

(S)-Pregabalin

sc-212896

Material Safety Data Sheet



The Power is Question

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

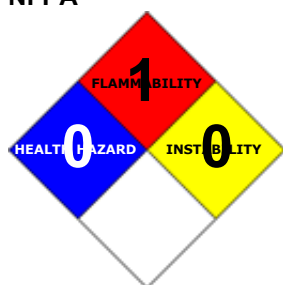
PRODUCT NAME

(S)-Pregabalin

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Company: Santa Cruz Biotechnology, Inc.

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PRODUCT USE

Pregabalin is an analogue of the neurotransmitter gamma-aminobutyric acid (GABA). It has analgesic and anticonvulsant activity.

SYNONYMS

C8-H17-N-O2, C8-H17-N-O2, "(S)-(+)-3-aminomethyl-5-methylhexanoic acid", "(S)-(+)-3-aminomethyl-5-methylhexanoic acid", "3-(aminomethyl)-5-methyl-hexanoic acid", "3-(aminomethyl)-5-methyl-hexanoic acid", pregabalin, "analgesic/anticonvulsant", Lyrica

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS

None

EMERGENCY OVERVIEW

RISK

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Although ingestion is not thought to produce harmful effects, the material may still be damaging to the health of the individual following ingestion, especially where pre-existing organ (e.g. liver, kidney) damage is evident. Present definitions of harmful or toxic substances are generally based on doses producing mortality (death) rather than those producing morbidity (disease, ill-health). Gastrointestinal tract discomfort may produce nausea and vomiting. In an occupational setting however, ingestion of insignificant quantities is not thought to be cause for concern.

■ Accidental ingestion of the material may be damaging to the health of the individual.

■ The material may mimic the actions of the major inhibitory neurotransmitter of the brain, GABA, (gamma-aminobutyric acid) in inhibiting the electrical activity of certain elements of the nervous system. GABA is a putative amino-acid, produced within certain neurones (presynaptic cells) and is released into the synapse, between neurones, on the arrival of an action potential; GABA then interacts with post-synaptic neurones, slowing their rate of firing.

Certain GABA congeners may produce lightheadedness, ataxia, mood elevation and muscle incoordination. Side-effects of uptake of GABA analogues and congeners (such as the isoxazole derivative, muscimol, isolated from hallucinogenic mushrooms), by neurones, may include dizziness, ataxia, euphoria, muscle twitches, and initial psychic stimulations followed by dream-filled sleep. More severe ingestions may produce visual disturbances, fever, confusion, myoclonus, mydriasis, seizures and coma. Residual headache may persist for several days. The congener muscimol is structurally related to GABA, crosses the blood-brain barrier easily, in contrast to GABA, and inhibits the firing of some central neurones. GABA, when introduced directly to the brain by injection (i.e. intrathecally), produces the same effect and similar outcomes to those produced by muscimol.

Another amino-acid, with a similar structure to both GABA and muscimol, is ibotenic acid (also derived from mushrooms). Effects of ingestion are similar to those produced by muscimol. Ibotenic acid, however, binds to a different receptor, NMDA, which is normally activated by the putative neurotransmitter glutamic acid but now is inhibited by the action of ibotenic acid. NMDA receptors, in contrast to GABA receptors, when activated, normally cause neurones to fire. Systemic administration of ibotenic acid and muscimol to laboratory animals produces central inhibition of motor activity with little change to peripheral autonomic activity. Both compounds induce EEG changes in cats, rabbits and rats and thus within the central nervous system both compounds behave as false inhibitory neurotransmitters.

GABA and its congeners inhibit the excitation of cells, of neurological origin, by allowing anions, such as chloride, to enter the cell thus altering the electric potential of the cell. The GABA receptor acts as a gateway for influx of chloride ion.

One subtype of receptor for GABA, the GABA-A receptor also contains binding sites for anxiolytic barbiturates, benzodiazepines, neurosteroids and, probably, ethanol. These anxiolytic groups potentiate the function of the chloride channels linked to the receptor.

The whole receptor complex can be formed only by the interaction of several individual subunits, each of which is a membrane-spanning protein. Several different types of subunit have been identified and named the alpha-, beta-, and delta-subunits. The receptor may be made from any of up to five possible combinations of these subunits so that the number of possible subtypes of GABA-A receptor is huge and may, in part, explain their variable response to each anxiolytic agent. However, receptors made from any combination of two or three subunit types express much of the function of the native receptor.

EYE

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

SKIN

■ The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, 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

■ Long-term exposure to the product is not thought to produce chronic effects adverse to the health (as classified using animal models); nevertheless exposure by all routes should be minimized as a matter of course.

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

		Min	Max
Flammability:	1		
Toxicity:	2		
Body Contact:	0		
Reactivity:	1		
Chronic:	0		

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

NAME	CAS RN	%
pregabalin	148553-50-8	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

-
- If swallowed do NOT induce vomiting.
- If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.
- Observe the patient carefully.
- Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious.
- Give water to rinse out mouth, then provide liquid slowly and as much as casualty can comfortably drink.
- Seek medical advice.

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

- Treat symptomatically.

In overdoses up to 15 g, no unexpected adverse reactions were reported.

The most commonly reported adverse events observed when pregabalin was taken in overdose included affective disorder, somnolence, confusional state, depression, agitation and restlessness.

There is no specific antidote for pregabalin. Treatment of pregabalin overdose should be symptomatic and supportive.

Consider administration of activated charcoal in the event of a potentially toxic ingestion. Activated charcoal is most effective when administered within 1-hour of ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via nasogastric tube once the airway is protected.

Haemodialysis may be useful in patients with severe toxicity or those with significant renal impairment. Standard haemodialysis procedures result in significant clearance of pregabalin (approximately 50% in 4 hours). Emesis is not recommended because of the potential for CNS depression and seizures.

Management

Pharmacokinetics: Pregabalin steady-state pharmacokinetics are similar in healthy volunteers, patients with epilepsy receiving anti-epileptic drugs and patients with chronic pain.

Absorption: Pregabalin is rapidly absorbed when administered in the fasted state, with peak plasma concentrations occurring within 1 hour following both single and multiple dose administration. Pregabalin oral bioavailability is estimated to be = 90% and is independent of dose. Following repeated administration, steady state is achieved within 24 to 48 hours. The rate of pregabalin absorption is decreased when given with food resulting in a decrease in C_{max} by approximately 25-30% and a delay in T_{max} to approximately 2.5 hours. However, administration of pregabalin with food has no clinically significant effect on the extent of pregabalin bioavailability.

Elimination: Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug. Renal clearance (CL_r) derived from Phase I studies was 73 ml/min.

Pregabalin mean elimination half-life is 6.3 hours. Pregabalin plasma clearance and renal clearance are directly proportional to creatinine clearance.

Pregabalin clearance is reduced in patients with impaired renal function

Renal impairment: Pregabalin clearance is directly proportional to creatinine clearance. In addition, pregabalin is effectively removed from plasma by haemodialysis (following a four hour haemodialysis treatment plasma pregabalin concentrations are reduced by approximately 50%). Because renal elimination is the major elimination pathway, dosage reduction in patients with renal impairment and dosage supplementation following haemodialysis is necessary (see Dosage and Administration, Patients with Renal Impairment, Table 6).

Hepatic impairment: No specific pharmacokinetic studies were carried out in patients with impaired liver function. Since pregabalin does not undergo significant metabolism and is excreted predominantly as unchanged drug in the urine, impaired liver function would not be expected to significantly alter pregabalin plasma concentrations.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

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

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), other pyrolysis products typical of burning organic material.

May emit poisonous 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

-
- 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

- 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 (AEGl) (in ppm)

AEGl 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.

AEGl 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.

AEGl 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

- pregabalin: CAS:148553-50-8

MATERIAL DATA

PREGABALIN:

- 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).

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

Mixes with water.

State	Divided Solid	Molecular Weight	159.23
Melting Range (°F)	356- 365	Viscosity	Not Applicable
Boiling Range (°F)	Not Applicable	Solubility in water (g/L)	Miscible
Flash Point (°F)	Not Available	pH (1% solution)	Not Available
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

White to off-white solid; mixes with water, basic and acidic aqueous solutions

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

pregabalin

TOXICITY AND IRRITATION

- No significant acute toxicological data identified in literature search.

Pregabalin undergoes negligible metabolism in humans. Following a dose of radiolabelled pregabalin, approximately 98% of the radioactivity recovered in the urine was unchanged pregabalin. The N-methylated derivative of pregabalin, the major metabolite of pregabalin found in urine, accounted for 0.9% of the dose. In preclinical studies, there was no indication of racemisation of pregabalin S-enantiomer to the R-enantiomer.

In vitro studies show that pregabalin binds to an auxiliary subunit (α2-delta protein) of voltage-gated calcium channels in the central nervous system, potentially displacing [3H]-gabapentin. Two lines of evidence indicate that binding of pregabalin to the α2-d site is required for analgesic and anticonvulsant activity in animal models: (1) Studies with the inactive R -enantiomer and other structural derivatives of pregabalin and (2) Studies of pregabalin in mutant mice with defective drug binding to the α2-d protein. In addition, pregabalin reduces the release of several neurotransmitters, including glutamate, noradrenaline, and substance P. The significance of these effects for the clinical pharmacology of pregabalin is not known.

Pregabalin does not show affinity for receptor sites or alter responses associated with the action of several common drugs for treating seizures or pain. Pregabalin does not interact with either GABAA or GABAB receptors; it is not converted metabolically into GABA or a GABA agonist; it is not an inhibitor of GABA uptake or degradation.

Pregabalin prevents pain-related behaviours in animal models of neuropathic and post-surgical pain, including hyperalgesia and allodynia.

Pregabalin is also active in animal models of seizures, including maximal electroshock tonic extensor seizures in mice or rats, threshold clonic seizures from pentylenetetrazol, behavioural and electrographic seizures in hippocampal kindled rats, and tonic and clonic seizures in DBA/2 audiogenic mice. Pregabalin does not reduce the incidence of spontaneous absence seizures in Genetic Absence Epilepsy in Rats from Strasbourg (GAERS).

Mutagenesis: Pregabalin is not genotoxic based on results of in vitro and in vivo tests. It was not mutagenic in bacteria or in mammalian cells in vitro, not clastogenic in mammalian systems in vitro and in vivo, and did not induce unscheduled DNA synthesis in mouse or rat hepatocytes.

Carcinogenesis: Two-year carcinogenicity studies with pregabalin were conducted in rats and mice. No increased incidence of tumours was observed in rats at exposures (plasma AUC) up to 25 times the expected human exposure at the maximum recommended clinical dose of 600 mg/day. In mice, no increased incidence of tumours was found at exposures similar to the expected maximum human exposure, but an increased incidence of haemangiosarcoma was observed at exposures 6 to 33 times the expected maximum human exposure. The precise non-genotoxic mechanism of pregabalin-induced tumour formation is not fully characterised. However, available data show that platelet changes associated with the formation of this tumour in mice are not seen in rats, monkeys or humans. Although long-term data in humans are limited, these findings in mice are thought not to pose a risk to humans.

Fertility: Preclinical data: In male rats, oral administration of high doses of pregabalin resulted in reversible decreased sperm motility and fertility. These were not observed at exposures (plasma AUC) up to 11 times the expected human exposure at the maximum recommended clinical dose of 600 mg/day. There were also no drug-related effects on sperm parameters in a long term monkey study with exposures up to 8 times the expected maximum human exposure. In female rats, oestrus cycles were prolonged by high oral doses of pregabalin, but fertility was unaffected, and an increase in post-implantation loss also occurred. No adverse effects were seen at an exposure approximately 50 times the expected maximum human exposure.

Human data: In a double-blind, placebo-controlled clinical trial to assess the effect of pregabalin on sperm motility, 30 of 46 healthy male subjects were exposed to pregabalin at 600 mg/day for 3 months. Pregabalin did not exhibit detrimental effects on the reproductive function of healthy male subjects, as measured by semen analysis.

Teratogenesis: Pregabalin was not teratogenic in mice, rats or rabbits. Fetal developmental toxicity was not observed after treatment of pregnant mice and rabbits with oral doses that resulted in respective pregabalin exposures that were 30 times and 17 times the expected human exposure at the maximum recommended clinical dose of 600 mg/day. Increased fetal skeletal variations were seen in rats at oral doses resulting in exposures = 17 times the expected maximum human exposure, but lower doses were not tested in a full study.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

PREGABALIN:

- DO NOT discharge into sewer or waterways.

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

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

† 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

pregabalin (CAS: 148553-50-8) is found on the following regulatory lists;

"US Drug Enforcement Administration (DEA) Controlled Substances Schedule V", "US FDA Controlled Substances Schedule V"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

■ Ingestion may produce health damage*.

* (limited evidence).

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■ 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.

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