SAFETY DATA SHEETS

This SDS packet was issued with item:

078502280

The safety data sheets (SDS) in this packet apply to the individual products listed below. Please refer to invoice for specific item number(s).

078919756

Material Data Safety Sheet – Buprenex®

Section 1. PRODUCT AND COMPANY IDENTIFICATION

Product Name:	Buprenex® (buprenorphine hydrochloride) 0.3mg/mL Injection.
National Drug Code:	12496-0757
Product Description:	A mu-opioid partial agonist used for the relief of moderate to severe pain.
Manufacturer:	Reckitt Benckiser Healthcare (U.K.) Ltd. Dansom Lane Hull, England HU8 7DS Telephone: 011 44 1482 326151
Distributor:	Reckitt Benckiser Pharmaceuticals Inc. 10710 Midlothian Turnpike Suite 430 Richmond VA 23235 Telephone: (804) 379-1090, Monday – Friday 9:00 a.m. - 5:00 p.m.

Section 2. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS No.	Proportion (%w/w)
Buprenorphine hydrochloride	53152-21-9	<1
Glucose	50-99-7	<1
Water	7732-18-5	to 100

Section 3. HAZARD IDENTIFICATION

Buprenex® is a potent opioid analgesic that can produce sedation and respiratory depression.

Keep out of reach of children.

Sedation and respiratory depression may be intensified when exposure is in combination with other central nervous system depressants.

Eye	May cause irritation to the eyes.
Skin	Prolonged exposure may lead to systemic drug exposure. May irritate skin.
Mucus Membranes	Readily absorbed sublingually and through the lining of the mouth. Acute effects may include nausea, dizziness/vertigo, hypoventilation, sweating, hypotension, vomiting, miosis,and headache.
Inhalation	Well absorbed through the lungs. Acute effects may include nausea, dizziness/vertigo, hypoventilation, sweating, hypotension, vomiting, miosis, headache.
Ingestion	Poorly absorbed by ingestion, but systemic exposure may include nausea, dizziness/vertigo, respiratory distress, sweating, hypotension, vomiting, miosis, headache.

Section 4. FIRST AID MEASURES

Eye	Rinse eyes with a large quantity of water. If irritation persists, seek medical attention.
Skin	Remove contaminated clothing and rinse the affected area with water.
Mucus Membranes	Rinse thoroughly with water.
Inhalation	Move to fresh air. Seek medical attention if symptoms occur.
Ingestion	Do not administer anything by mouth to unconscious person. Seek medical attention.

Note to Physicians: Respiratory and cardiac status of the patient should be monitored carefully. In the event of depression of respiratory or cardiac function, primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated.
High doses of naloxone hydrochloride, 10-35mg/70kg may be of limited value in the management of buprenorphine overdose. Doxapram (a respiratory stimulant) has also been used.

Section 5. FIRE FIGHTING MEASURES

Buprenex® is an aqueous solution and is not flammable. Dry buprenorphine decomposes at temperatures above 140 °F.

Specific Dangers:	HCl fumes may be released
Suitable Extinguishing Media:	As for surrounding fire.
Extinguishing media which must not be used:	No information available.
Protection of Firefighters:	Vapor may be toxic, especially if inhaled. Firefighters should wear self-contained breathing apparatus and protective clothing appropriate for fighting a typical chemical fire.

Section 6. ACCIDENTAL RELEASE MEASURES

Personal Precautions:	Wear suitable gloves, safety glasses and overalls. Avoid contact with eyes and skin. Wash thoroughly after handling waste and before eating or drinking.
Environmental Precautions:	Environmental hazards have not been identified.
Spills:	Mop up with damp cloth or sweep into plastic bags. Dispose of waste in accordance with requirements for Schedule III narcotics under the U.S. Controlled Substances Act. When performing clean-up operation, wear personal protective equipment such as impervious gloves and eye protection.

Section 7. HANDLING AND STORAGE

General Handling:	Handle in accordance with requirements for Schedule III narcotics under the U.S. Controlled Substances Act. Avoid crushing containers or rough treatment that may break ampules. When handling pharmaceutical products, avoid all contact and inhalation of dust, fumes, mist, or vapors associated with the product.
Storage:	Store in secure place at temperature above freezing and below 104 °F.

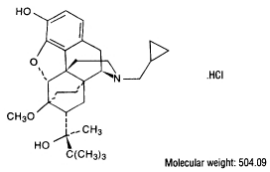
Section 8. EXPOSURE CONTROL/PERSONAL PROTECTION

Engineering Controls:	Under normal conditions with undamaged ampules, no exposure is likely. Ensure adequate ventilation when handling bulk quantities.
Personal Protection:	When handling bulk quantities, wear suitable gloves, safety glasses, and overalls. In case of breakage, avoid contact with eyes and skin, and avoid exposure to mist if produced by spill. Wash thoroughly after handling waste and before eating or drinking.
Exposure Limits:	Exposure limits are not known.

Section 9. PHYSICAL AND CHEMICAL PROPERTIES OF BUPRENEX®

Physical State:	Liquid in glass ampules (5/pack)
Color:	Colorless
Odor:	Odorless
pH:	4.5
Vapor Pressure:	Negligible at Standard Room Temperature.

Buprenorphine HCl ($C_{29}H_{41}NO_4$.HCl) - the active ingredient of Buprenex®



pKa: 8.42, 9.92

Section 10. STABILITY AND REACTIVITY

Buprenex® is stable under normal storage conditions, and is not corrosive or highly reactive. High temperature causes decomposition of buprenorphine that can include the formation of oxides of carbon and HCl.

Protect Buprenex® from prolonged exposure to light. Avoid excessive heat (over 104 °F or 40 °C).

Section 11. TOXICOLOGICAL INFORMATION

This product is intended for therapeutic use only when prescribed by a physician. Potential adverse reactions from prescribed doses and overdoses are described in the package insert.

Acute Effects (buprenorphine):

Oral LD_{50}:	Mouse: 260.1-261.4 mg/kg
	Rat: >600 mg/kg
Intravenous LD_{50}:	Mouse: 23.8-29.1 mg/Kg
	Rat: 21.3-40 mg/Kg
Intraperitoneal LD_{50}:	Mouse: 96.7-100.9 mg/kg
	Rat: 234.2-367.5 mg/kg
Intramuscular LD_{50}:	Rat: >100mg/kg

Subcutaneous LD_{50}:	Mouse: >150 mg/kg Rat: >600 mg/kg
Dermal LD_{50}:	Rat: >100mg/kg
Inhalation:	Maximum concentration producing no toxicological effects in rats was 0.1 mg/L and the LC_{50} was >0.92 mg/L.
Skin irritation:	Mild irritant to skin of albino rabbits by the Draize System.
Sensitization:	Not phototoxic and not a sensitizer in guinea pigs.

Chronic Effects (buprenorphine):

Carcinogenicity:	Rats exposed in the diet with up to 56 mg/kg/day buprenorphine for 27 months experienced dose-related increases in testicular interstitial cell tumors. Statistically significant dose-related increases in testicular interstitial cell tumors occurred, according to the trend test adjusted for survival. Pair-wise comparison of the high dose against control failed to show statistical significance. Buprenorphine was not carcinogenic to mice at doses of 8, 50, and 100 mg/kg/day for 86 weeks.
Mutagenicity:	Not found to be mutagenic in the following tests: • Recombinant, gene convertant, or forward mutations in yeasts. • *Bacillus subtllis* "rec" assay • CHO cells for clastogenicity • Chinese hamster bone marrow and spermatogonia cell test. • Mouse lymphoma L5178Y assay. Mutagenicity potential was found with the following tests: • Green-Tweets (E.Coli) survival test. • DNA synthesis inhibition test with testicular tissue from mice. • Unscheduled DNA synthesis test using testicular cells from mice. Equivocal tests: • Ames test
Reproductive Effects:	No evidence of impaired fertility in rats with daily buprenorphine ingestion of up to 80mg/kg or up to 5mg/kg by subcutaneous or intramuscular injection.
Developmental Effects:	Buprenorphine was not teratogenic in rats and rabbits at the following exposure levels: • Subcutaneous Injection: 5 mg/kg/day • Intramuscular Injection: 5 mg/kg/day • Intravenous Injection: 0.8 mg/kg/day In rabbits, there were pre-implantation losses of embryos at oral doses of 1mg/kg/day or greater and post-implantation losses with intravenous doses of 0.2mg/kg/day or greater.

Section 12. ECOLOGICAL INFORMATION

The environmental effects of buprenorphine have not been determined. Buprenorphine is light-sensitive and biodegradable.

Section 13. DISPOSAL CONSIDERATIONS

If ampules are broken, beware of glass shards or exposure to wet packaging material. Use protective clothing such as latex gloves. Sweep or wet-vacuum waste and dispose of it in a hazard container or by incineration. If waste is dry, use a dust mask.

Section 14. TRANSPORTATION INFORMATION

U.S. DOT Classification: Not Regulated.

Section 15. REGULATORY INFORMATION

Buprenex® is a Schedule III narcotic under the U.S. Controlled Substances Act and is marketed as a prescription product in accordance with regulations of the U.S. Food and Drug Administration. It should be protected against pilfering or misuse.

California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins under California Proposition 65 at levels which would be subject to the proposition.

Prepared by Reckitt Benckiser Pharmaceuticals Inc., John Pitts, Technical Expert

The information contained in this document applies to this specific material as supplied. It may not be valid for this material if it is used in combination with any other materials. It is the user's responsibility to satisfy oneself as to the suitability and completeness of this information for a particular use.

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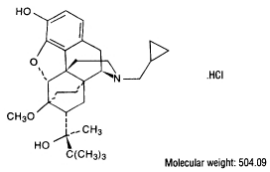

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