

Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

Titan Ag

Chemwatch: 3194-323

Version No: 3.1

Safety Data Sheet according to Work Health and Safety Regulations (Hazardous Chemicals) 2023 and ADG requirements

Chemwatch Hazard Alert Code: 2

Initial Date: 08/01/2025

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SECTION 1 Identification of the substance / mixture and of the company / undertaking

Product Identifier

Product name	Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)
Chemical Name	Not Applicable
Synonyms	Not Available
Proper shipping name	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (contains tebuconazole)
Chemical formula	Not Applicable
Other means of identification	Not Available

Relevant identified uses of the substance or mixture and uses advised against

Relevant identified uses	Agricultural fungicide.
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Details of the manufacturer or importer of the safety data sheet

Registered company name	Titan Ag
Address	Princes Street Marina, Suite 15/16 Princes Street Newport NSW 2106 Australia
Telephone	+61 2 9999 6655
Fax	+61 2 9999 0483
Website	https://www.titanag.com.au/
Email	titanorders@titanag.com.au

Emergency telephone number

Association / Organisation	Titan Ag
Emergency telephone number(s)	1800 033 111 (24 hours)
Other emergency telephone number(s)	Not Available

SECTION 2 Hazards identification

Classification of the substance or mixture

Poisons Schedule	S5
Classification [1]	Acute Toxicity (Oral) Category 4, Reproductive Toxicity Category 2, Hazardous to the Aquatic Environment Acute Hazard Category 1, Hazardous to the Aquatic Environment Long-Term Hazard Category 1
Legend:	1. Classified by Chemwatch; 2. Classification drawn from HCIS; 3. Classification drawn from Regulation (EU) No 1272/2008 - Annex VI

Label elements

Hazard pictogram(s)	
Signal word	Warning

Hazard statement(s)

H302	Harmful if swallowed.
H361d	Suspected of damaging the unborn child.
H410	Very toxic to aquatic life with long lasting effects.

Precautionary statement(s) Prevention

P202	Do not handle until all safety precautions have been read and understood.
P280	Wear protective gloves and protective clothing.

P264	Wash all exposed external body areas thoroughly after handling.
P270	Do not eat, drink or smoke when using this product.
P273	Avoid release to the environment.

Precautionary statement(s) Response

P308+P313	IF exposed or concerned: Get medical advice/ attention.
P391	Collect spillage.
P301+P312	IF SWALLOWED: Call a POISON CENTER/doctor/physician/first aider if you feel unwell.
P330	Rinse mouth.

Precautionary statement(s) Storage

P405	Store locked up.
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Precautionary statement(s) Disposal

P501	Dispose of contents/container to authorised hazardous or special waste collection point in accordance with any local regulation.
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No further product hazard information.

SECTION 3 Composition / information on ingredients

Substances

See section below for composition of Mixtures

Mixtures

CAS No	%[weight]	Name
107534-96-3	35-45	tebuconazole
Not Available	balance	Ingredients determined not to be hazardous
Legend:	1. Classified by Chemwatch; 2. Classification drawn from HCIS; 3. Classification drawn from Regulation (EU) No 1272/2008 - Annex VI; 4. Classification drawn from C&L; * EU IOELVs available	

SECTION 4 First aid measures

Description of first aid measures

Eye Contact	If this product comes in contact with the eyes: ▶ Immediately hold eyelids apart and flush the eye continuously with 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. ▶ Continue flushing until advised to stop by the Poisons Information Centre or a doctor, or for at least 15 minutes. ▶ Transport to hospital or doctor without delay. ▶ Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.
Skin Contact	If skin or hair contact occurs: ▶ Flush skin and hair with running water (and soap if available). ▶ Seek medical attention in event of irritation.
Inhalation	▶ If fumes or combustion products are inhaled remove from contaminated area. ▶ Lay patient down. Keep warm and rested. ▶ Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures. ▶ Apply artificial respiration if not breathing, preferably with a demand valve resuscitator, bag-valve mask device, or pocket mask as trained. Perform CPR if necessary. ▶ Transport to hospital, or doctor, without delay.
Ingestion	▶ 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 SDS 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 SDS. 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.

Indication of any immediate medical attention and special treatment needed

As in all cases of suspected poisoning, follow the ABCDEs of emergency medicine (airway, breathing, circulation, disability, exposure), then the ABCDEs of toxicology (antidotes, basics, change absorption, change distribution, change elimination).
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.

Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

- ▶ **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.

SECTION 5 Firefighting measures

Extinguishing media

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

Special hazards arising from the substrate or mixture

Fire Incompatibility	▶ Avoid contamination with oxidising agents i.e. nitrates, oxidising acids, chlorine bleaches, pool chlorine etc. as ignition may result
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Advice for firefighters

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 water delivered as a fine spray to control fire and cool adjacent area. ▶ Avoid spraying water onto liquid pools. ▶ 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.
Fire/Explosion Hazard	▶ Combustible. ▶ Slight fire hazard when exposed to heat or flame. ▶ Heating may cause expansion or decomposition leading to violent rupture of containers. ▶ On combustion, may emit toxic fumes of carbon monoxide (CO). ▶ May emit acid smoke. ▶ Mists containing combustible materials may be explosive. Combustion products include: ▶ carbon dioxide (CO₂) - hydrogen chloride - phosgene - nitrogen oxides (NO_x) ▶ other pyrolysis products typical of burning organic material.
HAZCHEM	•3Z

SECTION 6 Accidental release measures

Personal precautions, protective equipment and emergency procedures

See section 8

Environmental precautions

See section 12

Methods and material for containment and cleaning up

Minor Spills	Environmental hazard - contain spillage. ▶ Clean up all spills immediately. ▶ Avoid breathing vapours and contact with skin and eyes. ▶ Control personal contact with the substance, by using protective equipment. ▶ Contain and absorb spill with sand, earth, inert material or vermiculite. ▶ Wipe up. ▶ Place in a suitable, labelled container for waste disposal.
Major Spills	Environmental hazard - contain spillage. Moderate hazard. ▶ Clear area of personnel and move upwind. ▶ Alert Fire Brigade and tell them location and nature of hazard. ▶ Wear breathing apparatus plus protective gloves. ▶ Prevent, by any means available, spillage from entering drains or water course. ▶ No smoking, naked lights or ignition sources. ▶ Increase ventilation. ▶ Stop leak if safe to do so. ▶ Contain spill with sand, earth or vermiculite. ▶ Collect recoverable product into labelled containers for recycling. ▶ Absorb remaining product with sand, earth or vermiculite. ▶ Collect solid residues and seal in labelled drums for disposal. ▶ Wash area and prevent runoff into drains. ▶ If contamination of drains or waterways occurs, advise emergency services.

Personal Protective Equipment advice is contained in Section 8 of the SDS.

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Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

SECTION 7 Handling and storage

Precautions for safe handling

Safe handling	▶ Avoid skin 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. ▶ Avoid smoking, naked lights or ignition sources. ▶ 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. ▶ Use good occupational work practice. ▶ Observe manufacturer's storage and handling recommendations contained within this SDS. ▶ Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions.
Other information	▶ Store in original containers. ▶ Keep containers securely sealed. ▶ No smoking, naked lights or ignition sources. ▶ 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 storage and handling recommendations contained within this SDS.

Conditions for safe storage, including any incompatibilities

Suitable container	▶ Glass container is suitable for laboratory quantities ▶ Metal can or drum ▶ Packaging as recommended by manufacturer. ▶ Check all containers are clearly labelled and free from leaks.
Storage incompatibility	High nitrogen compounds are often unstable or explosive; the tendency is exaggerated by attachment of azide or diazonium groups, or a high-nitrogen heterocyclic nucleus. High-nitrogen chemical families include ▶ azides ▶ diazoazoles ▶ diazonium salts ▶ hydrazinium salts ▶ N-nitro compounds ▶ tetrazoles ▶ tetrazines ▶ triazenes ▶ triazoles ▶ Avoid reaction with oxidising agents

SECTION 8 Exposure controls / personal protection

Control parameters

Occupational Exposure Limits (OEL)

INGREDIENT DATA

Not Available

MATERIAL DATA

Exposure controls

Appropriate engineering controls	For potent pharmacological agents: Solutions Handling: ▶ Solutions can be handled outside a containment system or without local exhaust ventilation during procedures with no potential for aerosolisation. If the procedures have a potential for aerosolisation, an air-purifying respirator is to be worn by all personnel in the immediate area. ▶ Solutions used for procedures where aerosolisation may occur (e.g., vortexing, pumping) are to be handled within a containment system or with local exhaust ventilation. ▶ In situations where this is not feasible (may include animal dosing), an air-purifying respirator is to be worn by all personnel in the immediate area. If using a ventilated enclosure that has not been validated, wear a half-mask respirator equipped with HEPA cartridges until the enclosure is validated for use. ▶ Ensure gloves are protective against solvents in use. Unless written procedures, specific to the workplace are available, the following is intended as a guide: ▶ For Laboratory-scale handling of Substances assessed to be toxic by inhalation. Quantities of up to 25 grams may be handled in Class II biological safety cabinets*; Quantities of 25 grams to 1 kilogram may be handled in Class II biological safety cabinets* or equivalent containment systems; Quantities exceeding 1 kg may be handled either using specific containment, a hood or Class II biological safety cabinet*. ▶ HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapours. ▶ The need for respiratory protection should also be assessed where incidental or accidental exposure is anticipated. Dependent on levels of contamination, PAPR, full face air purifying devices with P2 or P3 filters or air supplied respirators should be evaluated. When handling: Quantities of up to 25 grams, an approved respirator with HEPA filters or cartridges should be considered; Quantities of 25 grams to 1 kilogram, a half-face negative pressure, full negative pressure, or powered helmet-type air purifying respirator should be considered. Quantities in excess of 1 kilogram, a full face negative pressure, helmet-type air purifying, or supplied air respirator should be considered. Written procedures, specific to a particular work-place, may replace these recommendations * For Class II Biological Safety Cabinets, Types B2 or B3 should be considered. Where only Class I, open fronted Cabinets are available, glove panels may be added, Laminar flow cabinets do not provide sufficient protection when handling these materials unless especially designed to do so. Pilot Plant and Production ▶ Wear appropriate gloves; lab coat, nylon coveralls or disposable Tyvek suit; safety glasses, safety shoes, and disposable booties. Use good manufacturing practices (i.e., cGMPs). ▶ Protective garment (coveralls, Tyvek, lab coat) is not to be worn outside the work area.
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Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

	▶ Clean/dirty/decontamination areas are to be established. ▶ Negative/positive air pressure relationships and buffer zones required (i.e., ante-room/degowning room/airlock). ▶ Area access is to be restricted. ▶ High-energy operations such as milling, particle sizing, spraying or fluidising should be done within an approved emission control or containment system. ▶ Develop cleaning procedures and techniques that limit potential exposure
Individual protection measures, such as personal protective equipment	    
Eye and face protection	▶ Safety glasses with side shields. ▶ Chemical goggles.[AS/NZS 1337.1, EN166 or national equivalent] ▶ Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lenses 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].
Skin protection	See Hand protection below
Hands/feet protection	▶ Wear chemical protective gloves, e.g. PVC. ▶ Wear safety footwear or safety gumboots, e.g. Rubber The selection of suitable gloves does not only depend on the material, but also on further marks of quality which vary from manufacturer to manufacturer. Where the chemical is a preparation of several substances, the resistance of the glove material can not be calculated in advance and has therefore to be checked prior to the application. The exact break through time for substances has to be obtained from the manufacturer of the protective gloves and has to be observed when making a final choice. Personal hygiene is a key element of effective hand care. 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. Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: · 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, AS/NZS 2161.1 or national equivalent). · 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, AS/NZS 2161.10.1 or national equivalent) 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, AS/NZS 2161.10.1 or national equivalent) is recommended. · Some glove polymer types are less affected by movement and this should be taken into account when considering gloves for long-term use. · Contaminated gloves should be replaced. As defined in ASTM F-739-96 in any application, gloves are rated as: · Excellent when breakthrough time > 480 min · Good when breakthrough time > 20 min · Fair when breakthrough time < 20 min · Poor when glove material degrades For general applications, gloves with a thickness typically greater than 0.35 mm, are recommended. It should be emphasised that glove thickness is not necessarily a good predictor of glove resistance to a specific chemical, as the permeation efficiency of the glove will be dependent on the exact composition of the glove material. Therefore, glove selection should also be based on consideration of the task requirements and knowledge of breakthrough times. Glove thickness may also vary depending on the glove manufacturer, the glove type and the glove model. Therefore, the manufacturers technical data should always be taken into account to ensure selection of the most appropriate glove for the task. Note: Depending on the activity being conducted, gloves of varying thickness may be required for specific tasks. For example: · Thinner gloves (down to 0.1 mm or less) may be required where a high degree of manual dexterity is needed. However, these gloves are only likely to give short duration protection and would normally be just for single use applications, then disposed of. · Thicker gloves (up to 3 mm or more) may be required where there is a mechanical (as well as a chemical) risk i.e. where there is abrasion or puncture potential 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.
Body protection	See Other protection below
Other protection	▶ Overalls. ▶ P.V.C apron. ▶ Barrier cream. ▶ Skin cleansing cream. ▶ Eye wash unit.

Respiratory protection

Type A Filter of sufficient capacity. (AS/NZS 1716 & 1715, EN 143:2000 & 149:2001, ANSI Z88 or national equivalent)

Selection of the Class and Type of respirator will depend upon the level of breathing zone contaminant and the chemical nature of the contaminant. Protection Factors (defined as the ratio of contaminant outside and inside the mask) may also be important.

Required minimum protection factor	Maximum gas/vapour concentration present in air p.p.m. (by volume)	Half-face Respirator	Full-Face Respirator
up to 10	1000	A-AUS / Class1	-
up to 50	1000	-	A-AUS / Class 1
up to 50	5000	Airline *	-
up to 100	5000	-	A-2
up to 100	10000	-	A-3
100+			Airline**

* - Continuous Flow ** - Continuous-flow or positive pressure demand

A(All classes) = Organic vapours, B AUS or B1 = Acid gasses, B2 = Acid gas or hydrogen cyanide(HCN), B3 = Acid gas or hydrogen cyanide(HCN), E = Sulfur dioxide(SO₂), G = Agricultural chemicals, K = Ammonia(NH₃), Hg = Mercury, NO = Oxides of nitrogen, MB = Methyl bromide, AX = Low boiling point organic compounds(below 65 degC)

▶ Cartridge respirators should never be used for emergency ingress or in areas of unknown vapour concentrations or oxygen content.

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Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

- ▶ The wearer must be warned to leave the contaminated area immediately on detecting any odours through the respirator. The odour may indicate that the mask is not functioning properly, that the vapour concentration is too high, or that the mask is not properly fitted. Because of these limitations, only restricted use of cartridge respirators is considered appropriate.
- ▶ Cartridge performance is affected by humidity. Cartridges should be changed after 2 hr of continuous use unless it is determined that the humidity is less than 75%, in which case, cartridges can be used for 4 hr. Used cartridges should be discarded daily, regardless of the length of time used

SECTION 9 Physical and chemical properties

Information on basic physical and chemical properties

Appearance	Whitish liquid with characteristic odor; mixes with water.		
Physical state	Liquid	Relative density (Water = 1)	1.08-1.10
Odour	Not Available	Partition coefficient n-octanol / water	Not Available
Odour threshold	Not Available	Auto-ignition temperature (°C)	Not Available
pH (as supplied)	6-8	Decomposition temperature (°C)	Not Available
Melting point / freezing point (°C)	Not Available	Viscosity (cSt)	Not Available
Initial boiling point and boiling range (°C)	Not Available	Molecular weight (g/mol)	Not Applicable
Flash point (°C)	Not Available	Taste	Not Available
Evaporation rate	Not Available	Explosive properties	Not Available
Flammability	Not Applicable	Oxidising properties	Not Available
Upper Explosive Limit (%)	Not Available	Surface Tension (dyn/cm or mN/m)	Not Available
Lower Explosive Limit (%)	Not Available	Volatile Component (%vol)	Not Available
Vapour pressure (kPa)	Not Available	Gas group	Not Available
Solubility in water	Miscible	pH as a solution (1%)	Not Available
Vapour density (Air = 1)	Not Available	VOC g/L	Not Available
Heat of Combustion (kJ/g)	Not Available	Ignition Distance (cm)	Not Available
Flame Height (cm)	Not Available	Flame Duration (s)	Not Available
Enclosed Space Ignition Time Equivalent (s/m3)	Not Available	Enclosed Space Ignition Deflagration Density (g/m3)	Not Available

SECTION 10 Stability and reactivity

Reactivity	See section 7
Chemical stability	▶ Unstable in the presence of incompatible materials. ▶ Product is considered stable. ▶ Hazardous polymerisation will not occur.
Possibility of hazardous reactions	See section 7
Conditions to avoid	See section 7
Incompatible materials	See section 7
Hazardous decomposition products	See section 5

SECTION 11 Toxicological information

Information on toxicological effects

a) Acute Toxicity	There is sufficient evidence to classify this material as acutely toxic.
b) Skin Irritation/Corrosion	Based on available data, the classification criteria are not met.
c) Serious Eye Damage/Irritation	Based on available data, the classification criteria are not met.
d) Respiratory or Skin sensitisation	Based on available data, the classification criteria are not met.
e) Mutagenicity	Based on available data, the classification criteria are not met.
f) Carcinogenicity	Based on available data, the classification criteria are not met.
g) Reproductivity	There is sufficient evidence to classify this material as toxic to reproductivity
h) STOT - Single Exposure	Based on available data, the classification criteria are not met.
i) STOT - Repeated Exposure	Based on available data, the classification criteria are not met.
j) Aspiration Hazard	Based on available data, the classification criteria are not met.
Inhaled	The material is not thought to produce respiratory irritation (as classified by EC Directives using animal models). Nevertheless inhalation of vapours, fumes or aerosols, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress. Inhalation of vapours or aerosols (mists, fumes), generated by the material during the course of normal handling, may be damaging to the health of the individual.
Ingestion	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 (including triazoles and azoles) 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,

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Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

	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.
Skin Contact	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, puncture wounds 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.
Eye	Limited evidence exists, or practical experience suggests, that the material may cause eye irritation in a substantial number of individuals and/or is expected to produce significant ocular lesions which are present twenty-four hours or more after instillation into the eye(s) of experimental animals. Repeated or prolonged eye contact may cause inflammation characterised by temporary redness (similar to windburn) of the conjunctiva (conjunctivitis); temporary impairment of vision and/or other transient eye damage/ulceration may occur.
Chronic	On the basis, primarily, of animal experiments, concern has been expressed that the material may produce carcinogenic or mutagenic effects; in respect of the available information, however, there presently exists inadequate data for making a satisfactory assessment. Repeated or long-term occupational exposure is likely to produce cumulative health effects involving organs or biochemical systems. Harmful: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed. Serious damage (clear functional disturbance or morphological change which may have toxicological significance) is likely to be caused by repeated or prolonged exposure. As a rule the material produces, or contains a substance which produces severe lesions. Such damage may become apparent following direct application in subchronic (90 day) toxicity studies or following sub-acute (28 day) or chronic (two-year) toxicity tests. Exposure to the material may cause concerns for humans owing to possible developmental toxic effects, generally on the basis that results in appropriate animal studies provide strong suspicion of developmental toxicity in the absence of signs of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are not a secondary non-specific consequence of other toxic 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. Azole fungicides are broad spectrum antifungal compounds used in agriculture and in human and veterinary medicine. The mechanism of antifungal action relies on inhibition of CYP51 (sterol 14-demethylase), resulting in inhibition of fungal cell growth. Known adverse health effects of azole fungicides are mainly linked to cytochrome P450 (CYP) inhibition. The relatively poor selectivity of the agricultural azoles for the fungal CYP51 over the human homolog raises the concern that exposure to azole fungicide residues might disrupt sterol biosynthesis and other endogenous downstream cytochrome P450 metabolic systems, such as human steroidogenesis and phase I metabolism of xenobiotics in the liver. Agricultural azoles have the general ability to inhibit the P450 enzymes in steroidogenesis, albeit with different potencies. Since the introduction of large-scale use of azole antifungals increasing evidence of hepatotoxicity and associated hepatic tumors has been reported with liver tissue concentrations of ketoconazole and itraconazole being reported as 22- and 10-fold higher, respectively, than plasma levels indicating azole toxicity in the liver being more acute than in other tissues. Additionally, azole fungicide-induced neurotoxicity has been reported. Several azole fungicides induced a nonspecific inhibition of voltage-gated calcium channels (VGCCs), each with varying potency. These findings demonstrate modulation of intracellular calcium ion via inhibition of VGCCs as a novel mode of action of azole fungicides Calcium plays a pivotal role in neuronal survival and functioning. Triazoles are important antifungal compounds, and all drugs in this class inhibit ergosterol synthesis by blocking the 14-alpha-demethylase enzyme, resulting in the accumulation of toxic methylsterols that may culminate in fungal death. Triazole pesticides all contain a triazole ring with nitrogen atoms at the 1,2 and 4 positions. 1,2,4-Triazole (1,2,4-T) and its conjugates, triazole alanine (TA), triazole acetic acid (TAA), triazole pyruvic acid, and triazole lactic acid are the metabolic products of plant, fungal and animal bioconversion. These compounds all possess potentially significant toxicological properties. Following application of a triazole-derivative fungicide, biological and/or chemical processes may cause the triazole ring to be released from the parent compound. In rats and livestock, 1,2,4-triazole is relatively stable and is the terminal form of the triazole ring. In plants, the 1,2,4-triazole molecule may become conjugated to serine. The resulting compound, triazole alanine, may be oxidised to form triazole acetic acid. Triazole alanine and triazole acetic acid are the primary terminal forms of the triazole ring in plants, though some 1,2,4-triazole may remain. The degree of formation of any given form of the triazole ring is highly dependent on the nature and properties of the parent compound. Although other triazole conjugates such as triazole lactic acid and triazole pyruvate have been observed in plant metabolism studies, TA and TAA are the predominant conjugates that need to be included in the dietary risk assessment. Although for most pesticides, mammals convert only a small proportion to free triazole (less than 25%), two compounds (tetraconazole and flusilazole) demonstrate relatively high conversion (68-77%) in rat metabolism studies. Available acute data indicate that 1,2,4-triazole is slightly toxic by the oral route (with oral LD50 values ranging from 666 mg/kg in rabbits to 3650 mg/kg in mice) and slightly to moderately toxic by the dermal route (dermal LD50s were less than 2000 mg/kg in rabbits, and 3000-4000 mg/kg in rats). Limited available information indicates that 1,2,4-triazole is slightly irritating or non-irritating to the skin, but severely irritating to the eye. Based on the limited acute toxicity data, as well as the available developmental toxicity data (see below), it appears that rabbits may be substantially more susceptible to 1,2,4-triazole than are rats or mice. Studies indicate that 1,2,4-triazole affects the central and peripheral nervous systems, reproductive tissues of both sexes, and the hematological system. Developmental and reproductive effects have been noted for this compound. Based on the available metabolism data from rats and livestock, 1,2,4-triazole may form in humans following exposure to parent triazole compounds. Relative to triazole alanine, fewer studies are available depicting the toxicological effects of the other triazole conjugates. It is assumed that the triazole conjugates are all toxicologically equivalent to triazole alanine. The available studies found developmental skeletal effects, decreased body weight and body weight gain, and decreased leukocytes and triglycerides. A number of target organs and critical effects have been identified. 1,2,4-triazole targets the nervous system, both central and peripheral, as brain lesions (most notably in the cerebellum) were seen in both rats and mice, and peripheral nerve degeneration was also seen in the subchronic neurotoxicity study in rats. In addition, brain weight decreases were seen in several studies, including in the offspring in the reproductive toxicity study. In the subchronic/neurotoxicity study, there is evidence that effects progress over time, with an increase in incidence of clinical signs (including tremors and muscle fasciculations) during weeks 8 and 13 that were not seen during earlier evaluations. There is no evidence that exposure to triazole alanine results in neurotoxicity. No clinical signs of neurotoxicity, changes in brain weights, changes in brain gross or microscopic pathology, or any other neurotoxic effects were observed in the short-term rat studies, the subchronic rat and dog feeding studies, the rat developmental toxicity study, or the two-generation reproduction study. Effects were also seen on reproductive organs in both sexes, most notably ovaries (in rats) and testes (in rats and mice), in both the reproductive toxicity and subchronic toxicity studies. Hematological changes, including slightly decreased hemoglobin and/or hematocrit, have also been seen in multiple studies and species (in rats at doses of 33 mg/kg/day and above, and in mice at doses of 487 mg/kg/day and above). 1,2,4-triazole also causes developmental toxicity in both rats and rabbits, including malformations, at doses similar to those inducing maternal toxicity (decreased body weight gain in rats and clinical signs and mortality in rabbits). Developmental toxicity was also seen in the reproductive toxicity study, with offspring showing adverse effects on multiple endpoints (including decreased brain and body weight) at doses lower than those at which effects were seen in parents. In addition, reproductive toxicity was seen in both sexes: at the highest dose (3000 ppm), only two F1 litters (one pup/litter) were produced, and neither survived to adulthood. Triazole alanine showed increased incidences of skeletal findings in the offspring at the mid and high doses, while no treatment-related effects were seen in the dams up to the limit dose. The skeletal findings included unossified odontoid processes at 300 and 1000 mg/kg/day, with partially ossified transverse processes of the 7th cervical vertebra (bilateral), unossified 5th sternebra, and partially ossified 13th thoracic centrum observed only at 1000 mg/kg/day.

Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

Available mutagenicity data are limited but negative. A large number of parent triazole-derivative pesticides have been classified as carcinogens (most also non-mutagenic), but the relevance of that finding to expected effects of free triazole may be limited. The types of tumors associated with exposure to the parent chemicals are most commonly hepatocellular adenomas/carcinomas in mice. Other tumor types vary considerably (including liver tumors, thyroid tumors, ovarian tumors, testicular tumors, and bladder tumors). None of the tumor types are clearly associated with the proportion of free triazole formed in available rat metabolism studies. Evidence indicates that the parent triazole compounds appear to result in a tumor response subsequent to perturbation of liver metabolism, specifically xenobiotic and fatty acid metabolic pathways. In addition the thyroid response appears to be secondary to perturbation of thyroid homeostasis. Thus, the conazoles appear to drive a tumor response secondary to epigenetic effects and not from direct interaction with the DNA. An epigenetic mode of action would be consistent with a nonlinear process.

Azole antifungals cause hepatotoxicity by inducing the expression of liver cytochrome P450 enzymes (CYP1, CYP2, and CYP3 families), which in turn increases the abundance of reactive oxygen species in liver cells, resulting in lipid peroxidation and DNA damage. In addition, azole antifungals have the potential to inhibit liver P450 enzymes, interfering in the phase I metabolism of xenobiotics.

Disruption of the endocrine system, by azoles, can lead to impaired reproduction, alterations in sexual differentiation, impaired growth and development, and the formation of hormone-dependent cancers. Azole antifungals disrupt the endocrine system by inhibiting several highly substrate-selective cytochrome P450 enzymes involved in mammalian steroid hormone biosynthesis. These include aromatase (CYP19) (which catalyzes the C-10 demethylation of androgens to estrogens), CYP11A (which converts cholesterol to pregnenolone), steroid 21-hydroxylase (CYP21), aldosterone synthase (CYP11B2), steroid 11 β -hydroxylase (CYP11B1), steroid 17 α -hydroxylase/17,20-lyase (CYP17), and lanosterol 14 α -demethylase (CYP51), disturbing the in vivo hormonal balance.

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 difference between the imidazoles and the triazoles involves the mechanism of inhibition of the cytochrome P450 enzyme. The N3 of the imidazole compound binds to the heme iron atom of ferric cytochrome P450, whereas the N4 of the triazoles bind to the heme group. The triazoles have been shown to have a higher specificity for the cytochrome P450 than imidazoles, thereby making them more potent than the imidazoles.

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 α -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.

Aromatase is another target enzyme of azole compounds. In steroidogenesis, it converts androgens into the corresponding oestrogens. The importance of androgens and oestrogens 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 oestrogen-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 α -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 α -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 α -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 α -demethylase and/or aromatase, but the overall view strongly suggests a connection with disturbed steroidogenesis.

Zam et al; Environmental Health Perspectives-3/1/2003

Some azoles have been associated with prolongation of the QT interval on the electrocardiogram.

Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)	TOXICITY	IRRITATION
	Not Available	Not Available
tebuconazole	TOXICITY	IRRITATION
	dermal (rat) LD50: >5000 mg/kg ^[2]	Not Available
	Inhalation (Rat) LC50: >0.8 mg/L4h ^[2]	
	Oral (Mouse) LD50; 2000 mg/kg ^[2]	
Legend:	1. Value obtained from Europe ECHA Registered Substances - Acute toxicity 2. Value obtained from manufacturer's SDS. Unless otherwise specified data extracted from RTECS - Register of Toxic Effect of chemical Substances	

TEBUCONAZOLE	(aerosol) NOEL (2 y)* for rats, 300 mg/kg diet for dogs, 100 mg/kg " for mice, 20 mg/kg " ADI 0.03 mg/kg b.w. * Toxicity Class WHO III; EPA III * Side effects of antiestrogens include hot flashes, osteoporosis, breast atrophy, vaginal dryness, and vaginal atrophy. In addition, they may cause depression and reduced libido. The antiestrogen withdrawal response is a paradoxical improvement in breast cancer caused by discontinuation of antiestrogen therapy for breast cancer. It has been documented rarely with the selective estrogen receptor modulators (SERMs) tamoxifen and raloxifene. The phenomenon indicates that these agents can somehow result in stimulation of breast cancer tumor progression under certain circumstances. One proposed theory for the mechanism is that the sensitivity of breast cells to estrogens shifts with estrogen deprivation, and upon antiestrogen withdrawal, endogenous estrogen acts in the manner of high-dose estrogen therapy in the breast to inhibit breast cancer growth and induce breast cancer cell death. The antioestrogen withdrawal syndrome is analogous to but less common and well-known than the antiandrogen withdrawal syndrome, a phenomenon in which paradoxical improvement in prostate cancer occurs upon discontinuation of antiandrogen therapy. aromatase inhibitors (AIs) are commonly used in breast cancer treatment, but they can cause various side effects, primarily due to estrogen depletion. Common side effects include musculoskeletal problems like joint pain (arthralgia), muscle stiffness, and bone loss leading to osteoporosis and fractures. Additionally, women may experience menopausal symptoms such as hot flashes, vaginal dryness, and sexual dysfunction. Other potential side effects include fatigue, insomnia, and an increased risk of cardiovascular events. ther Common Side Effects: Fatigue: Many patients report feeling tired or weak. Insomnia: Sleep disturbances are also common.
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Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

Cardiovascular Events: While less frequent, there's a slightly increased risk of heart problems, especially in women with pre-existing conditions.

Weight Gain: Als can contribute to weight gain.

Mood Changes: Some women experience depression or mood swings.

Less Common but Serious Side Effects:

Liver Problems: Als can occasionally affect liver function.

Skin Reactions: Skin rashes and other skin changes can occur.

Cardiovascular Risks: Some studies suggest an increased risk of heart attack or stroke.

Cytochrome P450 (CYP) enzyme modulators can cause adverse effects, primarily through drug-drug interactions. Specifically, CYP inhibitors can increase the concentration of other drugs in the body, leading to toxicity or adverse reactions, while CYP inducers can decrease drug concentrations, potentially causing therapeutic failure.

CYP inhibitors, particularly those affecting CYP3A4, can cause a range of adverse effects due to their impact on drug metabolism. These effects include increased risk of toxicity from other drugs, arrhythmias like torsades de pointes, rhabdomyolysis, and even potentially fatal outcomes

depending on the specific CYP inhibitor and the other drugs involved, adverse effects can include gastrointestinal disorders, liver damage, and neurological problems.

CYP inhibitors can reduce the metabolism of other drugs, leading to higher concentrations in the bloodstream and potentially increasing the risk of side effects and toxicity

People metabolize drugs differently, and factors like age, sex, genetics, and other medical conditions can influence how CYP inhibitors affect them.

Incidents of liver injury or failure among modern antifungal medicines are very low to non-existent. However, some can cause allergic reactions in people.[

There are also many drug interactions. Patients must read in detail the enclosed data sheet(s) of any medicine. For example, the azole antifungals such as ketoconazole or itraconazole can be both substrates and inhibitors of the P-glycoprotein, which (among other functions) excretes toxins and drugs into the intestines.] Azole antifungals also are both substrates and inhibitors of the cytochrome P450 family CYP3A4,[] causing increased concentration when administering, for example, calcium channel blockers, immunosuppressants, chemotherapeutic drugs, benzodiazepines, tricyclic antidepressants, macrolides and SSRIs.[35]

Before oral antifungal therapies are used to treat nail disease, a confirmation of the fungal infection should be made.[Approximately half of suspected cases of fungal infection in nails have a non-fungal cause.[The side effects of oral treatment are significant and people without an infection should not take these drugs.[

Azoles are the group of antifungals which act on the cell membrane of fungi. They inhibit the enzyme 14-alpha-sterol demethylase, a microsomal CYP, which is required for biosynthesis of ergosterol for the cytoplasmic membrane. This leads to the accumulation of 14-alpha-methylsterols resulting in impairment of function of certain membrane-bound enzymes and disruption of close packing of acyl chains of phospholipids, thus inhibiting growth of the fungi. Some azoles directly increase permeability of the fungal cell membrane.

Antifungal resistance is a subset of antimicrobial resistance, that specifically applies to fungi that have become resistant to antifungals.

Resistance to antifungals can arise naturally, for example by genetic mutation or through aneuploidy. Extended use of antifungals leads to development of antifungal resistance through various mechanisms.

Some fungi (e.g. *Candida krusei* and fluconazole) exhibit intrinsic resistance to certain antifungal drugs or classes, whereas some species develop antifungal resistance to external pressures. Antifungal resistance is a One Health concern, driven by multiple extrinsic factors, including extensive fungicidal use, overuse of clinical antifungals, environmental change and host factors.]

Unlike resistance to antibacterials, antifungal resistance can be driven by antifungal use in agriculture. Currently there is no regulation on the use of similar antifungal classes in agriculture and the clinic.

The emergence of *Candida auris* as a potential human pathogen that sometimes exhibits multi-class antifungal drug resistance is concerning and has been associated with several outbreaks globally. The WHO has released a priority fungal pathogen list, including pathogens with antifungal resistance

conazoles are azole antifungals used in agricultural and pharmaceutical products. Exposure to conazole fungicides leads to several toxic endpoints, including reproductive and endocrine. The results of animal experiments have shown that various conazole fungicides at high doses affect the structure and functions of reproductive organs. In males, adverse effects of conazole fungicides are manifested in the testes, prostate, sperm viability, fertility and sexual behaviour. Reduced testis weight, testis atrophy and reduced or absent sperm production were frequently observed. In female genitalia, structural changes in the ovaries and uterus have been observed. The extent of the changes depends on the dose and duration of treatment. Triazoles affected the expression of multiple genes involved in steroid hormone metabolism and modulate enzyme activity of multiple cytochrome P450 (CYP) and other metabolic enzymes in mammalian liver and other tissues. Conazole fungicides act as endocrine disruptors. Conazoles have been reported to reduce oestradiol and testosterone production and to increase progesterone concentration, indicating the inhibition of enzymes involved in the conversion of progesterone to testosterone. The reproductive effects are consistent with impairment of testosterone homeostasis. The disruption in steroid homeostasis is a common mode of action, leading to abnormal reproductive development and diminished reproductive function. At high doses, azole fungicides affect reproductive organs and fertility in several species.

The relatively poor selectivity of the agricultural azoles for the fungal CYP51 over the human homolog raises the concern that exposure to azole fungicide residues might disrupt sterol biosynthesis and other endogenous downstream cytochrome P450 metabolic systems, such as human steroidogenesis and phase I metabolism of xenobiotics in the liver.

agricultural azoles have the general ability to inhibit the P450 enzymes in steroidogenesis, albeit with different potencies. Since the introduction of large-scale use of azole antifungals increasing evidence of hepatotoxicity and associated hepatic tumors has been reported with liver tissue concentrations of ketoconazole and itraconazole being reported as 22- and 10-fold higher, respectively, than plasma levels (58), indicating azole toxicity in the liver being more acute than in other tissues.

Rapidly multiplying cancer cells synthesize greater amounts of cholesterol to build their membranes.

Sterol 14alpha-demethylase (CYP51) is potentially a specific drug target because of its role in the production of cholesterol in animals. Sterol biosynthesis is an essential metabolic pathway in most eukaryotes and in some bacteria. Sterols (cholesterol in humans, sitosterol in plants, ergosterol and its C24-alkylated derivatives in fungi and protozoa) are required components of eukaryotic membranes, where they control fluidity and permeability and modulate functions of membrane-bound enzymes, receptors, and ion channels. These sterols also serve as precursors for multiple regulatory molecules that are crucial for cell division, growth, and development.

Sterol biosynthesis is the target for many drugs. Statins, as inhibitors of HMG-CoA reductase (EC.1.1.1.34), act upstream in the pathway at the step of mevalonate production and serve as major cholesterol-lowering drugs in humans, while azoles, as inhibitors of fungal and protozoan cytochrome P450 sterol 14a-demethylase (CYP51, EC.1.14.13.70), act downstream in the pathway at its postsqualene portion and are widely used as antimicrobial agent.

Human CYP51 [<35% amino acid sequence identity with fungal and <25% identity with protozoan orthologs (9)] has also been considered as a drug target.

Due to the side effects of statins, alternative drugs that target cholesterol biosynthesis in humans more specifically would be highly desirable, and CYP51, the lanosterol demethylase, is a target of interest in that several more distal (post-lanosterol) steps in the cholesterol synthesis pathway are known to be associated with hereditary diseases when they are attenuated (40). For instance, a loss of the sterol 7-reductase (DHCR7) is associated with a severe disease, Smith-Lemli-Opitz syndrome (41). Deficiency in the 3β-hydroxysteroid dehydrogenase (NSDHL) is responsible for congenital hemidysplasia, ichthyosiform nevus, and limb defects (CHILD) syndrome (42). Mutations in the 7β-sterol isomerase (EBP) are associated with Conradi-Hünermann-Happle syndrome, or X-linked dominant chondrodysplasia punctate type 2 (CDPX2) (40), and mutations in sterol 5-desaturase (SC5D) cause lathosterolosis (43). Compared with these problems, attenuating lanosterol 14-demethylation seems very favourable.

It is now generally accepted that cancer cells have elevated levels of cholesterol in lipid rafts and contain more lipid rafts than their normal cell line counterparts (26, 27, 29, 31, 44). Enhanced expression of enzymes of the cholesterol pathway has been reported in many cancer cell types (31, 45–47). Furthermore, certain types of cancer exhibit CYP51 gene amplification (<https://www.cbioportal.org>). It is likely that the earlier attempts to develop human CYP51 inhibitors were unsuccessful because they concentrated on substrate analogs, which had rather low inhibitory potency (10) and could not compete in efficiency with statins.

Continued...

Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

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However, screening a variety of commercial and experimental inhibitors of microbial CYP51 orthologs revealed that most of them (including all clinical antifungals) weakly inhibit human CYP51 activity,

Present in all animals, plants, fungi, in some protozoa and bacteria, the CYP51 protein located in the inner face of the endoplasmic reticulum is a membrane monospanning enzyme. Its N-terminus includes an amphipathic helix, which links the catalytic subunit to the lipid bilayer.

Sterol synthesis is a very ancient pathway. After the appearance of molecular oxygen in the atmosphere, squalene-2,3-epoxide is formed and then cyclized to steroid precursors, such as lanosterol. Under the oxidative removal of methyl groups by CYP51, these precursors were transformed into ergosterol, which is critical in membrane permeability and fluidity in the fungal kingdom.

Cytochrome P450s (P450s, CYP) are an abundant hemease superfamily. As the first group of enzymes ranked as "superfamily," cytochrome P450s play an important role in the primary as well as secondary metabolic pathway.

These members are important for catalyzing the oxidative process of various organic substrates, and play a critical role during heterogeneous metabolism and steroid conversion in biological kingdoms.

Unlike other CYP enzymes, CYP51 has a strong specificity. It only catalyzes the demethylation of a very narrow range of substrates, including lanosterol, obtusifoliol, 24,25-dihydrolanosterol, 24-methylenedihydrolanosterol and 4 beta-desmethyl lanosterol. The CYP51-involved catalytic reaction consists of three steps, each of which requires one molecule of oxygen and two molecules of NADPH-sourced reduction equivalent. The first two steps are typical cytochrome P450 monooxygenation processes, during which the 14a methyl is converted to methyl alcohol and further converted to methyl aldehyde. And in the last step, the aldehyde group is transformed into formic acid and detached, accompanied with the synthesis of the delta-14, 15 double bond.

The 14a-demethylase is the only invariant P450 present in all sterol biosynthetic pathways, suggesting that all sterol 14a-demethylases share a common prokaryotic ancestor. CYP51s are widely distributed in the fungal kingdom. However, in different species of fungi, there are still differences in the types and subtypes, as shown in the phylogenetic tree.

As potential anticancer agents, human CYP51 inhibitors are expected to have generally the same mode of action as statins in vivo, yet present certain important advantages. First, their specificity for the biosynthesis of cholesterol would help to avoid side effects of statins due to inhibition of other metabolic pathways. Second, as with systemic clinical antifungal azoles, which kill pathogenic cells that invade multiple organs and tissues, they should have broad tissue distribution. Finally, because all mammalian CYP51 enzymes share very high amino acid sequence identity (e.g., human/mouse 88%, human/dog 96%), animal in vivo models should produce highly relevant outcomes in preclinical trials. Potential inhibitors of human CYP51 may also have advantages as alternative medications for treatment of other cholesterol-related human diseases. The dual occupancy may be important in the mechanism of human CYP51 inhibition.

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Acute Toxicity	✓	Carcinogenicity	✗
Skin Irritation/Corrosion	✗	Reproductivity	✓
Serious Eye Damage/Irritation	✗	STOT - Single Exposure	✗
Respiratory or Skin sensitisation	✗	STOT - Repeated Exposure	✗
Mutagenicity	✗	Aspiration Hazard	✗

Legend: ✗ – Data either not available or does not fill the criteria for classification
✓ – Data available to make classification

Toxicity

Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)	Endpoint	Test Duration (hr)	Species	Value	Source
	Not Available	Not Available	Not Available	Not Available	Not Available
tebuconazole	Endpoint	Test Duration (hr)	Species	Value	Source
	NOEC(ECx)	672h	Crustacea	0.001mg/L	4
	EC50	72h	Algae or other aquatic plants	2.09-3.01mg/l	4
	EC50	48h	Crustacea	2.1-3.94mg/L	4
	EC50	96h	Algae or other aquatic plants	1.45mg/L	4
	LC50	96h	Fish	6.4mg/l	Not Available
Legend: Extracted from 1. IUCLID Toxicity Data 2. Europe ECHA Registered Substances - Ecotoxicological Information - Aquatic Toxicity 3. US EPA, Ecotox database - Aquatic Toxicity Data 4. ECETOC Aquatic Hazard Assessment Data 5. NITE (Japan) - Bioconcentration Data 6. METI (Japan) - Bioconcentration Data 7. Vendor Data					

Very 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.

Triazole fungicides share common metabolites, the triazole compounds 1,2,4-triazole (free triazole), triazole alanine, and triazole acetic acid. In environmental fate studies, all three forms of triazole (1,2,4-T, TA, and TAA) have been found and there is evidence that the three can inter-convert in soil and aquatic systems.

As a plant metabolite, and given the wide use of triazole-derivative pesticides (used as fungicides on many crops as well as on turf) free triazole is found in a variety of food commodities, including animal byproducts. 1,2,4-triazole appears to be relatively stable in the environment, and may be found in rotational crops as well as in water.

Studies indicate that 1,2,4-triazole affects the central and peripheral nervous systems, reproductive tissues of both sexes, and the hematological system. Developmental and reproductive effects have been noted for this compound. Based on the available metabolism data from rats and livestock, 1,2,4-triazole may form in humans following exposure to parent triazole compounds.

The available studies on triazole conjugates found developmental skeletal effects, decreased body weight and body weight gain, and decreased leukocytes and triglycerides following exposure in animals.

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.

Persistence and degradability

Ingredient	Persistence: Water/Soil	Persistence: Air
tebuconazole	HIGH	HIGH

Bioaccumulative potential

Ingredient	Bioaccumulation
tebuconazole	LOW (LogKOW = 3.7)

Mobility in soil

Ingredient	Mobility
tebuconazole	LOW (Log KOC = 20660)

SECTION 13 Disposal considerations

Waste treatment methods

Product / Packaging disposal	- 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 SDS 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.
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Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)

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. If it has been contaminated, it may be possible to reclaim the product by filtration, distillation or some other means. 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 or consult manufacturer for recycling options.
- ▶ Consult State Land Waste Authority for disposal.
- ▶ Bury or incinerate residue at an approved site.
- ▶ Recycle containers if possible, or dispose of in an authorised landfill.

SECTION 14 Transport information

Labels Required

	
Marine Pollutant	
HAZCHEM	•3Z

Land transport (ADG)

14.1. UN number or ID number	3082	
14.2. UN proper shipping name	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (contains tebuconazole)	
14.3. Transport hazard class(es)	Class	9
	Subsidiary Hazard	Not Applicable
14.4. Packing group	III	
14.5. Environmental hazard	Environmentally hazardous	
14.6. Special precautions for user	Special provisions	274 331 335 375 AU01
	Limited quantity	5 L

Environmentally Hazardous Substances meeting the descriptions of UN 3077 or UN 3082 are not subject to this Code when transported by road or rail in;

(a) packagings;

(b) IBCs; or

(c) any other receptacle not exceeding 500 kg(L).

- Australian Special Provisions (SP AU01) - ADG Code 7th Ed.

Air transport (ICAO-IATA / DGR)

14.1. UN number	3082	
14.2. UN proper shipping name	Environmentally hazardous substance, liquid, n.o.s. (contains tebuconazole)	
14.3. Transport hazard class(es)	ICAO/IATA Class	9
	ICAO / IATA Subsidiary Hazard	Not Applicable
	ERG Code	9L
14.4. Packing group	III	
14.5. Environmental hazard	Environmentally hazardous	
14.6. Special precautions for user	Special provisions	A97 A158 A197 A215
	Cargo Only Packing Instructions	964
	Cargo Only Maximum Qty / Pack	450 L
	Passenger and Cargo Packing Instructions	964
	Passenger and Cargo Maximum Qty / Pack	450 L
	Passenger and Cargo Limited Quantity Packing Instructions	Y964
	Passenger and Cargo Limited Maximum Qty / Pack	30 kg G

Sea transport (IMDG-Code / GGVSee)

14.1. UN number	3082
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14.2. UN proper shipping name	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (contains tebuconazole)	
14.3. Transport hazard class(es)	IMDG Class	9
	IMDG Subsidiary Hazard	Not Applicable
14.4. Packing group	III	
14.5 Environmental hazard	Marine Pollutant	
14.6. Special precautions for user	EMS Number	F-A, S-F
	Special provisions	274 335 375 969
	Limited Quantities	5 L

14.7. Maritime transport in bulk according to IMO instruments

14.7.1. Transport in bulk according to Annex II of MARPOL and the IBC code

Not Applicable

14.7.2. Transport in bulk in accordance with MARPOL Annex V and the IMSBC Code

Product name	Group
tebuconazole	Not Applicable

14.7.3. Transport in bulk in accordance with the IGC Code

Product name	Ship Type
tebuconazole	Not Applicable

SECTION 15 Regulatory information

Safety, health and environmental regulations / legislation specific for the substance or mixture

tebuconazole is found on the following regulatory lists

Australia Hazardous Chemical Information System (HCIS) - Hazardous Chemicals
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 5

Additional Regulatory Information

Not Applicable

National Inventory Status

National Inventory	Status
Australia - AIC / Australia Non-Industrial Use	No (tebuconazole)
Canada - DSL	No (tebuconazole)
Canada - NDSL	No (tebuconazole)
China - IECSC	Yes
Europe - EINEC / ELINCS / NLP	Yes
Japan - ENCS	Yes
Korea - KECI	Yes
New Zealand - NZIoC	Yes
Philippines - PICCS	Yes
USA - TSCA	No (tebuconazole)
Taiwan - TCSI	Yes
Mexico - INSQ	Yes
Vietnam - NCI	Yes
Russia - FBEPH	Yes
UAE - Control List (Banned/Restricted Substances)	Yes
Legend:	Yes = All CAS declared ingredients are on the inventory No = One or more of the CAS listed ingredients are not on the inventory. These ingredients may be exempt or will require registration.

SECTION 16 Other information

Revision Date	13/05/2026
Initial Date	08/01/2025

SDS Version Summary

Version	Date of Update	Sections Updated
3.1	10/10/2025	Classification change due to full database hazard calculation/update.
3.1	13/05/2026	Hazards identification - Classification

Titan Tebuconazole 430 (Titan Tebuconazole 430 SC Fungicide)**Other information**

Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

The SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

Definitions and abbreviations

- PC - TWA: Permissible Concentration-Time Weighted Average
- PC - STEL: Permissible Concentration-Short Term Exposure Limit
- IARC: International Agency for Research on Cancer
- ACGIH: American Conference of Governmental Industrial Hygienists
- STEL: Short Term Exposure Limit
- TEEL: Temporary Emergency Exposure Limit,
- IDLH: Immediately Dangerous to Life or Health Concentrations
- ES: Exposure Standard
- OSF: Odour Safety Factor
- NOAEL: No Observed Adverse Effect Level
- LOAEL: Lowest Observed Adverse Effect Level
- TLV: Threshold Limit Value
- LOD: Limit Of Detection
- OTV: Odour Threshold Value
- BCF: BioConcentration Factors
- BEI: Biological Exposure Index
- DNEL: Derived No-Effect Level
- PNEC: Predicted no-effect concentration
- MARPOL: International Convention for the Prevention of Pollution from Ships
- IMSBC: International Maritime Solid Bulk Cargoes Code
- IGC: International Gas Carrier Code
- IBC: International Bulk Chemical Code

- AIIC: Australian Inventory of Industrial Chemicals
- DSL: Domestic Substances List
- NDSL: Non-Domestic Substances List
- IECSC: Inventory of Existing Chemical Substance in China
- EINECS: European INventory of Existing Commercial chemical Substances
- ELINCS: European List of Notified Chemical Substances
- NLP: No-Longer Polymers
- ENCS: Existing and New Chemical Substances Inventory
- KECI: Korea Existing Chemicals Inventory
- NZIoC: New Zealand Inventory of Chemicals
- PICCS: Philippine Inventory of Chemicals and Chemical Substances
- TSCA: Toxic Substances Control Act
- TCSI: Taiwan Chemical Substance Inventory
- INSQ: Inventario Nacional de Sustancias Químicas
- NCI: National Chemical Inventory
- FBEPH: Russian Register of Potentially Hazardous Chemical and Biological Substances

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