SAFETY DATA SHEET

BUPRENORPHINE

Safety data sheet according to European Parliament and Council Regulation (EC) No. 1907/2006 (REACH) and Commission Regulation (EU) 2020/878.

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier

Product name
Buprenorphine

IUPAC name
(2*S*)-2-[(5*R*,6*R*,7*R*,14*S*)-17-cyclopropylmethyl-3-hydroxy-4,5-epoxy-6-methoxy-6,14-ethanomorphinan-7-yl]-3,3-dimethylbutan-2-ol

CAS no.
52485-79-7

EC no. (EINECS)
257-950-6

1.2 Relevant identified uses of the substance or mixture and uses advised against

Relevant uses
For industrial and professional use only [SU 3, SU 22].
Active Pharmaceutical Ingredient (API) for the manufacture of medicinal products and use in pharmaceutical research and development under controlled conditions.

Uses advised against
Not intended for consumer use [SU 21].
Not to be used as a finished medicinal product, for self-administration, or for end-use outside regulated facilities.

1.3 Details of the supplier of the safety data sheet

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Kanalholmen 8-12
DK-2650 Hvidovre
Denmark

Tel: +45 3679 4500
Fax: +45 3834 1572
info@COSynthesis.dk
www.cosynthesis.dk

1.4 Emergency telephone number

National poison information centres
Austria: +43 1 406 43 43 (VIZ), 24/7 service
Belgium: 070 245 245, 24/7 service, free of charge
Bulgaria: +359 2 9154 233, 24/7 service, free of charge
Croatia: +385 1 2348 342, 24/7 service, free of charge
Cyprus: 1401 (Poison Centre), 24/7 service
Czech Republic: +420 224 919 293; +420 224 915 402
Denmark: +45 82 12 12 12, 24/7 service, free of charge
Estonia: 16662; from abroad +372 7943 794
Finland: 0800 147 111, 24/7 service, free of charge
France: +33 (0)1 45 42 59 59 (ORFILA), 24/7 service, free of charge
Greece: +30 210 779 3777, 24/7 service
Hungary: +36 80 201 199, 24/7 service, free of charge
Iceland: +354 543 2222 / +354 543 1000, 24/7 service
Ireland: Public: +353 1 809 2166 (08:00–22:00); HCPs: +353 1 809 2566 (24/7)
Italy: +39 0382 24444 (CAV Pavia), 24/7 service
Latvia: +371 670 42473, 24/7 service
Lithuania: +370 5 2362052
Luxembourg: +352 8002 5500, 24/7 service, free of charge
Netherlands: +31 (0)88 755 8000 (NVIC) — for healthcare professionals only, 24/7
Norway: +47 22 59 13 00, 24/7 service, free of charge
Poland: 112 — poison centre contact via general emergency number
Portugal: +351 800 250 250 (Centro de Informação Antivenenos), 24/7 service

Romania: +40 21 318 3606
Slovakia: +421 2 5477 4166 (NTIC), 24/7 service
Slovenia: 112 — poison centre contact via general emergency number
Spain: +34 91 562 04 20 (Instituto Nacional de Toxicología), 24/7 service
Sweden: 112 — ask for Poisons Information
United Kingdom: NHS 111 (public, 24/7, Tel. 111 or 18001 111 for text relay); NPIS for healthcare professionals: +44 344 892 0111

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

The classification of this substance is based on self-classification in accordance with Regulation (EC) No 1272/2008 (CLP).

Repr. 2; H361d
Acute Tox. 4 (Inhalation); H332
Acute Tox. 4 (Oral); H302
STOT RE 2; H373
Eye Irrit. 2; H319

2.2 Label elements

Labelling according to Regulation (EC) No 1272/2008 [CLP]:

Signal words
Warning

Hazard statements
H302: Harmful if swallowed.
H332: Harmful if inhaled.
H319: Causes serious eye irritation.
H361d: Suspected of damaging the unborn child.
H373: May cause damage to organs (central nervous system) through prolonged or repeated exposure.

Precautionary statements
P261: Avoid breathing dust.
P280: Wear protective gloves and eye protection.
P308 + P313: IF exposed or concerned: Get medical attention.
P501: Dispose of contents and container in accordance with local/regional/national waste disposal regulations.

Additional hazard information
None.

2.3 Other hazards

This product contains no components considered to be persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

This product does not contain any substances considered to be endocrine disruptors in accordance with the criteria set out in Commission Delegated Regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605.

SECTION 3: Composition/information on ingredients

3.1 Substances

Substance
Buprenorphine (pure substance).

Chemical formula
$C_{29}H_{41}NO_4$

Molecular weight
467.64 g/mol

Component	Identifiers	Purity %	Classification	SCL / M-factors
Buprenorphine	CAS: 52485-79-7 EC: 257-950-6 REACH: - Index: -	≥ 99	Repr. 2; H361d Acute Tox. 4 (Inhalation); H332 Acute Tox. 4 (Oral); H302 STOT RE 2; H373 Eye Irrit. 2; H319	-

Additional information:
For full text of H-statements, see Section 16.

SECTION 4: First aid measures

4.1 Description of first aid measures

Take precautions to ensure your own safety before assisting others. Remove exposed individuals from the hazard area. Seek immediate medical attention for any significant exposure. Show this SDS to medical personnel.

In case of inhalation
IF INHALED: Move person to fresh air and keep comfortable for breathing. If symptoms such as wheezing, cough, or shortness of breath occur, obtain medical attention immediately. Individuals with pre-existing asthma or respiratory conditions may be more susceptible.

In case of ingestion
IF SWALLOWED: Rinse mouth thoroughly with water. Do NOT induce vomiting unless directed by medical personnel. Do not give anything by mouth to an unconscious person. Call a POISON CENTER or doctor immediately and describe the substance and amount ingested. Monitor for signs of CNS depression or respiratory difficulty.

In case of contact with skin
Remove contaminated clothing and rinse skin with soap and water for at least 15 minutes. Seek medical attention if irritation or systemic symptoms appear. Launder clothing before reuse.

In case of contact with eyes
Rinse eyes carefully with lukewarm water for several minutes while holding eyelids open. Remove contact lenses if present and easy to do so. Continue rinsing and seek medical attention if irritation persists.

In case of burns
Not applicable.

4.2 Most important symptoms and effects, both acute and delayed

Acute effects
Harmful if swallowed or inhaled. Systemic symptoms of over-exposure resemble those of potent opioids: sedation, drowsiness, miosis (pupil constriction), nausea, vomiting, constipation, hypotension and in severe cases respiratory depression and coma. Coughing or wheezing may indicate respiratory sensitisation. Causes serious eye irritation.

Delayed effects
Prolonged or repeated low-level exposure may lead to physical dependence or tolerance (similar to other opioid agonists). May cause damage to the central nervous system through prolonged or repeated exposure. Possible reproductive effects at high doses observed in animal studies (foetotoxicity).

4.3 Indication of any immediate medical attention and special treatment needed

If the substance has been ingested or inhaled, seek medical attention immediately. Provide medical personnel with all available information, including the substance name, estimated dose, time of exposure, and the patient's clinical condition, to ensure appropriate treatment. Ensure that emergency responders and medical staff are aware of the potent opioid nature of the compound and the possibility of prolonged toxicity.

Notes for the doctor
This substance is buprenorphine, a potent semisynthetic opioid. Toxic effects are primarily due to μ-opioid receptor agonism leading to central nervous system and respiratory depression. Treatment is primarily supportive and symptomatic.

Airway and ventilation:
Maintain a patent airway and ensure adequate oxygenation. Mechanical ventilation may be required in cases of severe respiratory depression.

Antidote:
Naloxone (an opioid antagonist) should be administered promptly in symptomatic cases. Because the duration of effect of buprenorphine may exceed that of naloxone, repeated doses or continuous infusion may be necessary. Observe the patient for recurrence of respiratory depression.

Circulation:
Monitor cardiac rhythm and blood pressure. Treat hypotension with fluids and vasopressors if required.

Seizures:
Although uncommon, treat seizures with intravenous benzodiazepines under controlled conditions.

Aspiration and gastrointestinal decontamination:
Gastric lavage is generally not recommended unless ingestion is recent and life-threatening. Administration of activated charcoal may be considered within one hour of ingestion in alert patients with protected airway.

Allergic or respiratory sensitisation:
In cases of acute asthmatic or allergic response, administer bronchodilators and corticosteroids as indicated.

Observation:
Monitor for at least 24 hours after significant exposure due to possible delayed recurrence of respiratory depression.

SECTION 5: Firefighting measures

5.1 Extinguishing media

Suitable extinguishing media
Use an extinguishing agent appropriate for the surrounding fire. Water spray (fog), dry chemical powder, carbon dioxide, or alcohol-resistant foam can be used.

Unsuitable extinguishing media
Do not use water jet directly, as it may spread burning material.

5.2 Special hazards arising from the substance or mixture

The product is not classified as flammable, but if involved in a fire it can decompose and produce toxic and irritating fumes or smoke.

Fine dust of the substance, if dispersed in air, could potentially form an explosive dust-air mixture in the presence of an ignition source (general caution for organic powders).

Hazardous combustion products
Oxides of carbon (CO, CO_2), oxides of nitrogen (NO_x), and other toxic gases. In a fire, the material can contribute toxic smoke; inhalation of combustion products can be very hazardous.

5.3 Advice for firefighters

Evacuate area and fight fire from a safe distance or protected location. Firefighters should wear full protective gear and a self-contained breathing apparatus (SCBA) if there is potential exposure to fumes. Prevent runoff from fire control from entering waterways or drains if possible. Use water spray to keep fire-exposed containers cool. If large quantities of the material are stored, be aware that toxic fumes can accumulate; approach from upwind. Follow standard procedures for chemical fire situations.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

For non-emergency personnel
Evacuate non-essential personnel from the area. Do not breathe dust. Avoid contact with skin, eyes and clothing. Ventilate the area thoroughly.

For emergency responders
Emergency responders should wear appropriate personal protective equipment: gloves, protective clothing, eye protection, and in case of significant dust, a suitable respiratory protection (P3 filter or air-purifying respirator). If material is spilled in an enclosed area, consider using a respirator even for small spills.

Avoid generating airborne dust during cleanup. Remove any ignition sources if fine dust is present (to prevent dust explosion, although this material is not highly flammable, dust clouds of organics can ignite).

6.2 Environmental precautions

Prevent material from entering drains, surface water, or soil. The compound is pharmacologically active and may adversely affect aquatic life even at low concentrations. Notify authorities if large quantities enter the environment.

6.3 Methods and material for containment and cleaning up

For containment
For small spills, if possible, dampen the solid dust with water to minimize airborne dispersion. Carefully scoop, sweep, or vacuum (with explosion-proof vacuum) the spilled material into an appropriate closed container for disposal. Use inert absorbent material if needed (for example, wet paper towels or spill pads dampened with water) to wipe up residues. Avoid dry sweeping which can stir up dust; if sweeping is needed, lightly mist the spill first to suppress dust.

For cleaning up
Collect all contaminated materials (absorbents, used PPE, etc.) in a sealed plastic bag or container for disposal as hazardous waste. After removal of bulk material, wash the spill site with water and detergent to remove any remaining traces. Do not flush wash water into the environment; collect it for proper disposal.

Other information
For larger spills, personnel must wear respiratory protection and follow your organization's chemical spill response plan. Ventilate the area until cleanup is complete.

6.4 Reference to other sections

For more information, see Sections 8 (protective equipment) and 13 (disposal).

SECTION 7: Handling and storage

7.1 Precautions for safe handling

Technical measures
Handle only in a well-ventilated area or fume hood to avoid exposure to dust. Use engineering controls (local exhaust ventilation, closed processes) to minimize dust generation and airborne exposure. All handling should occur in an area with smooth, impermeable surfaces that can be easily cleaned. Keep containers closed when not in use. Handle over spill trays if possible to prevent dispersion of powder. Ensure that only authorized personnel have access, and that handling complies with applicable regulations (controlled psychotropic substance/opioid). Young persons under 18 years should not work with this product.

Measures to prevent fire
Not specifically applicable; substance is not classified as flammable. No special fire prevention measures beyond good housekeeping are required.

Measures to prevent aerosol and dust generation
Handle material in closed systems or under local exhaust ventilation. Avoid open handling and transfer operations that may generate dust. Use spill trays or containment systems to prevent dispersion of powder. Minimize agitation, pouring, or mechanical processes that create airborne particles. Regularly clean work surfaces to avoid accumulation of dust.

Measures to protect the environment
Prevent dispersion of powder outside designated handling areas. Handle over spill trays if possible. Ensure cleaning procedures prevent release to the environment.

Advice on general occupational hygiene
Do not ingest. Avoid contact with skin and eyes – wear appropriate protective equipment (see Section 8). No eating, drinking or smoking in areas where this material is handled or stored. Wash hands and any exposed skin thoroughly with soap and water after handling. Remove and wash contaminated clothing before reuse. Employ good industrial hygiene practices: e.g., keep work areas clean, and periodically clean surfaces to prevent accumulation of powder. Workers should be trained about the hazards and proper handling procedures.

7.2 Conditions for safe storage, including any incompatibilities

Technical measures and storage conditions
Store in the original container, tightly closed, in a secure location. Keep in a cool, dry, and well-ventilated area.

Protect from direct sunlight, moisture/humidity, and physical damage. The substance is hygroscopic; exposure to humid air may cause degradation or clumping. Store away from incompatible materials, especially strong oxidizing agents, strong alkalis/bases, reactive metals, and strong reducing agents. Keep locked up or otherwise secured; access limited to authorized personnel (controlled opioid under national and international narcotics legislation).

Packaging material
Suitable: glass, stainless steel, or high-density polyethylene (HDPE). Ensure containers are labeled, tightly sealed, and intact to prevent leakage.

Requirements for storage rooms and vessels
Storage rooms should be cool, dry, well-ventilated, and secure against unauthorized access. Surfaces and fittings should be resistant to moisture and chemicals. Provide secondary containment or spill trays if possible.

Storage class
According to TRGS 510 (Germany): Storage class 6.1C (toxic hazardous substances, combustible solids). National regulations may apply (e.g. controlled drug storage requirements).

7.3 Specific end use(s)

This product is intended solely for research, analytical, or synthetic use in industrial or professional laboratories under controlled conditions. It must not be used as or incorporated into any medicinal or consumer product without appropriate authorisation. It is not intended for direct human or veterinary administration.

Use is restricted to professional users familiar with its handling and hazards. Refer to the appropriate technical literature for application details. No other specific uses are advised.

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

There are no occupational exposure limit (OEL) values specifically established for buprenorphine by EU, OSHA, ACGIH or other major standards.

For potent opioids, internal exposure guidelines (Occupational Exposure Band 3 or 4) correspond to airborne concentrations below 10 µg/m³ (8 h TWA).
Exposure should be kept as low as reasonably achievable (ALARA principle).

Always follow national regulations that may apply for chemical agents at the workplace; there may be a requirement to minimize exposure under directives for hazardous substances.

If available, general air-sampling methods for particulates can be used to verify adequate control of airborne dust levels, although no specific analytical method for buprenorphine in air has been standardised. Biological monitoring is not routinely performed for this substance in occupational settings; however, unexpected systemic absorption could, in principle, be detected through specialised opioid screening assays if clinically indicated.

8.2 Exposure controls

Appropriate engineering controls
Provide adequate general or local exhaust ventilation to keep airborne concentrations below any recommended guidelines and as low as possible. Enclose processes where feasible. If dust is generated (e.g. during weighing or mixing), perform these operations in a fume hood or ventilated enclosure. Use explosion-proof equipment for handling large quantities of fine powder. Implement dust control measures (e.g., use of dust extraction vacuum, wet methods for cleaning) to prevent accumulation of dust on surfaces. Emergency eye wash stations and safety showers should be available in areas where the substance is handled.

Personal protection equipment
Selection of PPE should be in accordance with EN standards and based on risk assessment:

Pictogram	Equipment	Marking	CEN standards	Remarks
	Disposable nitrile gloves. Thickness ≥0.12 mm; Breakthrough time >480 min	CE CAT III	EN ISO 374-1:2016; EN ISO 21420:2020	Change immediately if contaminated or torn. Wash hands after removal. Prevent skin absorption.
	Safety goggles with side shields or tightly fitting chemical goggles	CE CAT II	EN 166:2002; EN ISO 4007:2018	Required if dust formation or splashing is possible. Prevents serious eye exposure.
	Half-mask respirator with P3 particulate filter (or full-face if needed)	CE CAT III	EN 140:1998; EN 143:2000/A1:2006; EN 14387:2004+A1:2008	Use if ventilation is inadequate. Protects against fine powder dust (harmful if inhaled).
	Chemical-resistant clothing (e.g. lab coat, disposable coverall, apron)	CE CAT III	EN 13034:2005+A1:2009 (Type 6)	Recommended for bulk handling or risk of spills. Prevents contamination of personal clothes and reduces skin contact risk.
	Closed chemical-resistant footwear (e.g. safety shoes)	CE CAT II	EN ISO 20345:2011	Protects against accidental contamination and ensures safe laboratory/workplace practice.

Environmental exposure controls
Prevent spills or effluents from entering the environment. Use closed systems or secondary containment for processes to reduce the risk of accidental release. Air exhaust from ventilation should be filtered (HEPA) or scrubbed if possible to remove particulate before release.

All waste (solids, solutions) should be collected for proper disposal (see Section 13) rather than discharged. Given the potential ecological effects (see Section 12), even small quantities should be handled with care to avoid environmental contamination.

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Physical and chemical properties

(a) Physical state:	Solid crystalline fine powder.
(b) Colour:	White to off-white or light brown in color.
(c) Odour:	Odourless (no characteristic odor).
(d) Melting point/freezing point:	~217–218 °C
(e) Boiling point:	Not applicable (solid decomposes before boiling; no boiling point at atmospheric pressure).
(f) Flammability:	Not classified as flammable. The solid can burn if strongly heated, but it does not easily ignite under normal conditions.
(g) Lower and upper explosion limit:	Not applicable (solid material, no flammable vapor; dust explosion limits not determined, treat as any organic dust).
(h) Flash point:	Not applicable (non-volatile solid).
(i) Auto-ignition temperature:	No data available, but not expected to self-ignite. Likely >400 °C if any (organic powder, but no specific data).
(j) Decomposition temperature:	~210–230 °C (approximate, at which thermal decomposition with darkening and fume generation occurs).
(k) pH:	Not determined. The substance is very slightly soluble in water.

(l) Kinematic viscosity:	Not applicable (solid).
(m) Solubility:	Limited solubility in water (0.1–1 mg/mL), freely soluble in acetone (100–1000 mg/mL), soluble in methanol (33.3-100 mg/mL), slightly soluble in cyclohexane (1–10 mg/mL), and very freely soluble in N-methyl-2-pyrrolidone (NMP) (>1000 mg/mL).
(n) Partition coefficient: n-octanol/water:	~3.2–3.8.
(o) Vapour pressure:	Essentially zero at room temperature (solid with negligible vapor pressure). No measurable vapor pressure data available.
(p) Density:	Bulk solid approx. 1.15–1.25 g/cm³ (true density); bulk/tapped density depends on particle size and grade.
(q) Relative vapour density:	Not applicable (non-volatile solid). (If sublimation occurred, vapor density would be >1 as molecular weight is high, but practically no vapor).
(r) Particle characteristics:	Particle size: not specified; supplied as fine crystalline powder.
(s) Chemical family:	Semi-synthetic morphinan / thebaine- or oripavine-derived opioid.
	Belongs to the morphinan phenanthrene family of analgesic alkaloids containing a fused tricyclic morphinan framework with an epoxide bridge.
(t) Molecular structure:	Chiral compound with multiple stereocentres (notably 4R, 4aS, 6R, 7R, 7aR, 12bS).
	Structural description: rigid pentacyclic system incorporating a cyclopropylmethyl-substituted tertiary amine and two ether linkages.
	Functional groups: tertiary amine, secondary alcohol, aryl-O-methoxy substituents, and an ether bridge.
	The structure lacks oxidising or explosive functional groups and exhibits typical amphiphilic character (lipophilic core with one basic nitrogen).
(u) Stable isotopic composition:	Contains C, H, N and O in natural isotopic abundance (no radioactive isotopes).
(v) Surface tension:	Not applicable (solid).
(w) Evaporation rate:	Not applicable (non-volatile solid).

9.2 Other information

Information with regard to physical hazard classes

(x) Explosive properties:	Not explosive. The substance does not have chemical groups associated with explosive properties. Note: Finely dispersed dust in air could pose a dust explosion risk in the presence of an ignition source, as is common with organic powders, but this is a physical hazard of dust, not a chemical explosivity rating.
(y) Oxidising properties:	Not oxidizing (does not cause or enhance combustion of other materials).
(z) Corrosive to metals:	The mixture is not classified as corrosive to metals.

Other safety characteristics

No other relevant safety characteristics.

SECTION 10: Stability and reactivity

10.1 Reactivity

The substance is not considered reactive under normal conditions of use, handling, and storage. Buprenorphine is a stable organic compound that does not polymerise, auto-oxidise rapidly, or undergo hazardous reactions in contact with air or water. No self-accelerating decomposition or uncontrolled exothermic reaction is expected.

The tertiary amine function is weakly basic and may form salts with strong acids.
No known reaction hazard with common construction materials (stainless steel, glass, HDPE) under ambient conditions.

10.2 Chemical stability

Stable under recommended storage and handling conditions (see Section 7). When stored in tightly closed containers in a cool, dry, and well-ventilated place, the compound remains stable for extended periods. It may gradually darken or degrade on prolonged exposure to light, heat, or humidity due to slow oxidation or hydrolysis of ether linkages.

Solutions of the compound in polar organic solvents (e.g., methanol, DMSO) are stable for typical laboratory timescales but may degrade on extended storage, particularly in the presence of light and air.

10.3 Possibility of hazardous reactions

Hazardous polymerisation does not occur. The substance may react with strong oxidising agents (e.g., peroxides, nitric acid, permanganates, chromates) causing exothermic oxidation or combustion. Contact with strong acids will protonate the tertiary amine and may form salts (no violent reaction). Contact with strong bases or reducing agents can lead to decomposition or dealkylation with release of irritating fumes.

Dust suspended in air may form a combustible dust/air mixture, which under ignition conditions could produce a mild explosion; however, this is a physical, not chemical, hazard.

No other hazardous reactions are known under normal laboratory or storage conditions.

10.4 Conditions to avoid

Avoid exposure to high temperatures, open flame, or other ignition sources. Heating above ~150 °C should be avoided except in controlled conditions, as decomposition can begin and hazardous fumes may be emitted at elevated temperatures. Avoid moisture/humidity – the compound absorbs water from air and can degrade or become less stable when wet. Avoid direct sunlight or UV light – prolonged light exposure may cause chemical degradation or discoloration. Also avoid generating dust (as a dust explosion precaution and to avoid inhalation exposure). Any condition causing the formation of aerosols or dust clouds should be controlled.

10.5 Incompatible materials

Avoid contact with strong oxidising agents (e.g. peroxides, permanganates, nitric acid, perchlorates), which may cause exothermic oxidation and possible fire hazard. Avoid strong acids, which can form salts of the tertiary amine with heat release. Avoid strong bases or alkalis (e.g. sodium or potassium hydroxide, ammonia), which may promote decomposition of the ether and alcohol functions and lead to discoloration or degradation. Avoid reducing agents and reactive metals (e.g. sodium, potassium, lithium aluminium hydride), which can cause reductive cleavage of functional groups.

The substance is stable under normal conditions of handling and storage when kept dry and away from reactive materials.

10.6 Hazardous decomposition products

When heated to decomposition or combusted, it may produce toxic fumes including nitrogen oxides and carbon monoxide/carbon dioxide. Thermal decomposition may also yield other irritating or harmful low-molecular organic vapours, amine fumes, and phenolic/etheric residues.

Under strong oxidation, additional toxic smoke and irritant gases may form.
No hazardous decomposition occurs under normal storage and handling conditions.

SECTION 11: Toxicological information

11.1 Information on hazard classes as defined in Regulation (EC) No 1272/2008

Unless otherwise specified, data refer to buprenorphine (free base) and related data for buprenorphine compounds. Experimental data are limited; classification is primarily based on data for buprenorphine and known metabolites.

Acute toxicity
Oral LD_{50} values in rats range between 200 – 600 mg/kg, and in mice 150 – 300 mg/kg. By comparison, in humans, pharmacologically active doses are in the microgram range, and ingestion of only a few milligrams in a non-tolerant individual may produce marked opioid effects such as sedation, miosis, respiratory depression, and nausea. Larger single doses (tens of milligrams) could cause severe respiratory depression or fatal overdose.

No quantitative data are available for inhalation or dermal routes, but given its potency and capacity for systemic absorption through mucous membranes, airborne dust or aerosol exposure may produce pharmacological effects if inhaled.

Classification: Buprenorphine is harmful if swallowed or inhaled (Acute Tox. 4, H302 + H332). No data support classification for dermal toxicity.

Skin corrosion/irritation
Based on available data, the classification criteria are not met.

Serious eye damage/irritation
The substance meets the criteria for Eye Irrit. 2 (H319): causes serious eye irritation.

Respiratory or skin sensitisation
Based on available data, the classification criteria are not met.

Germ cell mutagenicity
Based on available data, the classification criteria are not met.

Carcinogenicity
Based on available data, the classification criteria are not met.

Reproductive toxicity
Classified as Repr. 2 (H361d) – Suspected of damaging the unborn child.

STOT-single exposure
Based on available data, the classification criteria are not met.

STOT-repeated exposure
Based on available data, the classification criteria are not met.

Aspiration hazard
Based on available data, the classification criteria are not met.

11.2 Information on other hazards

Endocrine disrupting properties
None known.

Other information
No evidence of neurotoxicity beyond opioid receptor-mediated CNS depression.
In overdose situations, symptoms can be reversed with naloxone, though repeated administration may be necessary because of longer receptor occupancy.

No data on human occupational exposure; risk assessment should treat this as a potent hazardous drug with controlled handling requirements similar to other active opioids.

SECTION 12: Ecological information

12.1 Toxicity

Results	
Short-term toxicity to fish -	**Long-term toxicity to fish** -
Short-term toxicity to aquatic invertebrates -	**Long-term toxicity to aquatic invertebrates** -
Toxicity to aquatic algae and cyanobacteria -	**Toxicity to microorganisms** -

No classification for the aquatic environment is assigned based on available data. Avoid release to the environment – the substance is pharmacologically active and may affect aquatic organisms even at low concentrations.

12.2 Information on other hazards

BOD5	COD	Biodegradable
No data available	No data available	No data available

No experimental data are available. Based on structural analogy (multi-ring morphinan skeleton with ether and tertiary amine groups), the substance is expected to undergo slow, partial biodegradation in the environment. It cannot be formally classified as readily biodegradable without test results. Hydrolysis and photolysis are not significant under environmental conditions.

12.3 Bioaccumulative potential

BCF	LogPow	Bioaccumulative potential
No experimental data available	≈ 3.2 – 3.8 (estimated)	Low to moderate

Based on moderate lipophilicity, some bioaccumulation may occur in aquatic organisms, but ionisation in natural waters and the large molecular size limit uptake. The substance does not meet the B or vB criteria under REACH.

12.4 Mobility in soil

Koc	Surface tension	Henry's constant
500 – 1500 (estimated)	No data available	< 1×10^{-6} Pa·m³/mol (estimated)

The substance is expected to be moderately adsorbed to soil and sediment due to its hydrophobic core, reducing mobility. Volatilisation from water or soil is negligible. If released, the compound would remain primarily in the aqueous and sediment phases.

12.5 Results of PBT and vPvB assessment

This substance is not considered to be persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

12.6 Endocrine disrupting properties

The substance is not known for endocrine-disrupting properties according to REACH Article 57(f) or Commission Delegated Regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 in a concentration of 0.1% or higher.

12.7 Other adverse effects

If released, the substance could potentially affect aquatic organisms through opioid-receptor-mediated mechanisms, even at sub-lethal concentrations. Laboratory studies with related opioids have shown altered locomotor activity, feeding behaviour, and respiratory patterns in fish and invertebrates, consistent with central nervous system depression typical of narcotic substances.

As a pharmaceutical compound of emerging environmental concern, buprenorphine and its analogues have been detected in surface waters and effluents from wastewater-treatment plants at low ng/L to µg/L levels in monitoring studies. Although environmental concentrations are generally low, chronic exposure could contribute to behavioural or reproductive disturbances in aquatic organisms over time.

Consequently, environmental release should be avoided, and all residues and solutions containing the substance should be treated as hazardous chemical waste.

12.8 Additional information

Environmental classification is based on read-across to structurally related opioids. Actual environmental impact will depend on local dilution and degradation conditions.

The substance should be regarded as potentially hazardous to aquatic life and managed under good laboratory and waste-management practices to avoid emissions to surface water.

Ozone layer: not ozone-depleting.

Water hazard class (Germany): WGK 3 (severely hazardous to water) – this is a worst-case classification often applied to pharmaceuticals. All releases should be avoided.

SECTION 13: Disposal considerations

13.1 Waste treatment methods

Disposal of the product/packaging
Dispose of this material as hazardous chemical waste. Do not discharge to sewer or natural environment. All unused substance, spill clean-up materials, and contaminated containers should be disposed of in accordance with local, regional, and national regulations (e.g., EU Directive 2008/98/EC on waste, and pertinent national legislation). Incineration at a licensed hazardous waste incinerator is the preferred method of disposal, as high-temperature incineration will destroy the active ingredient. If incineration is not possible, consult an approved chemical waste disposal contractor for alternatives.

You may mix the waste with a combustible solvent (if solid) to facilitate incineration. Do not mix this substance with incompatible waste (see Section 10) or general trash. Do not dispose of in household garbage.

Waste codes
Classification according to the European waste catalog (2018/C124/01) depends on the specifics of the disposal situation (contact your waste disposal contractor). A suggested code is shown below.

EWC code	Description	Hazard properties
Wastes from the manufacture, formulation, supply and use (MFSU) of pharmaceuticals		
07 05 13	Solid wastes containing hazardous substances	HP 10 (Toxic for reproduction)

Information on disposal of the packaging
Dispose of in accordance with Annex I and Annex II (Directive 2008/98/EC). The uncleaned packaging must be disposed of in the same way as the product.
EWC: 15 01 10.

Special precautions for waste treatment
This substance is a controlled drug (Schedule II / equivalent) in many jurisdictions; waste destruction may need to be documented to meet regulatory requirements. Follow any protocols for destruction of controlled substances (e.g., witnessing by authorized individuals). Ensure that waste is securely stored until disposal to prevent diversion or accidental exposure.

Applicable law
In accordance with Annex II to Regulation (EC) No 1907/2006 of the European Parliament and of the Council (REACH), European and national regulations concerning the handling of waste products are set out below:

EU legislation: Directives 2008/98/EC and 2014/955/EU.
Commission Regulation (EU) No 1357/2014.

SECTION 14: Transport information

14.1 UN or ID number Not dangerous goods

14.2 UN proper shipping name -

14.3 Transport hazard class(es) -

14.4	**Packing group**	-
14.5	**Environmental hazards**	None.
14.6	**Special precautions for user**	Preferably keep away from foodstuffs (including animal feeds). Mark packages with CLP labels as per CLP Article 33. Persons handling the substance should be aware of the associated health hazards and avoid handling damaged packages without PPE. In case of accident or spill, emergency responders should use appropriate protective equipment and avoid exposure (see Sections 6 and 8).
14.7	**Maritime transport in bulk according to IMO instruments**	Not applicable – this substance is not transported in bulk cargo form. Typically shipped in packaged form (drums, bottles, etc.). Annex II of MARPOL 73/78 and the IBC Code do not apply (solid, not a bulk liquid).

SECTION 15: Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII)	:	Not listed in REACH Annex XVII with specific restrictions for sale/use (aside from its classification as a controlled drug under narcotics legislation).
REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59)	:	Not applicable (not on the Candidate List).
REACH - List of substances subject to authorisation (Annex XIV)	:	Not listed in Annex XIV.
Regulation (EC) 1005/2009 on substances that deplete the ozone layer	:	Not listed.
Regulation (EU) 2019/1021 of the European Parliament and of the Council of 20 June 2019 on persistent organic pollutants	:	Not listed.
Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens, mutagens or reproductive toxicants at work	:	Not listed.
Directive 98/24/EC (Chemical Agents Directive)	:	General worker protection requirements apply.
Regulation (EU) No 528/2012 on biocidal products	:	Not applicable; substance is not used as or in a biocidal product.
Regulation (EU) 649/2012 concerning the export and import of hazardous chemical products	:	Not listed in Annex I (PIC list).
Regulation (EU) 2019/1148 on the marketing and use of explosives precursors	:	Not listed as a restricted or reportable precursor.
Directive 2012/18/EU on the control of major-accident hazards involving dangerous substances (Seveso)	:	Not subject to Seveso III.
Drug Precursors Regulation (273/2004)	:	Buprenorphine is a controlled opioid (psychotropic substance) under the narcotics legislation.
UN Convention on Psychotropic Substances (1971)	:	Buprenorphine is listed in Schedule III.
Directive 2001/83/EC (Community code for medicinal products)	:	Marketing and use limited to authorised medicinal purposes.
Other applicable legislation	:	National narcotics control legislation applies in all EU Member States. Handling is limited to licensed facilities

and authorised personnel; unauthorised handling is prohibited and subject to criminal penalties.

Specific provisions regarding the protection of persons or the environment

The product is covered by the criteria in Council Directive 94/33/EC of 22 June 1994 on the protection of young people at work. Accordingly, young people under the age of 18 should not use or be exposed to the product professionally.

In relation to pregnancy and breastfeeding, the substance is classified as a suspected reproductive toxicant (Repr. 2; H361d). Because of its potent opioid activity on the central nervous and respiratory systems, any exposure during pregnancy or lactation should be avoided or strictly minimised as a precautionary measure. Appropriate risk management, closed handling systems, and personal protective equipment are required for all professional use.

15.2 Chemical safety assessment

No chemical safety assessment has been prepared for this product.

SECTION 16: Other information

Applicable law
This safety data sheet has been prepared in accordance with the European Parliament and Council Regulation (EC) No. 1907/2006 (REACH) and Commission Regulation (EU) 2020/878, and following the official ECHA guidelines. This SDS shall be supplied in an official language of the country where the product is placed on the market.

The safety data sheet has been prepared by

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Classification according to Regulation (EC) 1272/2008 [CLP]

Classification	Classification procedure
Repr. 2; H361d	Weight-of-evidence and expert judgement.
Acute Tox. 4 (Inhalation); H332	Calculation method.
Acute Tox. 4 (Oral); H302	Calculation method.
STOT RE 2; H373	Weight-of-evidence and expert judgement.
Eye Irrit. 2; H319	Weight-of-evidence and expert judgement

Key literature references and sources for data
http://echa.europa.eu
http://eur-lex.europa.eu

Revision
This safety data sheet replaces version 3.0 of 12-12-2022. This safety data sheet has been updated with a new classification. Acute Tox. 3 (H301), Skin Irrit. 2 (H315) and STOT SE 3 (H335) have been replaced by Repr. 2 (H361d), Acute Tox. 4 (Inhalation and Oral) (H332 + H302), STOT RE 2 (H373) and Eye Irrit. 2 (H319), based on updated classification data from a REACH joint submission as well as a renewed evaluation of available toxicological data.

Advice in relation to training
Personnel handling this product must receive appropriate training in chemical safety in accordance with national legislation (e.g. AT-vejledning C.0.11 in Denmark and TRGS 555 in Germany). Also, a good working knowledge of this Safety Data Sheet is essential. Training should cover the hazards of the substance, label elements, personal protective equipment, and first aid/emergency procedures.

Hazard statements
H302: Harmful if swallowed.

H332: Harmful if inhaled.
H319: Causes serious eye irritation.
H361d: Suspected of damaging the unborn child.
H373: May cause damage to the central nervous system through prolonged or repeated exposure.

Abbreviations and acronyms

API: Active Pharmaceutical Ingredient
ADR: Agreement concerning the International Carriage of Dangerous Goods by Road
CAS: Chemical Abstracts Service
CLP: Classification, Labelling and Packaging Regulation (EC 1272/2008)
CNS: Central Nervous System
CSA: Chemical Safety Assessment
EC: European Community (Number)
EC_{50}: Effective concentration for 50% of organisms (ecotoxicity)
ECHA: European Chemicals Agency
ERG: Emergency Response Guide
GHS: Globally Harmonized System of Classification and Labelling
IATA: International Air Transport Association
IBC: Intermediate Bulk Container / International Bulk Chemical (Code)
IMDG: International Maritime Dangerous Goods (Code)
LC_{50}: Lethal concentration for 50% of organisms
LD_{50}: Lethal dose for 50% of organisms
OEL: Occupational Exposure Limit
PBT: Persistent, Bioaccumulative, Toxic
PPE: Personal Protective Equipment
REACH: Registration, Evaluation, Authorization and Restriction of Chemicals (EC 1907/2006)
RID: Regulations concerning the International Carriage of Dangerous Goods by Rail
SCBA: Self-Contained Breathing Apparatus
STOT: Specific Target Organ Toxicity (SE: single exposure; RE: repeated exposure)
SVHC: Substance of Very High Concern
vPvB: very Persistent and very Bioaccumulative
WGK: Wassergefährdungsklasse (German Water Hazard Class)