RECKITT BENCKISER PHARMACEUTICALS INC.

Material Safety Data Sheet

Section 1: PRODUCT AND COMPANY IDENTIFICATION

Product Name: Buprenex Injectable (a Schedule III controlled substance)
Generic Name: Buprenorphine Hydrochloride Injectable

NDC Number: 12496-0757-1 (clear glass ampule containing 1ml solution)

Manufacturer: Reckitt Benckiser Healthcare (UK) Ltd
Hull, UK HU8 7DS

Distributor: Reckitt Benckiser Pharmaceuticals Inc.
10710 Midlothian Turnpike, Suite 430
Richmond, Virginia 23235

Telephone: 1-877-782-6966 (Monday - Friday, 9:00AM - 8:00PM, EDT)

Section 2: HAZARDS IDENTIFICATION

Emergency Overview

This contains an active pharmaceutical ingredient that can affect body functions.

CAUTION:
This is a clear, colorless, sterile injectable that has potential adverse health effects if abused by injection or absorbed through mucous membranes

OSHA Regulatory Status: While this material is not considered hazardous by the OSHA Hazard Communication Standard (29 CFR 1910.1200), this MSDS contains valuable information critical to the safe handling and proper use of the product. This MSDS should be retained and available for employees and other users of this product.

Potential Health Effects:

Eyes	May cause redness, irritation, pupillary constriction, and/or allergic reaction.
Skin	Prolonged exposure may cause sedation, respiratory depression, nausea, vomiting, and/or allergic reaction.
Inhalation	May cause sedation, respiratory depression, nausea, vomiting, and/or allergic reaction.
Ingestion	May cause sedation, respiratory depression, nausea, vomiting, and/or allergic reaction.

Medical Conditions Aggravated by Exposure:

Compromised respiratory function (such as chronic obstructive pulmonary disease, cor pulmonale, decreased respiratory reserve or pre-existing respiratory depression), increased intracranial pressure, impairment of hepatic function, impairment of renal function, hypothyroidism, adrenal cortical insufficiency, CNS depression, toxic psychosis, prostatic hypertrophy or urethral stricture, acute alcoholism, delirium tremens and kyphoscoliosis.

Carcinogenicity: This product does not contain any carcinogens or potential carcinogens as listed by OSHA, IARC, or NTP.

Potential Environmental Effects: An accidental spill of product does not pose a significant environmental hazard. (See Section 6).

Section 3: COMPOSITION / INFORMATION ON INGREDIENTS

Chemical Name	CAS Number	Composition
Buprenorphine Hydrochloride	53152-21-9	0.324% w/w
Anhydrous Dextrose	50-99-7	Proprietary
Water for Injection	7732-18-5	Proprietary
Hydrochloric Acid (added for pH adjustment)	7647-01-0	Proprietary

Section 4: FIRST AID MEASURES

Eye Contact: Irrigate thoroughly for 5 - 15 minutes with clean water as soon as possible. If symptoms occur, seek medical attention.

Skin Contact: For prolonged exposure, remove any contaminated clothing and wash skin thoroughly with plenty of water. If symptoms occur, seek medical attention.

Inhalation: Remove to fresh air. If symptoms occur, seek medical attention.

Ingestion: Give two glasses of water to drink. Seek medical attention and show the container or product label to medical personnel. If overdose occurs, primary attention should be given to the re-establishment of adequate respiratory exchange.

Note to Physicians: Narcan (naloxone hydrochloride) may reverse respiratory depression (recommendation - initial naloxone hydrochloride bolus dose of 3 mg/70 kg, followed by 4mg/70 kg/h over 90 minutes' infusion, is needed to maintain persistent reversal of buprenorphine-induced respiratory depression. If an infusion is not possible, repeat bolus dose as needed). The duration of the effects of buprenorphine depends on the degree of exposure but is more prolonged than the effects of morphine.

Section 5: FIRE FIGHTING MEASURES

Flammable Properties: Not Flammable

Suitable Extinguishing Media: Use water, foam, or carbon dioxide.

Hazardous Combustion Products: HCl fumes, oxides of carbon and nitrogen may be released.

Section 6: ACCIDENTAL RELEASE MEASURES

Personal Precautions: Use personal protection recommended in Section 8.

Environmental Precautions: Prevent product from entering drains, sewers, ditches, and waterways. Notify local authorities if you cannot contain a major spill.

Methods for Containment: Special instructions are not necessary.

Methods for Clean-up:

Minor Spills: Use proper absorbent/adsorbent materials to collect or solidify the liquid. Scoop-up waste (product, glass, packaging material) and place in a sealed, liquid-proof container. Dispose in accordance with local, state and federal requirements, including Drug Enforcement Administration regulations for controlled substances.

Major Spills: Contain spill. Use proper absorbent/adsorbent materials to collect or solidify the liquid. Collect waste (product, glass, packaging material) into an appropriate labeled, liquid-proof container. Close lid tightly. Dispose in accordance with local, state, and federal requirements, including Drug Enforcement Administration regulations for controlled substances.

Section 7: HANDLING AND STORAGE

Handling: Buprenex is a controlled drug product and must be handled by authorized personnel according to the requirements of the Drug Enforcement Administration. Do not handle with bare hands.

Storage: Store in a secure place at temperatures below 104°F (40°C). Protect product from prolonged exposure to light.

Section 8: EXPOSURE CONTROLS / PERSONAL PROTECTION

Exposure Guidelines:	No exposure is likely under normal circumstances. Buprenex Injectable is in a glass ampule. OSHA PEL's (permissible exposure limits) nor ACGIH TLV's (American Conference of Governmental Industrial Hygienists threshold limit values) have been established for the components of Buprenex.
Engineering Controls:	Use in well ventilated areas.
Eye/Face Protection:	Wear safety glasses when handling bulk quantities or during clean-up of product spills.
Skin Protection:	Wear gloves (rubber, nitrile, or vinyl) and a disposable coverall when handling bulk quantities or during clean-up of product spills.
Respiratory Protection:	Disposable particulate respirator that meets or exceeds the NIOSH N95 standard.
General Hygiene Considerations:	Avoid contact with eyes or nose. Avoid prolonged contact with skin. Wash hands after handling.

Section 9: PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	A clear, colorless liquid.
Odor:	Odorless
Odor Threshold:	Not Available
Physical State:	Liquid
pH:	4.5
Melting/Freezing Point:	Approximately 32°F (0°C)
Initial Boiling Point and Boiling Range:	Approximately 212°F (100°C)
Flash Point:	Not Flammable
Evaporation Point:	Not Applicable
Flammability:	Not Flammable
Upper/Lower Flammability Limits:	Not Applicable
Vapor Pressure:	Approximately 760 mmHg at 212°F (100°C)
Vapor Density:	Approximately 598 gm/m^3 at 212°F (0°C)
Specific Gravity:	Approximately 1.000 kg/liter at 39.2°F (4°C)
Solubility:	Soluble
Partition Coefficient (n-octanol/water):	Not Applicable
Auto-ignition Temperature:	Not Applicable
Decomposition Temperature:	Not Available

Section 10: STABILITY AND REACTIVITY

Chemical Stability:	Stable at temperatures below 104°F (40°C).
Conditions to Avoid:	None known.
Incompatible Materials:	None known.
Hazardous Decomposition Products:	Products may include oxides of carbon and hydrogen chloride.
Possibility of Hazardous Reactions:	Will not occur.

Section 11: TOXICOLOGICAL INFORMATION

Acute Dose Effects:	Oral LD50 - 800mg/kg (mice) Intravenous LD50 - 72mg/kg (rats), 62mg/kg (rats)
Repeated Dose Effects:	See Carcinogenicity
Irritation:	Not Available
Corrosivity:	Not Available
Sensitization (Skin and Respiratory):	Not Available
Carcinogenicity:	Carcinogenicity studies of buprenorphine were conducted in Sprague-Dawley rats and CD-1 mice. Buprenorphine was administered in the diet to rats at doses of 0.6, 5.5, and 56 mg/kg/day (estimated exposure was approximately 5.7, 52, and 534 times the recommended human dose of 1.2 mg on a mg/m² basis) for 27 months. Statistically significant dose-related increases in testicular interstitial (Leydig's) 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. In an 86-week study in CD-1 mice, buprenorphine was not carcinogenic at dietary doses up to 100 mg/kg/day (estimated exposure was approximately 477 times the recommended human dose of 1.2 mg on a mg/m² basis).
Neurological Effects:	Not Available

Genetic Effects:

Buprenorphine was studied in a series of tests utilizing gene, chromosome, and DNA interactions in both prokaryotic and eukaryotic systems. Results were negative in yeast (Saccharomyces cerevisiae) for recombinant, gene convertant, or forward mutations; negative in Bacillus subtilis "rec" assay, negative for clastogenicity in CHO cells, Chinese hamster bone marrow and spermatogonia cells, and negative in the mouse lymphoma L5178Y assay. Results were equivocal in the Ames test: negative in studies in two laboratories, but positive for frame shift mutation at a high dose (5mg/plate) in a third study. Results were positive in the Green-Tweets (E. coli) survival test, positive in a DNA synthesis inhibition (DSI) test with testicular tissue from mice, for both in vivo and invitro incorporation of [^{3}H]thymidine, and positive in unscheduled DNA synthesis (UDS) test using testicular cells from mice.

Reproductive Effects:

Reproductive studies of buprenorphine in rats demonstrated no evidence of impaired fertility at daily oral doses up to 80 mg/kg (approximately 763 times the recommended human daily dose of 1.2 mg on a mg/m^2 basis) or up to 5 mg/kg intramuscular or subcutaneous (approximately 48 times the recommended human daily dose of 1.2 mg on a mg/m^2 basis).

Developmental Effects:

Significant increases in skeletal abnormalities (e.g., extra thoracic vertebra or thoraco-lumbar ribs) were noted in rats after subcutaneous administration of 1mg/kg/day and up (estimated exposure was approximately 9.5 times the recommended human daily dose of 1.2 mg on a mg/m^2 basis), but were not observed at oral doses up to 160mh/kg/day. Increases in skeletal abnormalities in rabbits after intramuscular administration of 5mg/kg/day (estimated exposure was approximately 95 times the recommended human daily dose of 1.2 mg on a mg/m^2 basis) were not statistically significant. Increases in skeletal abnormalities after oral administration were not observed in rats, and increases in rabbits (1 to 25 mg/kg/day) were not statisically significant.

Target Organ Effects: Not Available

Section 12: ECOLOGICAL INFORMATION

Ecotoxicological Information: Not Available.

Chemical Fate Information: Not Available

Section 13: DISPOSAL CONSIDERATIONS

Disposal:

Buprenex is a Schedule III controlled drug product. Disposal should be in accordance with applicable federal, state, and local laws / regulations, including Drug Enforcement Administration (DEA) requirements.

Section 14: TRANSPORTATION INFORMATION

Transport Information: Buprenex is not classified as hazardous for transport. No special labeling is required for road, sea, or air. Buprenex is a controlled drug product, and it should be transported in accordance with applicable federal, state, and local requirements.

Section 15: REGULATORY INFORMATION

USA Federal:

OSHA Regulatory Status: This material is not considered hazardous according to the OSHA Hazardous Communications Standard (29 CFR 1910.1200).

DEA Regulatory Status: This material is classified as a Schedule III drug by the DEA, under the Controlled Substances Act.

SARA 313: This product does not contain any chemicals which are subject to the reporting requirements of Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA).

CAA: This product does not contain any chemicals listed in the Clean Air Act, Section 112(r).

US State Regulations:

California Proposition 65: This product does not contain any chemicals listed in the Safe Drinking Water and Toxic Enforcement Act of 1986.

European Union: This is a licensed medicinal product and a Controlled Drug in Europe.

Section 16: OTHER INFORMATION

Prepared By: Clinical, Scientific, & Regulatory Affairs Department of Reckitt Benckiser Pharmaceuticals Inc.

Format: This MSDS was prepared in accordance with ANSI Z400.1-2004 ("American National Standard for Hazardous Industrial Chemicals - Material Safety Data Sheets - Preparation").

List of References: See Patient Package Insert for more information.
Buprenex is a registered trademark.

Disclaimer:

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