

Zonisamide

sc-203316



The Power to Question

Material Safety Data Sheet

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

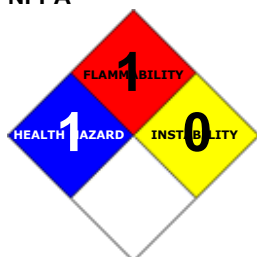
PRODUCT NAME

Zonisamide

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Company: Santa Cruz Biotechnology, Inc.

Address:

2145 Delaware Ave

Santa Cruz, CA 95060

Telephone: 800.457.3801 or 831.457.3800

Emergency Tel: CHEMWATCH: From within the US and

Canada: 877-715-9305

Emergency Tel: From outside the US and Canada: +800 2436

2255 (1-800-CHEMCALL) or call +613 9573 3112

PRODUCT USE

Zonisamide is an anti-epileptic. It is effective in various animal epilepsy models and humans with both partial and generalized epileptic seizures. Zonisamide sodium salt also scavenges nitric oxide (NO). A sulfonamide anticonvulsant approved for use as an adjunctive therapy in adults with partial-onset seizures for adults; infantile spasm, mixed seizure types of Lennox-Gastaut syndrome, myoclonic, and generalized tonic clonic seizure Has also been studied for obesity with significant positive effects on body weight Has been used off-label by psychiatrists as a mood stabilizer to treat bipolar depression. Sulfonamide antiseizure agent; blocks repetitive firing of voltage-sensitive sodium channels and reduces voltage-sensitive T-type calcium currents. Stimulates BKCa channels, modulates GABA, glutamate and monoamine neurotransmission, inhibits lipid peroxidation and scavenges hydroxyl and nitric oxide free radicals. Displays neuroprotective and anti-Parkinsonian activity

SYNONYMS

C8-H8-N2-O3-S, "1, 2-benzisoxazole-3-methanesulfonamide", "1, 2-benzisoxazole-3-methanesulfonamide", "3-(sulfamoylmethyl)-1, 2-benzisoxazole", "3-(sulfamoylmethyl)-1, 2-benzisoxazole", Aleviatin, Excegram, Exceglan, "anti-epileptic / anticonvulsant"

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Harmful if swallowed.

Possible risk of harm to the unborn child.

Toxic to soil organisms.

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.
- Antiepileptic drugs (AEDs) act as anticonvulsants and increase the risk of suicidal thoughts or behavior in patients taking

these drugs for any indication. Persons exposed to AEDs for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior (such as anxiety, agitation, hostility, pressured/rapid speech).

The increased risk of suicidal thoughts or behavior with AEDs was observed as early as one week after starting drug treatment with AEDs and persisted for the duration of treatment assessed. Because most trials included in the analysis did not extend beyond 24 weeks, the risk of suicidal thoughts or behavior beyond 24 weeks could not be assessed.

The finding of increased risk with AEDs of varying mechanisms of action and across a range of indications suggests that the risk applies to all AEDs used for any indication. The risk did not vary substantially by age (5-100 years) in the clinical trials analysed.

The relative risk for suicidal thoughts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar for the epilepsy and psychiatric indications.

■ Sulfonamides and their derivatives can cause extensive kidney damage, and destroy red blood cells. Overdose may cause an accumulation of acid in the blood or a diminished blood sugar level with confusion and coma resulting. Predisposed persons can develop hypersensitivity reactions, including for topical application. Deaths have occurred due to hypersensitivity, anemia, imbalances in blood cell distribution and kidney and liver damage. 2-5 grams can be fatal. Sulfonamides cross the placental barrier, are excreted in the breast milk and may produce adverse effects in the fetus/ embryo and newborn, including loss of certain white blood cells causing immune function deficiency, anemia, jaundice and kernicterus.

EYE

■ There is some evidence to suggest that this material can cause eye irritation and damage in some persons.
 ■ Eye drops with sulfonamides can cause local irritation, sensations of burning and stinging, blurred vision and loss of depth perception. The conjunctiva and cornea may become inflamed, and the cornea and lens may become clouded.

SKIN

■ Skin contact is not thought to produce harmful health effects (as classified using animal models). Systemic harm, however, has been identified following exposure of animals by at least one other route and the material may still produce health damage following entry through wounds, lesions or abrasions. Good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.

■ 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 either adverse health effects or irritation of the respiratory tract following inhalation (as classified using animal models). Nevertheless, adverse effects have been produced following exposure of animals by at least one other route and good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.

■ 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.

CHRONIC HEALTH EFFECTS

■ Results in experiments suggest that this material may cause disorders in the development of the embryo or fetus, even when no signs of poisoning show in the mother.

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

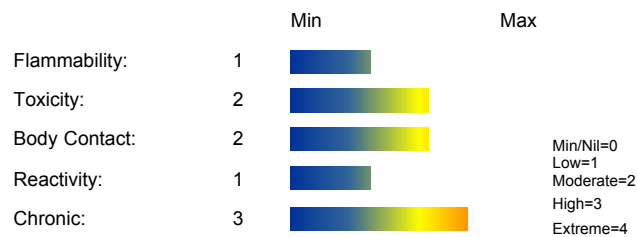
There is some evidence to provide a presumption that human exposure to the material may result in impaired fertility on the basis of: some evidence in animal studies of impaired fertility in the absence of toxic effects, or evidence of impaired fertility occurring at around the same dose levels as other toxic effects but which is not a secondary non-specific consequence of other toxic effects.

Prolonged oral treatment with sulfonamides has caused nausea, vomiting, diarrhea, abdominal pain, loss of appetite, inflammation of the mouth cavity, impaired folic acid absorption, exacerbation of porphyria, acidosis, liver damage with impaired blood clotting, jaundice and inflammation of the pancreas. Effects on the kidney include blood and crystals in the urine, painful and frequent urination or lack of urine with nitrogen retention. Nervous system symptoms include headache, drowsiness, trouble sleeping, dizziness, ringing in the ears, hearing loss, depression, hallucinations, inco-ordination, paralysis of muscles, numbness in the extremities, spinal cord damage and inflammation, convulsions and unconsciousness. Effects on the blood includes a change in blood cell distribution with loss of white blood cells and platelets, and anemia, which Africans seem to be more prone to developing than Europeans. Cyanosis can occur owing to complexes being formed by hemoglobin. Eye effects include inflamed cornea and conjunctiva with eyelid swelling and in severe cases, fear of the light. Allergies and cross-sensitivity is common, and can cause itches, wheals and sometimes a severe red rash with blisters that is often fatal. This class of drugs can scar the cornea and conjunctiva, swelling around the eyes, painful and inflamed joints, reduced sperm counts, pneumonia, fever, chills, hair loss, inflammation of vessels, lupus, reduced lung function, infertility, hypothyroidism and goiter, and increased urinary output. More seriously, the lungs may become permanently scarred and there may be irreversible damage to the nervous system and muscles. Inflammation of the skin has occurred after the drug is ingested and has traveled through the bloodstream. Skin effects often occur when there has been exposure in conjunction with UV light. Clothed areas are initially less likely to be affected but may be in later stages. Rarely there may be persistence of inflammation on light contact even after the drug has been removed.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung. Prime symptom is breathlessness; lung shadows show on X-ray.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS



NAME	CAS RN	%
zonisamide sodium	68291-98-5	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

-
- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.

- Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:
- For advice, contact a Poisons Information Center or a doctor.
- Urgent hospital treatment is likely to be needed.
- If conscious, give water to drink.
- 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.

- 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.

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.
 - 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 or hair contact occurs:
 - Flush skin and hair with running water (and soap if available).
 - Seek medical attention in event of irritation.

INHALED

- - If fumes or combustion products are inhaled remove from contaminated area.
 - Other measures are usually unnecessary.

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 edema .
- 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 hypovolemia are present use lactated Ringers solution. Fluid overload might create complications.
- Drug therapy should be considered for pulmonary edema.
- Hypotension with signs of hypovolemia 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.

For anticonvulsants:

It is recommended that the physician withdraw the drug slowly on the appearance of unusual depression, aggressiveness, or other behavioral alterations.

As with other anticonvulsants, it is important to proceed slowly when increasing or decreasing dosage, as well as when adding or eliminating other medication. Abrupt withdrawal of anticonvulsant medication may precipitate absence (petit mal) status.

Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):	Negligible
Upper Explosive Limit (%):	Not Available
Specific Gravity (water=1):	Not Available
Lower Explosive Limit (%):	Not Available

EXTINGUISHING MEDIA

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

FIRE FIGHTING

- - Alert Emergency Responders 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.
 - Use water delivered as a fine spray to control fire and cool adjacent 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.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- Combustible solid which burns but propagates flame with difficulty.
- 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 may burn rapidly and fiercely if ignited.
- 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.

Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), nitrogen oxides (NO_x), sulfur oxides (SO_x), other pyrolysis products typical of burning organic material.

May emit poisonous fumes.

May emit corrosive fumes.

FIRE INCOMPATIBILITY

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

PERSONAL PROTECTION

Glasses:

Chemical goggles.

Gloves:

Respirator:

Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- Environmental hazard - contain spillage.
- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.
- Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
- Dampen with water to prevent dusting before sweeping.
- Place in suitable containers for disposal.

MAJOR SPILLS

- Environmental hazard - contain spillage.
- Moderate hazard.
- CAUTION: Advise personnel in area.
- Alert Emergency Responders 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.

ACUTE EXPOSURE GUIDELINE LEVELS (AEG) (in ppm)

AEG 1: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

AEG 2: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.

AEG 3: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

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.

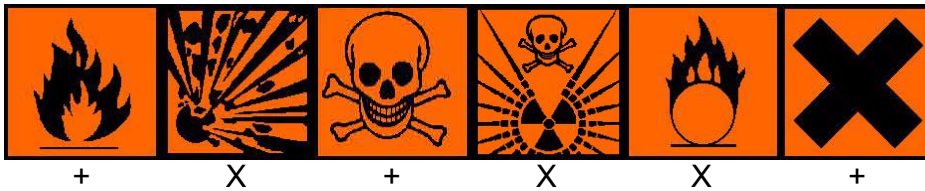
RECOMMENDED STORAGE METHODS

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

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.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS



X: Must not be stored together

O: May be stored together with specific preventions

+: May be stored together

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- zonisamide: CAS:68291-97-4
- zonisamide sodium: CAS:68291-98-5

MATERIAL DATA

ZONISAMIDE SODIUM:

ZONISAMIDE:

■ Airborne particulate or vapor must be kept to levels as low as is practicably achievable given access to modern engineering controls and monitoring hardware. Biologically active compounds may produce idiosyncratic effects which are entirely unpredictable on the basis of literature searches and prior clinical experience (both recent and past).

ZONISAMIDE:

■ 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.

Sensory irritants are chemicals that produce temporary and undesirable side-effects on the eyes, nose or throat. Historically occupational exposure standards for these irritants have been based on observation of workers' responses to various airborne concentrations. Present day expectations require that nearly every individual should be protected against even minor sensory irritation and exposure standards are established using uncertainty factors or safety factors of 5 to 10 or more. On occasion animal no-observable-effect-levels (NOEL) are used to determine these limits where human results are unavailable. An additional approach, typically used by the TLV committee (USA) in determining respiratory standards for this group of chemicals, has been to assign ceiling values (TLV C) to rapidly acting irritants and to assign short-term exposure limits (TLV STELs) when the weight of evidence from irritation, bioaccumulation and other endpoints combine to warrant such a limit. In contrast the MAK Commission (Germany) uses a five-category system based on intensive odour, local irritation, and elimination half-life. However this system is being replaced to be consistent with the European Union (EU) Scientific Committee for Occupational Exposure Limits (SCOEL); this is more closely allied to that of the USA.

OSHA (USA) concluded that exposure to sensory irritants can:

- cause inflammation
- cause increased susceptibility to other irritants and infectious agents
- lead to permanent injury or dysfunction
- permit greater absorption of hazardous substances and
- acclimate the worker to the irritant warning properties of these substances thus increasing the risk of overexposure.

PERSONAL PROTECTION



Consult your EHS staff for recommendations

EYE

■ When handling very small quantities of the material eye protection may not be required.
For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:

- Chemical goggles
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- 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.

- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers.
- Head covering.

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

-
- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.
- Eye wash unit.
- Ensure there is ready access to an emergency shower.
- For Emergencies: Vinyl suit

-
- 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 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 x PEL	P1	-	PAPR-P1
	Air-line*	-	-
50 x PEL	Air-line**	P2	PAPR-P2
100 x PEL	-	P3	-
		Air-line*	-
100+ x PEL	-	Air-line**	PAPR-P3

* - Negative pressure demand ** - Continuous flow

Explanation of Respirator Codes:

Class 1 low to medium absorption capacity filters.

Class 2 medium absorption capacity filters.

Class 3 high absorption capacity filters.

PAPR Powered Air Purifying Respirator (positive pressure) cartridge.

Type A for use against certain organic gases and vapors.

Type AX for use against low boiling point organic compounds (less than 65°C).

Type B for use against certain inorganic gases and other acid gases and vapors.

Type E for use against sulfur dioxide and other acid gases and vapors.

Type K for use against ammonia and organic ammonia derivatives

Class P1 intended for use against mechanically generated particulates of sizes most commonly encountered in industry, e.g. asbestos, silica.

Class P2 intended for use against both mechanically and thermally generated particulates, e.g. metal fume.

Class P3 intended for use against all particulates containing highly toxic materials, e.g. beryllium.

The local concentration of material, quantity and conditions of use determine the type of personal protective equipment required.

Use appropriate NIOSH-certified respirator based on informed professional judgement. In conditions where no reasonable estimate of exposure can be made, assume the exposure is in a concentration IDLH and use NIOSH-certified full face pressure demand SCBA with a minimum service life of 30 minutes, or a combination full facepiece pressure demand SAR with auxiliary self-contained air supply. Respirators provided only for escape from IDLH atmospheres shall be NIOSH-certified for escape from the atmosphere in which they will be used.

ENGINEERING CONTROLS

■ Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation. HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors. Barrier protection or laminar flow cabinets should be considered for laboratory scale handling. 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. Fume-hoods and other open-face containment devices are acceptable when face velocities of at least 1 m/s (200 feet/minute) are achieved. Partitions, barriers, and other partial containment technologies are required to prevent migration of the material to uncontrolled areas. For non-routine emergencies maximum local and general exhaust are necessary. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to effectively remove the contaminant.

Type of Contaminant:	Air Speed:
solvent, vapors, etc. evaporating from tank (in still air)	0.25-0.5 m/s (50-100 f/min.)
aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers (released at low velocity into zone of active generation)	0.5-1 m/s (100-200 f/min.)
direct spray, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)	1-2.5 m/s (200-500 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	1: Disturbing room air currents
2: Contaminants of low toxicity or of nuisance value only.	2: Contaminants of high toxicity
3: Intermittent, low production.	3: High production, heavy use
4: Large hood or large air mass in motion	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

PHYSICAL PROPERTIES

State	Divided Solid	Molecular Weight	212.2
Melting Range (°F)	320- 325.4	Viscosity	Not Applicable
Boiling Range (°F)	Not Applicable	Solubility in water (g/L)	Partly Miscible
Flash Point (°F)	Not Available	pH (1% solution)	Not Applicable
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not Applicable
Autoignition Temp (°F)	Not Available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not Available	Specific Gravity (water=1)	Not Available
Lower Explosive Limit (%)	Not Available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not Applicable

APPEARANCE

Off-white solid; does not mix well with water. Solubilities (mg/ml): water 0.8; 0.1N HCl 0.5. Sparingly soluble in chloroform, n-hexane. Soluble in methanol, ethanol, ethyl acetate and acetic acid pKa 10.2

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

-
- Presence of incompatible materials.
- Product is considered stable.
- Hazardous polymerization will not occur.

STORAGE INCOMPATIBILITY

- Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

zonisamide

TOXICITY AND IRRITATION

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

TOXICITY	IRRITATION
Oral (Rat) LD50: 1992 mg/kg	

Intraperitoneal (Rat) LD50: 733 mg/kg

Subcutaneous (Rat) LD50: 925 mg/kg

Intravenous (Rat) LD50: 672 mg/kg

Oral (Mouse) LD50: 1829 mg/kg

Intraperitoneal (Mouse) LD50: 699 mg/kg

Subcutaneous (Mouse) LD50: 1009 mg/kg

Intravenous (Mouse) LD50: 816 mg/kg

■ Reports suggest an association between the use of anticonvulsant drugs by women with epilepsy and an elevated incidence of birth defects in children born to these women. Data are more extensive with respect to phenytoin and phenobarbital, but these are also the most commonly prescribed anticonvulsants; less systematic or anecdotal reports suggest a possible similar association with the use of all known anticonvulsant drugs.

The frequency of major malformations, growth retardation, and hypoplasia of the midface and fingers, known as "anticonvulsant embryopathy", is increased in infants exposed to anticonvulsant drugs in utero. However, whether the abnormalities are caused by the maternal epilepsy itself or by exposure to anticonvulsant drugs is not known.

The reports suggesting an elevated incidence of birth defects in children of drug-treated epileptic women cannot be regarded as adequate to prove a definite cause and effect relationship. There are intrinsic methodologic problems in obtaining adequate data on drug teratogenicity in humans; the possibility also exists that other factors, eg, genetic factors or the epileptic condition itself, may be more important than drug therapy in leading to birth defects. The great majority of mothers on anticonvulsant medication deliver normal infants.

At least one study has shown a distinctive pattern of physical abnormalities in infants of mothers with epilepsy is associated with the use of anticonvulsant drugs during pregnancy, rather than with epilepsy itself (L.B. Holmes et al New England Jnl of Med, 344: 1132-1138; 2001).

It is important to note that anticonvulsant drugs should not be discontinued in patients in whom the drug is administered to prevent major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even minor seizures do not pose some hazard to the developing embryo or foetus.

Reproductive dysfunction in epilepsy is attributed to the seizures themselves and also to antiepileptic drugs (AEDs), which affect steroid production, binding, and metabolism. In turn, neuroactive steroids may influence neuronal excitability. A previous study in this cohort of consecutive women with epilepsy showed that patients with more frequent seizures had higher cortisol and lower dehydroepiandrosterone sulfate levels than those with rare or absent seizures. Actual hormone titers were not significantly correlated with seizure frequency scores (SFS) rather these hormonal changes were explained by AED treatments, mainly when enzyme-inducing AEDs (EIAED) polytherapies were given.

ZONISAMIDE SODIUM:

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

■ Reports suggest an association between the use of anticonvulsant drugs by women with epilepsy and an elevated incidence of birth defects in children born to these women. Data are more extensive with respect to phenytoin and phenobarbital, but these are also the most commonly prescribed anticonvulsants; less systematic or anecdotal reports suggest a possible similar association with the use of all known anticonvulsant drugs.

The frequency of major malformations, growth retardation, and hypoplasia of the midface and fingers, known as "anticonvulsant embryopathy", is increased in infants exposed to anticonvulsant drugs in utero. However, whether the abnormalities are caused by the maternal epilepsy itself or by exposure to anticonvulsant drugs is not known.

The reports suggesting an elevated incidence of birth defects in children of drug-treated epileptic women cannot be regarded as adequate to prove a definite cause and effect relationship. There are intrinsic methodologic problems in obtaining adequate data on drug teratogenicity in humans; the possibility also exists that other factors, eg, genetic factors or the epileptic condition itself, may be more important than drug therapy in leading to birth defects. The great majority of mothers on anticonvulsant medication deliver normal infants.

At least one study has shown a distinctive pattern of physical abnormalities in infants of mothers with epilepsy is associated with the use of anticonvulsant drugs during pregnancy, rather than with epilepsy itself (L.B. Holmes et al New England Jnl of Med, 344: 1132-1138; 2001).

It is important to note that anticonvulsant drugs should not be discontinued in patients in whom the drug is administered to prevent major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even minor seizures do not pose some hazard to the developing embryo or foetus.

Reproductive dysfunction in epilepsy is attributed to the seizures themselves and also to antiepileptic drugs (AEDs), which affect steroid production, binding, and metabolism. In turn, neuroactive steroids may influence neuronal excitability. A previous study in this cohort of consecutive women with epilepsy showed that patients with more frequent seizures had higher cortisol and lower dehydroepiandrosterone sulfate levels than those with rare or absent seizures. Actual hormone titers were not significantly correlated with seizure frequency scores (SFS) rather these hormonal changes were explained by AED treatments, mainly when enzyme-inducing AEDs (EIAED) polytherapies were given.

No significant acute toxicological data identified in literature search.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

ZONISAMIDE SODIUM:

ZONISAMIDE:

■ DO NOT discharge into sewer or waterways.

■ The sulfonamides are bipolar substances due to their polar functional groups with two pKa-values in the environmentally relevant pH-range. At low pH-values they are cationic due to protonation of the aniline group (pKa1). The isoelectric point is between pH 4 and 5, resulting in neutral species under slightly acidic conditions (pH 3 to 6). At higher pH-values the sulfonamides are anionic due to the deprotonation of the sulfonamide nitrogen group (pKa2). As a consequence of this speciation, the partitioning and the reactivity are pH-dependent which plays an important role for assessing their environmental behavior as well as for their extraction from different matrices for chemical analysis.

Antibiotic sulfonamides, a structurally related group of substances, contain a similar 4-aminobenzene sulfonamide backbone, and are used in agriculture, aquaculture, animal husbandry, and also as human medicines.

After animal medication, they are excreted in high percentages of the administered amount, either as active substance or as acetyl conjugate. In manure, these sulfonamides are persistent. Furthermore the acetyl conjugates are cleaved into the active sulfonamide during manure storage, possibly by nucleophilic attack of ammonium at the carbonyl carbon. Concentrations ranging from 0.1 to more than 10 mg sulfonamide/ kg liquid manure translate into loads of some few grams to several hundred grams per hectare per application that may reach agricultural soils. On a plot scale, losses of sulfonamide antibiotics by surface run-off have been reported to vary from 0.1 to 28% of the applied amount. One reason for this high variability might be the different irrigation intensities ranging from a few mm per day to 100mm/2h. In a field study carried out on a macroporous tile-drained clay soil relative losses of a sulfonamide antibiotic amounted to 0.48% and 0.01% in two subsequent years.

Competing with p-aminobenzoic acid in the enzymatic synthesis of dihydrofolic acid, sulfonamides inhibit the growth and reproduction of bacteria. Once released to the environment, sulfonamides distribute themselves among different environmental compartments, along with their degradation products, and are transported to surface water and groundwater. The physicochemical properties, the dosage applied and the nature of the environmental components with which they interact, govern

the whole process. Sulfonamides, as a class, are only partially sorptive, non persistent, and leachable . They cannot be characterised as readily biodegradable. Their adsorption to soil increases with the aromaticity and electronegativity of functional groups attached to the sulfonyl phenyl amine core. Preferential flow in clay soils has been identified as a mechanism responsible for surface water contamination by sulfonamides.

George W. Ware et al: Reviews of Environmental Contamination and Toxicology Vol 187, 2006 pp 67-101.

Twelve different sulfonamides were selected for a biodegradation study using a respirometric screening test and an activated sludge simulation test. A simple bacterial growth inhibition test was applied to show that the sulfonamides did not affect the bacteria at the concentration levels used. None of the compounds were degraded in the screening test, leading to the conclusion that sulfonamides cannot be classified as readily biodegradable. In the simulation test, primary degradation of mixtures of four compounds at concentration levels of 250 to 500 µg/L were tested and analysed using high-performance liquid chromatography. Biodegradation occurred after lag phases of 7 to 10 d at 20°C when nonadapted sludge was applied. Test compounds were degraded within a few days. At 6°C, degradation lag phases and degradation rates were three to four times longer. Sulfonamide adapted bacterial cultures were able to degrade either the same compounds as previously added or four other sulfonamides in a rapid and uniform way (t½ from 0.2 to 3 d). This finding shows that if capable of degrading one sulfonamide substance, these bacteria may also degrade many other sulfonamides. In practice, this implies that because the biodegradation rate is found to be identical for several sulfonamides in the sludge, the compounds may be assessed as a group by studying only a few compounds in applications such as environmental fate assessments. The mechanism for inducement of sulfonamide adaptation to the bacteria was not revealed in this study.

Flemming Ingerslev and Bent Halling-Sørensen: Environmental Toxicology and Chemistry pp 2467-2473.

Laboratory tests showed that phototoxicity resulting from exposure to continuous UVB light generally increased the acute toxicity of the sulfonamides in *D. magna* by up to 2.3-fold. However, pulsed UVB exposure resulted in a greater increase in phototoxicity. Compared to fluorescent light only (no UVB), pulsed UVB irradiation (96 h) resulted in 12.0-, 5.8-, and 4.4-fold increases in toxicity for sulfamethazine, sulfathiazole, and sulfamethoxazole, respectively. This suggests that the mode of UV irradiation is more important than the dose (UV-intensity × exposure time) for the photo-enhancement of sulfonamide toxicity. Natural sunlight enhanced the toxicity of the sulfonamides to an even greater degree, likely because of the contribution of UVA light. This study suggests that without taking into account the effects of UV irradiation, it is possible to underestimate the actual consequences of phototoxic sulfonamide antibiotics in the aquatic environment.

Jinyong Jung et al: Earth and Environmental Science. Vol 17, January 2008, pp 37-45.

■ Toxic to soil organisms.

ZONISAMIDE:

ZONISAMIDE SODIUM:

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

! Puncture containers to prevent re-use and bury at an authorized landfill.

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 equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.
- Dispose of by: Burial in a licensed land-fill or Incineration in a licensed 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

Regulations for ingredients

No data for zonisamide (CAS: , 68291-97-4)

No data for zonisamide sodium (CAS: , 68291-98-5)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- May produce discomfort of the eyes*.
- Limited evidence of a carcinogenic effect*.
- May affect fertility*.

* (limited evidence).

Reasonable care has been taken in the preparation of this information, but the author makes no warranty of merchantability or any other warranty, expressed or implied, with respect to this information. The author makes no representations and assumes no liability for any direct, incidental or consequential damages resulting from its use. For additional technical information please call our toxicology department on +800 CHEMCALL.

■ Classification of the mixture 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.

A list of reference resources used to assist the committee may be found at:

www.chemwatch.net/references.

■ The (M)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.

This document is copyright. Apart from any fair dealing for the purposes of private study, research, review or criticism, as permitted under the Copyright Act, no part may be reproduced by any process without written permission from CHEMWATCH. TEL (+61 3) 9572 4700.

Issue Date: Dec-17-2009

Print Date: Apr-21-2010