Benserazide·HCl (Ro 4-4602)

sc-200723

Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Benserazide·HCl (Ro 4-4602)

STATEMENT OF HAZARDOUS NATURE
CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA

SUPPLIER
Santa Cruz Biotechnology, Inc.
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Santa Cruz, California 95060
800.457.3801 or 831.457.3800
EMERGENCY:
ChemWatch
Within the US & Canada: 877-715-9305
Outside the US & Canada: +800 2436 2255
(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS
C10-H15-N3-O5.HCl, HOCH2CH(NH2)CONHNHCH2C6H2(OH)3, "serine, 2-(2, 3, 4-trihydroxybenyl)hydrazide, monohydrochloride, DL-", "DL-serine 2-(2, 3, 4-trihydroxybenzyl)hydrazine hydrochloride", "DL-serine, 2-[(2, 3, 4-trihydroxyphenyl)methyl]hydrazide, monohydrochloride", "Ro 4-4602", "dopaminergic antiparkinsonian amino-acid analogue", "peripheral decarboxylase inhibitor"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

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

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

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW

RISK

Irritating to eyes, respiratory system and skin.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

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

■ Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

■ Dopamine receptor agonists are pharmacological agents with diverse physical and chemical properties that share the capacity to stimulate dopamine receptors and provide an antiparkinsonian effect. Currently available dopamine agonists belong to 2 classes: ergot (bromocriptine, lisuride, pergolide, cabergoline) and non-ergot (apomorphine, ropinirole, pramipexole, rotigotine) derivatives, each having a different pharamacological profile and different affinity for the dopaminergic receptors and subtypes.

Dopamine agonists, in clinical studies and clinical experience, appear to impair the systemic regulation of blood pressure, with resulting postural hypotension, especially during dose escalation. Parkinson's disease patients, in addition, appear to have an impaired capacity to respond to a postural challenge

Acute orthostatic hypotension is a frequent adverse effect at commencement of dopamine (dopinergic) agonist (DA) therapy. DAs are increasingly used as first-line treatment of early Parkinson's disease because of the lower incidence of motor adverse effects.

Side effects caused by DAs are similar to those of levodopa, including nausea, vomiting, orthostatic hypotension, confusion, and hallucinations. Patients intolerant of one agonist may tolerate another. As is seen with all of the antiparkinsonian drugs, elderly and demented patients are much more susceptible to psychiatric side effects.

Dopamine agonists act directly on striatal dopamine receptors. Unlike levodopa, they do not require metabolic conversion to an active form, and so their effects are independent of the degenerative state of dopaminergic terminals. They can selectively stimulate subclasses of dopamine receptors, theoretically reducing the incidence of adverse effects. Dopamine agonists do not compete with circulating plasma amino acids for absorption and transport into the brain and they do not generate free radicals or induce oxidative stress It has been demonstrated that dopamine D receptor-selective agonists may protect against glutamate-induced neurotoxicity in cultured neurons

Ergot-related side effects such as Raynaud's phenomenon, erythromelalgia, and retroperitoneal or pulmonary fibrosis are uncommon with bromocriptine and pergolide, and do not occur at all with the nonergot agonists ropinirole and pramipexole. In epidemiologic studies looking at pergolide, the onset of pulmonary and/or retroperitoneal fibrosis has been found to occur an average of 2 years following the initiation of therapy. Cardiac evaluations (e.g. Echocardiogram) should be conducted periodically on all patients taking ergot DA to monitor for the development of valve abnormalities.

Dopamine receptor agonists decrease prolactin concentration. Thus, there is a potential for decreased milk production in postpartum women taking these agents. However, this is not generally considered problematic because these agents are contraindicated in women who are breast-feeding

"Non-motor" side-effects include oedema , somnolence , constipation , dizziness , hallucinations , and nausea

Frequent side-effects include:

· allergic reactions (skin rash, itching, hives, swelling of the face, lips or tongue)
· abnormal heart beat (fast, slow or irregular
· abrupt drowsiness, sleep
· anxiety, restlessness
· difficult breathing
· dizziness
· fainting spells
· hallucinations
· skin irritation, redness, swelling, or itching
· uncontrollable movements of the arms, face, hands, head, mouth shoulders, or upper body

Dopamine agonists are typically used for treating Parkinson's disease and certain pituitary tumors (prolactinoma), and may be useful for restless legs syndrome (RLS).

Dopamine agonists activate signaling pathways through the dopamine receptor and trimeric G-proteins ultimately leading to changes in gene transcription.

EYE

■ This material can cause eye irritation and damage in some persons.

SKIN

■ This material can cause inflammation of the skin oncontact in some persons.

■ The material may accentuate any pre-existing dermatitis condition.

■ Skin contact is not thought to have harmful health effects, however the material may still produce health damage following entry through wounds, lesions or abrasions.

■ 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 can cause respiratory irritation in some persons. The body's response to such irritation can cause further lung damage.

■ 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.

■ Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

CHRONIC HEALTH EFFECTS

■ Long-term exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems.
Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.
Exposure to the material may result in a possible risk of irreversible effects. The material may produce mutagenic effects in man. This concern is raised, generally, on the basis of
appropriate studies with similar materials using mammalian somatic cells in vivo. Such findings are often supported by positive results from in vitro mutagenicity studies.
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.
<\p>.
Benserazide produced developmental abnormalities in the rat skeleton No evidence was found for disorders invloving bone metabolism in man (1). Nevertheless the manufacturers recommend that benserazide should not be given to patients under 25 years of age or in pregnant women.
(1) Ziegler et al

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
benserazide hydrochloride	14919-77-8	>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.

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.

SKIN

■ If skin contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

INHALED

· If fumes or combustion products are inhaled remove from contaminated area. · Lay patient down. Keep warm and rested.

NOTES TO PHYSICIAN

■ Treat symptomatically.
Benserazide is rapidly absorbed (about 58%) in the gut following oral administration to Parkinsonian patients; simultaneous administration of levadopa slightly increases absorption. Benserazide is rapidly excreted in the urine in the form of metabolites, 70-77% being excreted within 12
hours.

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.

FIRE FIGHTING

· Alert Emergency Responders and tell them location and nature of hazard.
· Wear breathing apparatus plus protective gloves.

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.
Combustion products include: carbon monoxide (CO), carbon dioxide (CO2), hydrogen chloride, phosgene, nitrogen oxides (NOx), 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
· 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.

Section 7 - HANDLING AND STORAGE

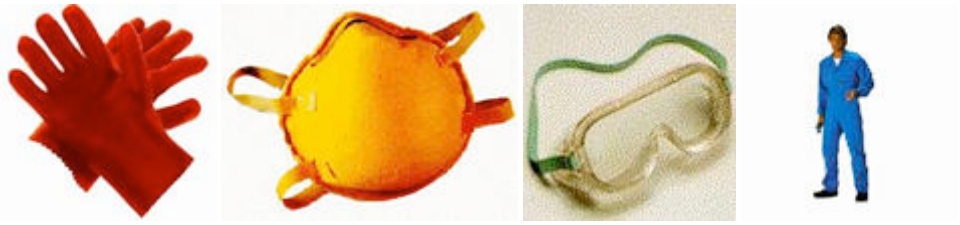
PROCEDURE FOR HANDLING
· Avoid all personal contact, including inhalation.
· Wear protective clothing when risk of exposure occurs.
Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.
· 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.
NOTE: Store in the dark.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS
The following materials had no OELs on our records
• benserazide hydrochloride: CAS:14919-77-8 CAS:14046-64-1

PERSONAL PROTECTION


RESPIRATOR
Particulate
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
· fluorocaoutchouc
· 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.

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.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.
Mixes with water.

State	Divided solid	Molecular Weight	293.74
Melting Range (°F)	294.8- 298.4	Viscosity	Not Applicable
Boiling Range (°F)	Not available	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

Solid; mixes with water. Unstable in neutral, alkaline or strongly acid media.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

· Presence of incompatible materials.
· Product is considered stable.

STORAGE INCOMPATIBILITY

■ Avoid reaction with oxidizing agents.

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

Section 11 - TOXICOLOGICAL INFORMATION

BENSERAZIDE HYDROCHLORIDE

TOXICITY AND IRRITATION

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

TOXICITY	IRRITATION
Oral (rat) LD50: 5300 mg/kg	Nil Reported
Intraperitoneal (rat) LD50: 2150 mg/kg	
Subcutaneous (rat) LD50: 5000 mg/kg	
Intraperitoneal (mouse) LD50: 1700 mg/kg	
Subcutaneous (mouse) LD50: 3300 mg/kg	

■ Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergenic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound. Key criteria for the diagnosis of RADS include the absence of preceding respiratory disease, in a non-atopic individual, with abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS. RADS (or asthma) following an irritating inhalation is an infrequent disorder with rates related to the concentration of and duration of exposure to the irritating substance. Industrial bronchitis, on the other hand, is a disorder that occurs as result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases. The disorder is characterised by dyspnea, cough and mucus production.
NOTE: Substance has been shown to be mutagenic in at least one assay, or belongs to a family of chemicals producing damage or change to cellular DNA.
Altered sleep time, ataxia, respiratory depression recorded.

Section 12 - ECOLOGICAL INFORMATION

No data

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.

Section 14 - TRANSPORTATION INFORMATION

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

Section 15 - REGULATORY INFORMATION

REGULATIONS

No data for benserazide hydrochloride (CAS: , 14919-77-8, 14046-64-1)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

■ Ingestion may produce health damage*.
■ Cumulative effects may result following exposure*.
■ Exposure may produce irreversible effects*.
* (limited evidence).

Ingredients with multiple CAS Nos

Ingredient Name CAS benserazide hydrochloride 14919-77-8, 14046-64-1

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