

EXPAREL® Safety Data Sheet

SAFETY DATA SHEET

Product Name: EXPAREL® (bupivacaine liposome injectable suspension)

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name and Address Pacira Pharmaceuticals, Inc.
10450 Science Center Drive
San Diego, CA 92121

Emergency Telephone ACT 1-888-785-7225

Pacira non-emergency (858) 625-2424

Product Name EXPAREL®

Synonyms DepoBupivacaine™, SKY0402

2. HAZARD INFORMATION

EMERGENCY OVERVIEW: This product is white to off-white aqueous suspension. This product can irritate contaminated skin, eyes, mucous membranes, and any other exposed tissues. This product is neither reactive nor flammable. Thermal decomposition of this product produces irritating vapors and toxic gases. Emergency responders must wear personal protective equipment (and have appropriate fire-extinguishing protection) suitable for the situation to which they are responding.

Physical Hazards Summary This product does not pose significant physical hazards.

Potential Health Hazards Summary Acute Toxicity, Oral, Category4

Potential Ecological Effects Summary None anticipated at amounts normally handled

2.1 Classification Of Product

U.S. OSHA classification Toxic



Classification as per EC 1272/2008 Acute Toxicity, Oral, Category 4
(CLP/GHS)

WHMIS classification D1B - Poisonous and infectious material - Other toxic effects

Hazardous Materials Information System (HMIS) Rating	Health	2
	Flammability	0
	Physical Hazard	0
	Protective Equipment	B

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2.2 Label Elements OSHA/GHS

General Warnings	P101 P102 P103 P403 P233	If medical advice is needed, have product container or label at hand. Keep out of reach of children. Read label before use Store in a well-ventilated place. Keep container tightly closed
Signal Word	WARNING	
Hazard statements	H301	Toxic if swallowed.
Precautionary statements	P301+P314 P264P280	IF SWALLOWED: Get medical advice/attention if you feel unwell. Wash hands thoroughly after handling. Wear protective gloves /protective clothing.
Hazard pictograms - GHS	P302 + P350+P314 	IF ON SKIN: Gently wash with plenty of soap and water. Get medical advice/attention if you feel unwell.
Hazard pictograms - WHMIS		

2.3 Unclassified Hazards None

2.4 Ingredients with unknown acute toxicity None

3. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name	Bupivacaine (USAN)
Synonym	1-butyl-2',6'-pipercoloxylidide
Chemical Name	(<i>RS</i>)-1-butyl- <i>N</i> -(2,6-dimethylphenyl)piperidine-2-carboxamide-1-butyl- <i>N</i> -(2,6-dimethylphenyl)-2-piperidinecarboxamide
Percent by Weight	1.3% (13.3 mg/mL)

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CAS Number 2180-92-9

4. FIRST AID MEASURES

Inhalation	Remove to fresh air and keep patient at rest
Skin	Wash with soap and water. Remove contaminated clothing and launder before reuse.
Eye	Rinse with flowing water for 15 minutes.
Ingestion	Wash out mouth with water provided person is conscious. Call a physician.

5. FIRE FIGHTING MEASURES

Conditions of flammability	Not flammable
Suitable Extinguishing Media	Water, Alcohol Foam, Carbon Dioxide, or Dry Chemical
Hazardous combustion products	Not Applicable
Special equipment for firefighters	During all firefighting activities, wear appropriate protective equipment.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions	Personnel involved in clean-up should wear appropriate personal protective equipment and minimize exposure. Adequate skin and respiratory protection should be worn when cleaning up spills.
Measures for Cleaning/Collecting	Contain the source of the spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly. Place in a bag and hold for proper waste disposal. Ventilate area and wash spill site after material pickup is complete.
Environmental precautions	Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

7. HANDLING AND STORAGE

Handling	All needles, syringes, vials, and other equipment or disposable clothing, which have been in contact with the material, should be disposed of properly.
Storage	Recommended storage is refrigeration at 2° to 8°C.
Special Precautions	No special precautions required for hazard control.

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8. EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1 Control Parameters

CHEMICAL NAME	CAS #	% w/w	EXPOSURE LIMITS IN AIR					
			ACGIH-TLVs		OSHA-PELs		IDLH mg/m ³	OTHER mg/m ³
			TWA mg/m ³	STEL mg/m ³	TWA mg/m ³	STEL mg/m ³		
Bupivacaine	2180-92-9	1.3	NE	NE	NE	NE	NE	Pacira Occupational Exposure Band (OEB): OEB 3 (control exposure to <100 µg/m ³)
Water and other components which are present in less than 1 percent concentration (0.1% concentration for potential carcinogens, reproductive toxins, respiratory tract sensitizers and mutagens).		Balance	None of the other components contribute significant additional hazards at the concentration present in this product. All pertinent hazard information has been provided in this document, per the requirements of the Federal Occupational Safety and Health Administration Standard (29 CFR 1910.1200), U.S. State equivalent Standards and Canadian Workplace Hazardous Materials Identification System Standards (CPR 4).					

8.2 Appropriate Engineering Controls.

Use with adequate ventilation to ensure exposure levels are maintained below the limits provided in this Section or as low as reasonably achievable. Ensure eyewash/safety shower stations are available near areas where this product is used.

8.3 Personal Protective Equipment

Respiratory protection:

None needed under normal conditions of use. Use NIOSH approved respirators if ventilation is inadequate to control mists or vapor. If respiratory protection is needed, use only protection authorized in the U.S. Federal OSHA Standard (29 CFR 1910.134), applicable U.S. State regulations, or the applicable local standards. Oxygen levels below 19.5% are considered IDLH by OSHA. In such atmospheres, use of a full-face piece pressure/demand SCBA or a full-face piece, supplied air respirator with auxiliary self-contained air supply is required under OSHA's Respiratory Protection Standard (1910.134).

Eye protection:

Use approved safety goggles or safety glasses, as described in OSHA 29 CFR 1910.133. Splash goggles with a faceshield may be needed if significant splash hazards exist.

Hand protection:

Wear chemical impervious gloves (e.g., Solvex™, Neoprene). Thin mil nitrile gloves are appropriate in a laboratory or clinical setting.

Body protection:

Lab coat or normal clinical body protection is adequate. If needed, use body protection appropriate for task (e.g., Tyvek suit,

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rubber apron) to protect from splashes and sprays.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	White to off white suspension
Odor	Odorless
Odor threshold	N/A
pH	5.8-7.4
Melting point/freezing point	N/A
Initial boiling point and boiling point range	N/A
Flash point	N/A
Evaporation rate	N/A
Flammability	Not flammable
Upper/lower flammability or explosive limits	Not flammable
Vapor Pressure	Approximately the same as that of water
Vapor density	N/A
Relative density	N/A
Solubility	EXPAREL is not solubilized by water
Partition coefficient:	
n-octanol/water	N/A
Auto-ignition temperature	N/A
Decomposition temperature	N/A

10. STABILITY AND REACTIVITY

Reactivity	Not determined
Chemical Stability	Stable
Hazardous Reactions	N/A
Conditions to avoid	N/A
Incompatibilities	N/A
Hazardous decomposition Products	N/A
Hazardous Polymerization	N/A

11. TOXICOLOGICAL INFORMATION

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Formal LD50 studies have not been conducted in mammals with EXPAREL

Toxicity data of bupivacaine HCl, analogous to the active ingredient in EXPAREL

		Test Type	Route of Administration	Value	Units	Species
AIPTAK	200,359,1972	LD50	SCU	43	MG/KG	RAT
AIPTAK	200,359,1972	LD50	IVN	6	MG/KG	RAT
ANESAV	89,1199,1998	LD50	PAR	30	MG/KG	RAT
AACRAT	60,385,1981	LD50	IPR	58700	UG/KG	MUS
AIPTAK	200,359,1972	LD50	SCU	59	MG/KG	MUS
ANPRBG	36,79,1989	LD50	IVN	6100	UG/KG	MUS
DDREDK	21,277,1990	LD50	IMS	22753	UG/KG	MUS
AIPTAK	200,359,1972	LD50	ORL	18	MG/KG	RBT
AIPTAK	200,359,1972	LD50	IVN	3400	UG/KG	RBT
AIPTAK	200,359,1972	LD50	PAR	48	MG/KG	RBT
AIPTAK	200,359,1972	LD50	ITR	11	MG/KG	RBT
NIIRDN	6,680,1982	LD50	IPR	50	MG/KG	GPG

Acute Toxicity

The main toxicological properties of EXPAREL are associated with the active ingredient bupivacaine. The bupivacaine-released form EXPAREL is chemically indistinguishable from bupivacaine hydrochloride. Therefore, the toxicological properties of EXPAREL are analogous to that of bupivacaine hydrochloride.

Data from the Registry of Toxic Effects of Chemical Substances (RTECS) for bupivacaine HCl (2', 6'-pipecoloxylidide, 1-butyl-, hydrochloride (±)) (#TK6125000), are presented below. Note: Only selected RTECS data is presented here. Please see actual entry in RTECS for complete information.

Skin corrosion/irritation

None anticipated from normal handling of this product. However, inadvertent contact with this product may be irritating to broken skin and mucous membranes and may produce numbness.

Ocular corrosion/irritation

None anticipated from normal handling of this product. However, inadvertent contact with this product with eyes may produce irritation, numbness, and blurred vision.

Respiratory or skin sensitization
through skin.

Pure bupivacaine HCl may be fatal if inhaled, swallowed, or absorbed

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May cause irritation.
 Prolonged or repeated exposure may cause allergic reactions in certain sensitive individuals.
 Exposure can cause anesthesia, CNS stimulation or depression, numbness of the tongue, tinnitus, anxiety, nervousness, dizziness, blurred vision, nausea, vomiting, tremors and convulsions.
 Overexposure can cause myocardial depression, decreased cardiac output, hypotension, respiratory arrest, ventricular arrhythmias, coma, cardiac arrest and death.

Germ cell mutagenicity	Data not available
Carcinogenicity	None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.
Reproductive Toxicity	Exposure during pregnancy can cause fetal bradycardia and death.
Aspiration hazard	None anticipated from normal use of this product.
Target Organ Effects	Target organ data of bupivacaine HCl, analogous to the active ingredient in EXPAREL Behavioral (anticonvulsant) Behavioral (somnolence) Behavioral (convulsions or effect on seizure threshold) Cardiac (EKG changes not diagnostic of above)

12. ECOLOGICAL INFORMATION

Aquatic Toxicity	Not determined for this product
Persistence/Biodegradability	Not determined for this product
Bioaccumulation	Not determined for this product
Mobility in Soil	Not determined for this product

13. DISPOSAL CONSIDERATIONS

Waste Disposal	Dispose of by incineration in accordance with applicable federal, state, and local regulations, or European Economic Community (EEC) regulations.
Container Handling and Disposal	Dispose of container and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

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ADR/ADG/DOT Status Not regulated

IATA status Not regulated

IMO status Not regulated

15. REGULATORY INFORMATION

PROGRAM	Bupivacaine
US EPA PROGRAMS	
Clean Air Act Hazardous Air Pollutants	NO
Safe Drinking Water Act	NO
RCRA F, K, P, U or D-lists	NO
SARA 302 RQ	NO
SARA 302 TPQ	NO
SARA 313 LISTED	NO
SARA CHEMICAL CATEGORIES	
SARA 311/312 ACUTE	YES
SARA 311/312 CHRONIC	NO
SARA 311/312 FIRE	NO
SARA 311/312 PRESSURE	NO
SARA 311/312 REACTIVITY	NO
EPA EXTREMELY HAZARDOUS SUBSTANCE	NO
CALIFORNIA SAFE DRINKING WATER ACT (Proposition 65)	
This product does not contain any chemical listed on the California Safe Drinking Water Act list (Proposition 65)	
US OSHA PROGRAMS	
PEL	NO
PSM	NO
CHEMICAL SECURITY PROGRAMS	
DHS CFATS	NO
CHEMICAL WEAPONS CONVENTION	
	NO
US DRUG ENFORCEMENT ADMINISTRATION	
DEA Controlled Substances	NO

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CHEMICAL INVENTORY PROGRAMS	
WHMIS	D1A
DSL	NO
NDSL	N/A
REACH Pre-registered List	NO
TSCA	NO
European Inventory of Existing Commercial Chemical Substances (EINECS)	NO
EU No-Longer Polymers List (NLP)	N/A
EEC Classification Packaging, and Labeling of Dangerous Substances(Annex 1)	Xn
Massachusetts RTK	NO
Pennsylvania RTK	YES
New Jersey RTK	YES
Australia	YES

16. OTHER INFORMATION

Notes The information contained in this Safety Data Sheet (SDS) is believed to be correct but must only be used as a guide. Pacira disclaims any express or implied warranty as to the accuracy of the information provided in this SDS, and shall not be held liable for any direct, incidental or consequential damages resulting from reliance on this information.

SDS Coordinator: John Sisco
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