high initial velocity into zone of very high rapid air motion).

Air Speed:

1- 2.5 m/s (200- 500 f/min.)

2.5- 10 m/s (500- 2000 f/min.)

Within each range the appropriate value depends on:
Lower end of the range Upper end of the range

- 1: Room air currents minimal or favourable to capture
- 2: Contaminants of low toxicity or of nuisance value only.
- 3: Intermittent, low production.
- 4: Large hood or large air mass in motion

- 1: Disturbing room air currents
- 2: Contaminants of high toxicity
- 3: High production, heavy use
- 4: Small hood- local control only

Simple theory shows that air velocity falls rapidly with distance away from the opening of a simple extraction pipe. Velocity generally decreases with the square of distance from the extraction point (in simple cases). Therefore the air speed at the extraction point should be adjusted, accordingly, after reference to distance from the contaminating source. The air velocity at the extraction fan, for example, should be a minimum of 1-2.5 m/s (200-500 f/min.) for extraction of gases discharged 2 meters distant from the extraction point. Other mechanical considerations, producing performance deficits within the extraction apparatus, make it essential that theoretical air velocities are multiplied by factors of 10 or more when extraction systems are installed or used.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE

White crystalline solid; does not mix well with water.

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	306.27
Melting Range (°C)	138-140	Viscosity	Not Applicable
Boiling Range (°C)	Not available	Solubility in water (g/L)	Partly miscible
Flash Point (°C)	Not available	pH (1% solution)	Not applicable
Decomposition Temp (°C)	Not available	pH (as supplied)	Not applicable
Autoignition Temp (°C)	Not available	Vapour Pressure (kPa)	Negligible
Upper Explosive Limit (%)	Not available.	specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapour Density (air=1)	>1
Volatile Component (%vol)	Negligible	Evaporation Rate	Not available

Section 10 - CHEMICAL STABILITY AND REACTIVITY INFORMATION

CONDITIONS CONTRIBUTING TO INSTABILITY

Presence of incompatible materials.

- Product is considered stable.
- Hazardous polymerisation will not occur.

Section 11 - TOXICOLOGICAL INFORMATION

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.

■ Aromatase inhibitors can cause mood swings, depression, weight gain, hot flushes, vaginal dryness, bloating and early menopause. Long-term use may result in bone weakness, increased risk of blood clots, gastrointestinal disturbance, and sweats.

Aromatase inhibitors reduce the level of oestrogen in post-menopausal women who have breast cancer sensitive to hormones. This reduces the growth of breast cancer in these women.

EYE

■ Although the material is not thought to be an irritant (as classified by EC Directives), direct contact with the eye may cause transient discomfort characterised 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 under EC Directives 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.

■ Open cuts, abraded or irritated skin should not be exposed to this material.

■ 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 by EC Directives using animal models). Nevertheless inhalation of dusts, or fumes, 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.

■ Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled. If prior damage to the circulatory or nervous systems has occurred or if kidney damage has been sustained, proper screenings should be conducted on individuals who may be exposed to further risk if handling and use of the material result in excessive exposures.

CHRONIC HEALTH EFFECTS

■ There has been some concern that this material can cause cancer or mutations but there is not enough data to make an assessment.

Based on experience with similar materials, there is a possibility that exposure to the material may reduce fertility in humans at levels which do not cause 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 foetus, at levels which do not cause significant toxic effects to the mother.

Azole fungicides show broad antifungal activity, and can be used to prevent or cure fungal infections. They are therefore important in agricultural production. They work by blocking the assembly of the cell membrane of fungi. Animal testing has shown inconclusive results regarding the effect of this group of fungicides on the reproductive organs in mammals.

Extensive structural activity data from the family of triazole pesticides suggests that may induce hepatocellular adenomas in animal models. The significance of this finding in human carcinogenicity is equivocal.

Administration to rats produced an increased incidence of hepatocellular adenomas.

Administration to pregnant rabbits produced reduced maternal weight gain, increases in foetal anatomical variants and delayed foetal ossification. Doses of 20-60 times the recommended human level, produced abortion

TOXICITY AND IRRITATION

■ unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

TOXICITY

Oral (rat) LD50: 1271 mg/kg
 Intraperitoneal (rat) LD50: >941 mg/kg
 Intravenous (rat) LD50: >200 mg/kg
 Oral (mouse) LD50: 1408 mg/kg
 Intraperitoneal (mouse) LD50: 1273 mg/kg
 Intravenous (mouse) LD50: >200 mg/kg
 Oral (dog) LD50: >300 mg/kg
 Intravenous (dog) LD50: >100 mg/kg
 Oral (woman) TDLo: 1456 mg/kg/26w – I
 Oral (man) TDLo: 1040 mg/kg/26w - I
 Oral (man) TDLo: 60 mg/kg/3w – I

IRRITATION

Nil Reported

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

FLUCONAZOLE::

Marine Pollutant:

Yes

- Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
- Do NOT allow product to come in contact with surface waters or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment wash-waters.

Wastes resulting from use of the product must be disposed of on site or at approved waste sites.

- For azole-containing substances.

Azole fungicides and systemically used antifungal drugs directly interfere with steroidogenesis by acting as potent inhibitors of steroidogenic enzymes and are known to cause endocrine disruption mainly via this mechanism.

An important P450 enzyme involved in the steroidogenesis is aromatase. Aromatase demethylates C10 and specifically converts androstenedione and testosterone. On the protein level, the amino acid sequence homology between aromatase from fish and humans is about 50% and between rats and humans is about 78%. In mammals, aromatase is mainly expressed in the brain and the gonads, but it is also found in placental, adipose, and bone tissue. The physiologic balance between different sex steroid hormones is crucial for the development, maintenance, and function of the reproductive system as well as for the differentiation of the sexual phenotype during ontogeny. Oestrogens (estrone and estradiol) are products of the androgens (androstenedione and testosterone), and the reaction is catalysed by aromatase. In mammals, differentiation of the male phenotype depends not only on testosterone but also on estradiol generated from testosterone by neuronal aromatase in central nervous system. Therefore, disturbances in aromatase expression and/or changes in its catalytic activity are expected to exhibit negative effects on reproduction parameters.

Azole-containing compounds produce profound effects in the environment. In part this is due to inhibition of several enzyme systems including those involving sterol 14[alpha]-demethylase. Sterol 14[alpha]-demethylase is a member of the superfamily of haeme-containing cytochrome P450 enzymes involved in metabolism of endogenous and xenobiotic substances. The antifungal effect of azoles is due to inhibition of sterol 14[alpha]-demethylase in fungi and yeast, thereby blocking the biosynthesis of ergosterol. The subsequent lack of ergosterol is detrimental because ergosterol is an essential sterol component in the membranes of fungi and yeast. Sterol 14[alpha]-demethylase is not only expressed in fungi and yeast but is also found in many other species ranging from bacteria to mammals. In plants, the sterol 14[alpha]-demethylase reaction metabolises obtusifoliosol and provides precursors for biosynthesis of phytosterols. In animals, the sterol 14[alpha]-demethylase reaction is part of the metabolic pathway leading to biosynthesis of cholesterol.

Cholesterol in turn is the substrate for the production of many other sterols (e.g., the sex steroid hormones).

The DNA sequences encoding sterol 14[alpha]-demethylase of many fungi and yeast are known, as well as the sequences of mice, rats, pigs, and humans. On the protein level, the amino acid sequences are highly conserved along the phylogenetic tree. This fact is considered by many authors as an indication of the pivotal role of sterol 14[alpha]-demethylase in all organisms. The homology of the amino acid sequence level between rats and humans is 93% and 40% between fungi and humans. In humans, the sterol 14[alpha]-demethylase is expressed in many different tissues.

- DO NOT discharge into sewer or waterways

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
fluconazole	HIGH		LOW	LOW

Section 13 - DISPOSAL CONSIDERATIONS

- Containers may still present a chemical hazard/ danger when empty.
- Return to supplier for reuse/ recycling if possible.

Otherwise:

- If container can not be cleaned sufficiently well to ensure that residuals do not remain or if the container cannot be used to store the same product, then puncture containers, to prevent re-use, and bury at an authorised landfill.

- Where possible retain label warnings and MSDS and observe all notices pertaining to the product. Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

- DO NOT allow wash water from cleaning or process equipment to enter drains.
- It may be necessary to collect all wash water for treatment before disposal.
- In all cases disposal to sewer may be subject to local laws and regulations and these should be considered first.
- Where in doubt contact the responsible authority.
- Recycle wherever possible.
- Consult manufacturer for recycling options or consult local or regional waste management authority for disposal if no suitable treatment or disposal facility can be identified.
- Dispose of by: burial in a land-fill specifically licenced to accept chemical and / or pharmaceutical wastes or Incineration in a licenced apparatus (after admixture with suitable combustible material)

- Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION



RISK

Risk Codes	Risk Phrases
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R22	■ Harmful if swallowed.
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R51/53	■ Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
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SAFETY

Safety Codes	Safety Phrases
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S53	■ Avoid exposure - obtain special instructions before use.
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S401	■ To clean the floor and all objects contaminated by this material, use water and detergent.
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S35	■ This material and its container must be disposed of in a safe way.
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S13	■ Keep away from food, drink and animal feeding stuffs.
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S46	■ If swallowed, IMMEDIATELY contact Doctor or Poisons Information Centre. (show this container or label).
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- S57 ■ Use appropriate container to avoid environmental contamination.
- S61 ■ Avoid release to the environment. Refer to special instructions/Safety data sheets.
- S60 ■ This material and its container must be disposed of as hazardous waste.

ANNEX 2: Indications of Danger

- N Dangerous for the environment
- Xn Harmful

REGULATIONS

fluconazole (CAS: 86386-73-4) is found on the following regulatory lists;

"European Customs Inventory of Chemical Substances (English)"

This safety data sheet is in compliance with the following EU legislation and its adaptations – as far as applicable - : 67/548/EEC, 1999/45/EC, 76/769/EEC, 98/24/EC, 92/85/EEC, 94/33/EC, 91/689/EEC, 1999/13/EC, as well as the following British legislation:

- The Control of Substances Hazardous to Health Regulations (COSHH) 2002
- COSHH Essentials
- The Management of Health and Safety at Work Regulations 1999

Section 16 - OTHER INFORMATION

Text of H-code(s) and P-sentence(s) are mentioned in Section 3

The information given in the safety data sheet is believed to be accurate and is based on our present knowledge .We take no guarantee with respect to such information and assume no liability resulting from its use.

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