INFORMATION ON THE ACTIVE INGREDIENTS FOR ALL RECKITT BENCKISER PHARMACEUTICALS PRODUCTS CAN BE OBTAINED FROM THE NATIONAL AND REGIONAL POISONS INFORMATION CENTRES .

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IN CASE OF EMERGENCY , CONTACT A MEDICAL PRACTITIONER OR

RECKITT BENCKISER PHARMACEUTICALS MEDICAL INFORMATION SERVICE
Tel: 0800 270 81 901
(OR FOR NORTH AMERICA call 1-877-SUBOXONE)

WHO WILL THEN DIRECT YOUR CALLS AS NECESSARY

In the case of reporting an adverse event, or product complaint please contact Reckitt Benckiser Pharmaceuticals pharmacovigilance

E-mail: pharmacovigilanceUS@rb.com
Tel: 1-877-SUBOXONE

OR
E.mail: QCHS.MI@quintiles.com
Tel: +800 270 81 901

OR (France only)
E.mail rbp-pv-infomed@rbp.com
Tel: 0800 909 972

Section 1, Identification

Active Pharmaceutical ingredient	Buprenorphine HCl (Schedule III controlled substance)
Product Name:	Temgesic / Buprenex / Buprex 0.3 mg/ml, 1 ml Injection Temgesic / Buprex Sublingual Tablets 0.2mg
National Drug Code:	Buprenex Injection: NDC 12496-0757-5
Generic Names:	Buprenorphine Injection Buprenorphine Sublingual Tablets
Product Type:	Opioid receptor partial agonist; analgesic
Use:	Relief of moderate to severe pain.
Appearance:	Injection - Colourless liquid in glass ampoules. Sublingual Tablets - White, to creamy white, tablets in blister pack.
Manufacturer:	RB Healthcare UK Limited Dansom Lane, Hull, UK, HU8 7DS Tel. +44 (1482) 326151
Marketing Authorisation holder:	RB Pharmaceuticals Ltd
US Distributor:	Reckitt Benckiser Pharmaceuticals Inc. 10710 Midlothian Turnpike Richmond, Virginia 23235 Tel. +(1) 877-782-6966

Section 2, Hazard(s) identification

Caution
This is a clear, colourless, sterile injection or a white, to creamy white, sublingual tablet, that has potential adverse health effects if abused by routes other than the intended medical application.

Emergency Overview
Buprenorphine Hydrochloride is a potent opiate type of analgesic. Precautions must be taken and procedures adopted to prevent excessive exposure. The side effects of buprenorphine exposure include: respiratory depression, nausea/vomiting, dizziness, pinpoint pupils, euphoria, headache, sweating and drowsiness.

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

Injection

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

Each glass ampoule contains 1ml of solution containing 324 micrograms of buprenorphine HCl in a 5% dextrose solution (0.3 mg/ml as buprenorphine), adjusted to pH 3.5 - 5.5 with hydrochloric acid.

Sublingual Tablet

Chemical Name	CAS Number	Composition
Buprenorphine Hydrochloride	53152-21-9	0.36 %w/w
Lactose	10039-26-6	Proprietary
Mannitol	69-65-8	Proprietary
Maize Starch	9005-25-8	Proprietary
Povidone K30	94800-10-9	Proprietary
Citric Acid Anhyd Gran	77-92-9	Proprietary
Sodium Citrate	6132-04-3	Proprietary
Magnesium Stearate Kosher	557-04-0	Proprietary

Each sublingual tablet contains 216 micrograms (0.2mg) of buprenorphine hydrochloride.

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: Buprenorphine is a opioid receptor partial agonist; competitive.

In the event of overdose, general supportive measures should be instituted, including close monitoring of respiratory and cardiac status of the patient. Symptomatic treatment of respiratory depression, following standard intensive care measures, should be performed. A patent airway and assisted or controlled ventilation must be assured. The patient should be transferred to an environment within which full resuscitation facilities are available. If the patient vomits, care must be taken to prevent aspiration of the vomitus. Use of an opioid antagonist (e.g., naloxone) is recommended, despite the modest effect it may have in reversing the respiratory

symptoms of buprenorphine compared to its effects on full agonist opioid agents. If naloxone is used, the long duration of action of buprenorphine should be taken into consideration when determining the length of treatment and medical surveillance needed to reverse the effects of an overdose. Naloxone can be cleared more rapidly than buprenorphine, allowing for a return of previously controlled buprenorphine overdose symptoms, so a continuing infusion may be necessary. Ongoing IV infusion rates should be titrated to patient response. If infusion is not possible, repeated dosing with naloxone may be required. Initial naloxone doses may range up to 2mg and be repeated every 2-3 minutes until a satisfactory response is achieved. Patients dosed with initial doses totalling greater than 4mg should be monitored closely.

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

As this is a controlled drug relevant local governmental law applies.

Personal Precautions: If waste is dusty, use personal protection recommended in Section Eight (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: Scoop-up product and dispose in accordance with local, state and federal requirements, including Drug Enforcement Administration regulations for controlled substances.
Major Spills: Contain spill. Shovel product into a clean, dry, and labelled 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

As this is a controlled drug relevant local governmental law applies.

Handling: Avoid prolonged contact with skin.
Storage: Store in a secure place in accordance with relevant local governmental law. Store in accordance with label instructions. Keep out of reach and sight of children.

Section 8, Exposure controls/personal protection

Exposure Guidelines: No exposure is likely under normal circumstances.
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 coverall when handling bulk quantities or during clean-up of product spills.
General Hygiene: Avoid contact with eyes or nose. Avoid prolonged contact with skin. Wash hands after handling.
Considerations: Wash hands after handling.

Section 9, Physical and chemical properties

	Injection	Sublingual Tablet
Appearance	A clear, colourless liquid	A white to creamy white tablet
Odour	Odourless	Odourless
Odour Threshold	Not Applicable	Not Applicable
Physical State	Liquid	Solid
pH	4.5	Not Applicable
Melting / Freezing Point	Approximately 0°C (32°F)	Not Applicable
Initial Boiling Point and Boiling Range	Approximately 100°C (212°F)	Not Applicable
Flash Point	Not Flammable	Not Flammable
Evaporation Point	Not Applicable	Not Applicable
Flammability	Not Flammable	Not Flammable
Upper/Lower Flammability Limits	Not Applicable	Not Applicable
Vapour Pressure	Approximately 760mmHg at 100°C (212°F)	Not Applicable
Vapour Density	Approximately 598gm/m^3 at 100°C (212°F)	Not Applicable
Specific Gravity	Approximately 1.000kg/l at 4°C (39.2°F)	Not Applicable
Solubility	Soluble	Partially Soluble
Partition Coefficient (n-octanol/water)	Not Applicable	Not Applicable
Auto-ignition Temperature	Not Applicable	Not Applicable
Decomposition Temperature	No applicable information was found.	No applicable information was found.

Section 10, Stability and reactivity

Physical and chemical Stability:
Injection: Store below 30°C (86°CF); protect from light, do not freeze
Sublingual Tablet: Store below 30°C (86°CF)
Conditions to Avoid: None known.
Incompatible Materials: Strong oxidisers.
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: No applicable information was found.
Corrosivity: No applicable information was found.
Sensitization (Skin and Respiratory): No applicable information was found.
Carcinogenicty: 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/m^2 basis) for 27 months. Statistically significant dose-related increases in testicular interstitial (Leydig's) cell tumours 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: No applicable information was found.
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 clastogeniciity in CHO cells, Chinese hamster bone marrow and spematogonia 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 in vitro incorporation of [³H]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/m² 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/m² 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/m² 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/m² 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 statistically significant.
Target Organ Effects: No applicable information was found.

Section 12, Ecological information

Ecotoxicological Information: No applicable information was found.
Chemical Fate Information: No applicable information was found.

Section 13, Disposal considerations

As this is a controlled drug relevant local governmental law applies.

Section 14, Transport information

As this is a controlled drug relevant local governmental law applies.

No special labelling required for Road, Sea and Air. Not classed as hazardous for transport.

Injection: Store at 20°C to 25°C (68°F to 77°F), with excursions permitted between 15°C and 30°C (between 59°F and 86°F), protect from prolonged exposure to light.

Sublingual Tablet: Store below 30°C (86°F). Excursions of down to -20°C (-4°C) or up to 60°C (140°C) for a maximum of 1 week in total (combined) are permitted.

Keep out of reach and sight of children.

Section 15, Regulatory information

As this is a controlled drug relevant local governmental law applies.

UK: This is a Schedule III drug under the Misuse of Drugs Regulations, 1985.

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

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 Clear 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.

Section 16, Other information

Temgesic/Buprenex/Buprex are Trademarks.

List of References: See Patient Package Insert for more information.

This document complements the technical usage instructions but does not replace them. The information contained herein is based on our best current technical knowledge of the product concerned, and is given in good faith. The attention of recipients is drawn to (amongst other things) the element of risk consequent to use of the product for a purpose other than that for which it was intended.

In no way does this document remove the need of the recipient of the product to fully understand and apply statutory requirements. It is the recipient's sole responsibility to take due precautions relative to the use made of the product.

All information contained herein is included only to assist the recipient in fulfilling his or her statutory duty connected with the use of hazardous materials.

This list of information must not be considered as exhaustive, and does not exonerate the recipient from taking other precautions described in documents other than those mentioned, concerning the storage and use of the product, for which he or she remains the sole person responsible.