Candesartan Celexetil Ester

sc-204666

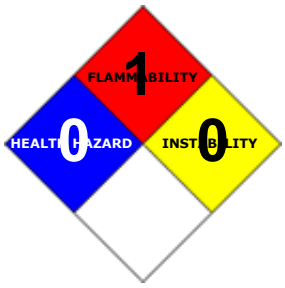
Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Candesartan Celexetil Ester

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
Antihypertensive. Normally given by mouth. Following oral administration, the prodrug undergoes hydrolysis at the ester link to form the active drug, candesartan which is achiral. Candesartan blocks the vasoconstrictor and aldosterone secreting effects of angiotensin II (the principal pressor agent of the renin-angiotensin system) by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues such as vascular smooth muscle and the adrenal gland. Blockade of the angiotensin II receptor inhibits the negative regulatory feedback of angiotensin II on renin secretion, but the resulting increased plasma renin activity and angiotensin II circulating levels do not overcome the effect of candesertan on blood pressure.

SYNONYMS
C33-H34-N6-O6, "1H-benzimidazole-7-carboxylic acid, 2-ethoxy-1-[(2' -(1H-tetrazol-5-", "yl)(1, 1' -biphenyl)-4-yl)methyl]-, 1-[((cyclohexyloxy)carbonyl)oxy]ethyl", ester, "1H-benzimidazole-7-carboxylic acid, 2-ethoxy-1-[(2' -(1H-tetrazol-5-", "yl)(1, 1' -biphenyl)-4-yl)methyl]-, 1-[((cyclohexyloxy)carbonyl)oxy]ethyl", ester, "(+/-)-[((cyclohexyloxy)carbonyl)oxy]ethyl-2-ethoxy-1-[(2' -(1H-tetrazol-", "5-yl)(1, 1' -biphenyl)-4-yl)methyl]-1H-benzimidazole-7-carboxylate", "(+/-)-[((cyclohexyloxy)carbonyl)oxy]ethyl-2-ethoxy-1-[(2' -(1H-tetrazol-", "5-yl)(1, 1' -biphenyl)-4-yl)methyl]-1H-benzimidazole-7-carboxylate", Atacand, TCV-116, antihypertensive, "angiotensin II competitive inhibitor", "angiotensin II competitive inhibitor"

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.
■ Considered an unlikely route of entry in commercial/industrial environments.
■ At sufficiently high doses the material may be nephrotoxic(i.e. poisonous to the kidney).
■ At sufficiently high doses the material may be cardiotoxic (i.e. poisonous to the heart).

EYE

■ Although the material is not thought to be an irritant, direct contact with the eye may produce transient discomfort characterized by tearing or conjunctival redness (as with windburn).

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.

INHALED

■ The material is not thought to produce adverse health effects or irritation of the respiratory tract (as classified using animal models). Nevertheless, 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

■ Principal routes of exposure are usually by skin contact/absorption and inhalation of generated dust.
■ The use of drugs that directly act on the renin-angiotensin system can cause foetal and neonatal morbidity and death. Typical of drugs of the this type are the ACE (angiotensin converting enzyme) inhibitors
In pregnancy during the second and third trimesters, ACE inhibitors may cause injury and even death to the developing foetus. Neonatal hypotension, renal failure, skull hypoplasia, oligohydramnios (insufficient amounts of amniotic fluid), associated with foetal limb contractures, craniofacial malformations, hypoplastic lung development and intra-uterine growth retardation, have been reported. It is not known whether exposure limited to the first trimester produces adverse foetal outcomes. Exposure in utero may be associated with hypotension and decreased renal perfusion in the foetus. ACE inhibitors have been associated with foetal death in utero.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS

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

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

NAME	CAS RN	%
candesartan cilexetil	145040-37-5	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

■
- Immediately give a glass of water.
- First aid is not generally required. If in doubt, contact a Poisons Information Center or a doctor.

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

INHALED

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

NOTES TO PHYSICIAN

■ Treat symptomatically.
If symptomatic hypotension occurs, supportive treatment is indicated.
The active drug is mainly excreted unchanged in the urine and faeces. It undergoes minor hepatic conversion by O-deethylation to an inactive metabolite. Elimination half-life is approximately 9 hours.

Candesartan cannot be removed by haemodialysis.

Section 5 - FIRE FIGHTING MEASURES

Upper Explosive Limit (%):	Not available.
Specific Gravity (water=1):	Not available
Lower Explosive Limit (%):	Not available
Relative Vapor Density (air=1):	>1

EXTINGUISHING MEDIA

■

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

FIRE FIGHTING

■

- 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

■

- Solid which exhibits difficult combustion or is difficult to ignite.
- 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) and nitrogen oxides (NOx).

FIRE INCOMPATIBILITY

■ Avoid contamination with strong oxidizing agents as ignition may result.

PERSONAL PROTECTION

Glasses:
Chemical goggles.
Gloves:
Respirator:
Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

■

- Clean up all spills immediately.
- Avoid contact with skin and eyes.
- Wear impervious gloves and safety glasses.
- Use dry clean up procedures and avoid generating dust.
- Sweep up or vacuum up (consider explosion-proof machines designed to be grounded during storage and use).
- Place spilled material in clean, dry, sealable, labeled container.

MAJOR SPILLS

■

- Clear area of personnel and move upwind.
- Alert Emergency Responders and tell them location and nature of hazard.
- Control personal contact by using protective equipment and dust respirator.
- Prevent spillage from entering drains, sewers or water courses.
- Avoid generating dust.
- Sweep, shovel up.
- Recover product wherever possible.
- Put residues in labeled plastic bags or other containers for disposal.
- 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

■

- Limit all unnecessary personal contact.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- When handling DO NOT eat, drink or smoke.
- Always wash hands with soap and water after handling.
- Avoid physical damage to containers.
- Use good occupational work practice.
- Observe manufacturer's storing and handling recommendations.

RECOMMENDED STORAGE METHODS

■

- Polyethylene or polypropylene container.
- Packing as recommended by manufacturer
- Check all containers are clearly labeled and free from leaks.

STORAGE REQUIREMENTS

■

- Keep dry.
- 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.
- Protect containers against physical damage.
- Check regularly for leaks.
- Observe manufacturer's storing and handling recommendations.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS

+	+	+	+	X	+

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

• candesartan cilexetil: CAS:145040-37-5

MATERIAL DATA

CANDESARTAN CILEXETIL:
CEL TWA: 0.05 mg/m3 (AstraZeneca)
■ 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
No special equipment needed when handling small quantities of substance.

For bulk handling wear:
Chemical goggles or
Face shield.

HANDS/FEET

Rubber gloves
PVC gloves
Protective shoe covers
Head covering.

OTHER

No special equipment when handling small quantities of substance otherwise:
Coveralls
For Emergencies:
Vinyl suit
Safety shower

RESPIRATOR

High Efficiency Dust Respirator (P2, P3)
For non-routine emergencies wear full face mask self-contained breathing apparatus.

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 65ºC).
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

Solid.
Does not mix with water.

State	Divided solid	Molecular Weight	610.67
Melting Range (°F)	Not available	Boiling Range (°F)	Not available
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)	>1	Volatile Component (%vol)	Negligible
Evaporation Rate	Not applicable		

APPEARANCE

White to off-white powder; does not mix well with water. A racemic mix containing one chiral centre at the cyclohexyloxycarbonyloxy ethyl ester group.

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

candesartan cilexetil

TOXICITY AND IRRITATION

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

TOXICITY	IRRITATION
Oral (rat) LD50: >2000 mg/kg	Nil Reported
Intraperitoneal (rat) LD50: 940 mg/kg	
Oral (mouse) LD50: >2000 mg/kg	
Intraperitoneal (mouse) LD50: 807 mg/kg	
Oral (dog) LD50: >2000 mg/kg	

Somnolence, muscle weakness, respiratory depression, effects on newborn recorded.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:
CANDESARTAN CILEXETIL:
EC50 (algae): >12 mg/l/72h*
EC50 (Daphnia magna): >16 mg/l/48h*
LC50 (fish): >17 mg/l/96h* *[AstraZeneca]

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

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

- Consult manufacturer for recycling options and recycle where possible .
- Consult Waste Management Authority for disposal.
- Incinerate residue at an approved site.
- Recycle containers where possible, or dispose of in an authorized landfill.

Section 14 - TRANSPORTATION INFORMATION

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

Section 15 - REGULATORY INFORMATION

candesartan cilexetil (CAS: 145040-37-5) is found on the following regulatory lists;
"Canada Controlled Drugs and Substances Act Schedule I"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE
■ Ingestion may produce health damage*.
■ May possibly be harmful to the fetus/ embryo*.
* (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.

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