

Cisapride

sc-203894



The Power to Question

Material Safety Data Sheet

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

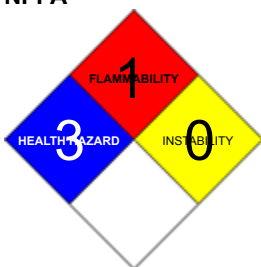
PRODUCT NAME

Cisapride

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

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EMERGENCY

ChemWatch

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Outside the US & Canada: +800 2436 2255

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

SYNONYMS

C23-H29-Cl-F-N3-O4, "cisapride monohydrate", 4-amino-5-chloro-N-[1-[3-(4-fluorophenoxy)propyl]-3-, methoxypiperidin-4-yl]-2-methoxybenzamide, "benzamide, 4-amino-5-chloro-N-[1-[3-(4-fluorophenoxy)propyl]-3-", methoxy-, (+/-)-cis-4-amino-5-chloro-N-1-[3-(4-fluorophenoxy)propyl]-3-, methoxypiperidin-4-yl)-2-methoxybenzamide, cis-4-amino-5-chloro-N-[1-[3-(4-fluorophenoxy)propyl]-3-methoxy-4-, piperidiny]-2-methoxybenzamide, cis-4-amino-5-chloro-N-[1-[3-(p-fluorophenoxy)propyl]-3-methoxy-4-, piperidiny]-o-anisamide, Acenaline, Alimix, Cipril, Prepulsid, Propulsid, Risamol, "R 51619", "peristaltic stimulant", "gastrokinetic agent", gastroprokinetic, "serotonin 5-HT4 receptor agonist"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability	1		
Toxicity	2		
Body Contact	3		
Reactivity	1		
Chronic	2		

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



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Harmful by inhalation.

Risk of serious damage to eyes.

Possible risk of harm to the unborn child.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ The material is not thought to produce adverse health effects following ingestion (as classified by EC Directives using animal models). Nevertheless, adverse systemic 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.

EYE

■ If applied to the eyes, this material causes severe eye damage.

SKIN

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

■ Open cuts, abraded or irritated skin should not be exposed to this material.

■ Entry into the blood-stream, through, for example, cuts, abrasions 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

■ Inhalation of dusts, generated by the material, during the course of normal handling, may be harmful.

■ The material is not thought to produce respiratory irritation (as classified by EC Directives using animal models). Nevertheless inhalation of dusts, or fumes, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.

■ 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.

If prior damage to the circulatory or nervous systems has occurred or if kidney damage has been sustained, proper screenings should be conducted on individuals who may be exposed to further risk if handling and use of the material result in excessive exposures.

CHRONIC HEALTH EFFECTS

■ Based on experience with animal studies, exposure to the material may result in toxic effects to the development of the foetus, at levels which do not cause significant toxic effects to the mother.

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

NAME	CAS RN	%
cisapride	81098-60-4	>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 Centre or a doctor.

EYE

If this product comes in contact with the eyes

- Immediately hold eyelids apart and flush the eye continuously with running water.
- Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.
- Continue flushing until advised to stop by the Poisons Information Centre or a doctor, or for at least 15 minutes.

- Transport to hospital or doctor without delay.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN

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.
- Lay patient down. Keep warm and rested.
- Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures.
- Apply artificial respiration if not breathing, preferably with a demand valve resuscitator, bag-valve mask device, or pocket mask as trained. Perform CPR if necessary.
- Transport to hospital, or doctor.

NOTES TO PHYSICIAN

- Treat symptomatically.

Oral bioavailability of cisapride is approximately 33%. It is primarily inactivated by hepatic metabolism by CYP3A4 with a half life of 10 hours. The dose of the drug should be reduced in case of liver diseases.

In instances of overdose, patients should be evaluated for possible QT prolongation and ventricular arrhythmias, including torsades de pointes. Treatment should include gastric lavage and/or activated charcoal, close observation and general supportive measures.

Reports of overdose with Propulsid (cisapride) also include an adult who took 540 mg and for 2 hours experienced retching, borborygmi, flatulence, stool frequency and urinary frequency.

Single oral doses of cisapride at 4000 mg/kg, 160 mg/kg, 1280 mg/kg and 640 mg/kg were lethal in adult rats, neonatal rats, mice, and dogs, respectively. Symptoms of acute toxicity were ptosis, tremors, convulsions, dyspnea, loss of righting reflex, catalepsy, catatonia, hypotonia and diarrhea

Section 5 - FIRE FIGHTING MEASURES

Vapor 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 Fire Brigade and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.
- Prevent, by any means available, spillage from entering drains or water courses.
- 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; it is estimated that most organic dusts are combustible (circa 70%) - according to the circumstances under which the combustion process occurs, such materials may cause fires and / or dust explosions.
- 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 (420 micron or less) may burn rapidly and fiercely if ignited - particles exceeding this limit will generally not form flammable dust clouds; once initiated, however, larger particles up to 1400 microns diameter will contribute to the propagation of an explosion.
- In the same way as gases and vapors, dusts in the form of a cloud are only ignitable over a range of concentrations; in principle, the concepts of lower explosive limit (LEL) and upper explosive limit (UEL) are applicable to dust clouds but only the LEL is of practical use; - this is because of the inherent difficulty of achieving homogeneous dust clouds at high temperatures (for dusts the LEL is often called the "Minimum Explosible Concentration", MEC)
- A dust explosion may release of large quantities of gaseous products; this in turn creates a subsequent pressure rise of explosive force capable of damaging plant and buildings and injuring people.
- Usually the initial or primary explosion takes place in a confined space such as plant or machinery, and can be of sufficient force to damage or rupture the plant. If the shock wave from the primary explosion enters the surrounding area, it will disturb any settled dust

layers, forming a second dust cloud, and often initiate a much larger secondary explosion. All large scale explosions have resulted from chain reactions of this type.

- 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.
- All movable parts coming in contact with this material should have a speed of less than 1-meter/sec
- A sudden release of statically charged materials from storage or process equipment, particularly at elevated temperatures and/ or pressure, may result in ignition especially in the absence of an apparent ignition source
- One important effect of the particulate nature of powders is that the surface area and surface structure (and often moisture content) can vary widely from sample to sample, depending of how the powder was manufactured and handled; this means that it is virtually impossible to use flammability data published in the literature for dusts (in contrast to that published for gases and vapors).
- Autoignition temperatures are often quoted for dust clouds (minimum ignition temperature (MIT)) and dust layers (layer ignition temperature (LIT)); LIT generally falls as the thickness of the layer increases.

Combustion products include carbon monoxide (CO), carbon dioxide (CO₂), hydrogen chloride, phosgene, hydrogen fluoride, nitrogen oxides (NO_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

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 Services 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.

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 authorization or permit.

RECOMMENDED STORAGE METHODS

- Glass container is suitable for laboratory quantities
- 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 area protected from environmental extremes.
- 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

For major quantities

- Consider storage in bunded areas - ensure storage areas are isolated from sources of community water (including stormwater, ground water, lakes and streams).
- Ensure that accidental discharge to air or water is the subject of a contingency disaster management plan; this may require consultation with local authorities.
- Store at room temperature.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- cisapride CAS81098-60-4

PERSONAL PROTECTION



RESPIRATOR

- Particulate. (AS/NZS 1716 & 1715, EN 1432000 & 1492001, ANSI Z88 or national equivalent)

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], [AS/NZS 1336 or national equivalent]

HANDS/FEET

Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739, AS/NZS 2161.1 or national equivalent).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- 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, latex/ nitrile). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Change gloves frequently and when contaminated, punctured or torn.
- Wash hands immediately after removing gloves.
- Protective shoe covers. [AS/NZS 2210]
- 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

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.

When handling quantities up to 500 gram in either a standard laboratory with general dilution ventilation (e.g. 6-12 air changes per hour) is preferred. Quantities up to 1 kilogram may require a designated laboratory using fume hood, biological safety cabinet, or approved vented enclosures. Quantities exceeding 1 kilogram should be handled in a designated laboratory or containment laboratory using appropriate barrier/ containment technology.

Manufacturing and pilot plant operations require barrier/ containment and direct coupling technologies.

Barrier/ containment technology and direct coupling (totally enclosed processes that create a barrier between the equipment and the room) typically use double or split butterfly valves and hybrid unidirectional airflow/ local exhaust ventilation solutions (e.g. powder containment booths). Glove bags, isolator glove box systems are optional. HEPA filtration of exhaust from dry product handling areas is required.

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.

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.

The following protective devices are recommended where exposures exceed the recommended exposure control guidelines by factors of

10; high efficiency particulate (HEPA) filters or cartridges

10-25; loose-fitting (Tyvek or helmet type) HEPA powered-air purifying respirator.

25-50; a full face-piece negative pressure respirator with HEPA filters

50-100; tight-fitting, full face-piece HEPA PAPR

100-1000; a hood-shroud HEPA PAPR or full face-piece supplied air respirator operated in pressure demand or other positive pressure mode.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

State	Divided Solid	Molecular Weight	465.95
Melting Range (°F)	230	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	Vapor 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

<+> enantiomer itself has the major pharmacologic effects and does not induce many of the detrimental side effects of the mixture>
 Odorless crystalline powder; does not mix well with water. Soluble in 2-propoanol, acetone. The commercial preparations of this drug are the racemic mixture of both enantiomers of the compound. The (+) enantiomer itself has the major pharmacologic effects and does not induce many of the detrimental side effects of the mixture

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

cisapride

TOXICITY AND IRRITATION

CISAPRIDE

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

TOXICITY	IRRITATION
Intravenous (Dog) TDLo 0.1 mg/kg	
Intravenous (Guinea pig) TDLo 0.1285 mg/kg	
Intravenous (Guinea pig) TDLo 0.0421 mg/kg	

Intravenous (Guinea pig) TDLo 0.1 mg/kg

Intravenous (Dog) TDLo 0.03 mg/kg

Oral (Rat) TDLo 1 mg/kg

Intraperitoneal (Mouse) TDLo 1 mg/kg

Oral (Mouse) TDLo 1 mg/kg

Intraperitoneal (Rat) TDLo 10 mg/kg

Oral (Dog) TDLo 0.6 mg/kg

Intravenous (Dog) TDLo 1 mg/kg

Intravenous (Rabbit) TDLo 1.44 mg/kg

Intravenous (Rabbit) TDLo 0.28 mg/kg

Oral (Rat) TDLo 3 mg/kg

Intravenous (Dog) TDLo 0.3 mg/kg

Oral (Rat) TDLo 200 mg/kg

Oral (Human) TDLo 0.9 mg/kg

Oral (Rat) LD50 4166 mg/kg

Intraperitoneal (Rat) LD50 3435 mg/kg

Subcutaneous (Rat) LD50 >2250 mg/kg

Intravenous (Rat) LD50 27.4 mg/kg

Oral (Mouse) LD50 8715 mg/kg

Intraperitoneal (Mouse) LD50 >1000 mg/kg

Subcutaneous (Mouse) LD50 >1000 mg/kg

Intravenous (Mouse) LD50 32.2 mg/kg

Intravenous (Rat) TDLo 0.5 mg/kg

Intravenous (Guinea pig) TDLo 0.3 mg/kg

May reduce or disturb heart rate, which in some cases have been reported to be fatal with cisapride. Causes gastrointestinal effects. May cause convulsions and tremor. Can cause an allergic reaction.

Serious cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation, torsades de pointes, and QT prolongation have been reported in patients taking Propulsid. From July 1993 through May 1999, more than 270 such cases have been spontaneously reported, including 70 fatalities. In approximately 85% of these cases the events occurred when Propulsid was used in patients with known risk factors. These risk factors included the administration of other drugs which caused QT prolongation, inhibited the cytochrome P450 3A4 enzymes that metabolise cisapride, or depleted serum electrolytes; or the presence of disorders that may have predisposed patients to arrhythmias. In approximately 0.7% of these cases, the events occurred in the absence of identified risk factors; in the remaining cases, risk factor status was unknown. Because the cases were reported voluntarily from a population of unknown size, estimates of adverse event frequency cannot be made.

Most patients had disorders that may have predisposed them to arrhythmias with Propulsid. These include history of prolonged electrocardiographic QT intervals or known family history of congenital long QT syndrome; history of ventricular arrhythmias, ischemic or valvular heart disease; other structural heart defects; cardiomyopathy; congestive heart failure; clinically significant bradycardia; sinus node dysfunction; second or third degree atrioventricular block; respiratory failure; or conditions that result in electrolyte disorders (hypokalemia, hypocalcemia, and hypomagnesemia), such as severe dehydration, vomiting, or malnutrition; eating disorders; renal failure; or the administration of potassium-wasting diuretics or insulin in acute settings. Propulsid is contraindicated in patients with these conditions

Carcinogenesis, mutagenesis, impairment of fertility

In a twenty-five month oral carcinogenicity study in rats, cisapride at daily doses up to 80 mg/kg was not tumorigenic. For a 50 kg person of average height (1.46 m² body surface area), this dose represents 50 times the maximum recommended human dose (1.6 mg/kg/day) on a mg/kg basis and 7 times the maximum recommended human dose (54.4 mg/m²) on a body surface area basis. In a nineteen month oral carcinogenicity study in mice, cisapride at daily doses up to 80 mg/kg was not tumorigenic. This dose represents 50 times the maximum recommended human dose on a mg/kg basis and about 4 times the maximum recommended human dose on a body surface area basis.

Cisapride was not mutagenic in the in vitro Ames test, human lymphocyte chromosomal aberration test, mouse lymphoma cell forward mutation test, and rat hepatocyte UDS test and in vivo rat micronucleus test, male and female mouse dominant lethal mutations tests, and sex linked recessive lethal test in male *Drosophila melanogaster*.

Fertility and reproductive performance studies were conducted in male and female rats. Cisapride was found to have no effect on fertility and reproductive performance of male rats at oral doses up to 160 mg/kg/day (100 times the maximum recommended human dose on a

mg/kg basis and 14 times the maximum recommended human dose on a mg/m2 basis). In the female rats, cisapride at oral doses of 40 mg/kg/day and higher prolonged the breeding interval required for impregnation. Similar effects were also observed at maturity in the female offspring (F1) of the female rats (F0) treated with oral doses of cisapride at 10 mg/kg/day or higher. Cisapride at an oral dose of 160 mg/kg/day also exerted contragestational/pregnancy disrupting effects in female rats (F0).

Teratogenic effects

Oral teratology studies have been conducted in rats (doses up to 160 mg/kg/day) and rabbits (doses up to 40 mg/kg/day). There was no evidence of a teratogenic potential of cisapride in rats or rabbits. Cisapride was embryotoxic and foetotoxic in rats at a dose of 160 mg/kg/day (100 times the maximum recommended human dose on a mg/kg basis and 14 times the maximum recommended human dose on a mg/m2 basis) and in rabbits at a dose of 20 mg/kg/day (approximately 12 times the maximum recommended human dose on a mg/kg basis) or higher. It also produced reduced birth weights of pups in rats at 40 and 160 mg/kg/day and adversely affected the pup survival. There are no adequate and well-controlled studies in pregnant women. Cisapride should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the mother and the foetus.

Section 12 - ECOLOGICAL INFORMATION

No data

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
cisapride	No Data Available	No Data Available		

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. In most instances the supplier of the material should be consulted.

- DO NOT allow wash water from cleaning or process equipment to enter drains.
- It may be necessary to collect all wash water for treatment before disposal.
- In all cases disposal to sewer may be subject to local laws and regulations and these should be considered first.
- Where in doubt contact the responsible authority.
- Recycle wherever possible.
- Consult manufacturer for recycling options or consult local or regional waste management authority for disposal if no suitable treatment or disposal facility can be identified.
- Dispose of by: burial in a land-fill specifically licenced to accept chemical and / or pharmaceutical wastes or Incineration in a licenced 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

cisapride (CAS: 81098-60-4) is found on the following regulatory lists;

"US FDA Maximum Recommended Therapeutic Dose (MRTD) Database"

Section 16 - OTHER INFORMATION

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

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.

■ For detailed advice on Personal Protective Equipment, refer to the following U.S. Regulations and Standards:

OSHA Standards - 29 CFR:

1910.132 - Personal Protective Equipment - General requirements

1910.133 - Eye and face protection

1910.134 - Respiratory Protection

1910.136 - Occupational foot protection

1910.138 - Hand Protection

Eye and face protection - ANSI Z87.1

Foot protection - ANSI Z41

Respirators must be NIOSH approved.

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