SAFETY DATA SHEET

Butorphic® (butorphanol tartrate injection) CIV

1. IDENTIFICATION

Product Identifier: Butorphic® (butorphanol tartrate injection) CIV

Synonyms: Morphinan-3, 14-diol, 17-(cyclobutylmethyl)-,(-)-, [S-(R*,R*)] - 2,3 -dihydroxybutanedioate (1:1) (salt).

National Drug Code (NDC): 59399-112-20
59399-112-50

Recommended Use: For Animal Use Only. Butorphic® is indicated for the relief of pain associated with colic in adult horses and yearlings.

Company: Akorn, Inc.
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Lake Forest, Illinois 60045

Contact Telephone: 1-800-932-5676

E mail: customer.service@akorn.com

Emergency Phone Number: CHEMTREC 1-800-424-9300 (U.S. and Canada)

2. HAZARD(S) IDENTIFICATION

Physical Hazards: Not classifiable.

Health Hazards: Reproductive Toxicity – Effects on or via lactation — Category 1B

Symbol(s):

Signal Word: Danger.

Hazard Statement(s):

H360 May damage fertility or the unborn child.

Precautionary Statement(s):

P201 Obtain special instructions before use.

P202 Do not handle until all safety precautions have been read and understood.

P260 Do not breathe dust/fume/gas/mist/vapors/spray.

P263 Avoid contact during pregnancy/while nursing.

P264 Wash hands thoroughly after handling.

P270 Do not eat, drink or smoke when using his product.

P280	Wear protective gloves/protective clothing/eye protection/face protection.
P308 + P313	IF exposed or concerned: Get medical advice/ attention.
P405	Store locked up.
P501	Dispose of contents/container in accordance with local/regional/national/international regulations.

Hazards Not Otherwise Classified: Not classifiable.

Supplementary Information: Opioid analgesic. Ingestion of this material may cause effects similar to those seen in clinical use including dry mouth, drowsiness, headache, dizziness, nausea, vomiting, weakness, anxiety, and dilated pupils. Cases of severe overdose may lead to respiratory depression, hypotension, coma, convulsions, cardiac arrhythmia, and tachycardia.

3. COMPOSITION / INFORMATION ON INGREDIENTS

Ingredient	Chemical Name	CAS Number	Chemical Formula	Molecular Weight	Percentage
Butorphanol Tartrate	morphinan-3, 14-diol, 17-(cyclobutylmethyl)-,(-)-, [S-(R*,R*)] - 2,3 - dihydroxybutanedioate (1:1) (salt)	58786-99-5	$C_{21}H_{29}NO_2 \bullet C_4H_6O_6$	477.55	1%

The formula also contains Citric Acid, 3.3 mg; Sodium Citrate 6.4 mg; Sodium Chloride, 4.7 mg; Benzethonium Chloride, 0.1 mg; and Water for injection.

4. FIRST AID MEASURES

Ingestion: If a person vomits place them in the recovery position so that vomit will not reenter the mouth and throat. Rinse mouth with water. If swallowed, seek medical advice immediately and show the container or label. Treat symptomatically and supportively. Ensure that medical personnel are aware of the material(s) involved and take precautions to protect themselves.

Eye Contact: Remove from source of exposure. Flush with copious amounts of water for at least 15 minutes. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.

Skin Contact:	Remove from source of exposure. Remove and isolate contaminated clothing and shoes. Flush with copious amounts of water for at least 20 minutes. Use soap. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.
Inhalation:	Remove from source of exposure. Move individual(s) to fresh air. Give artificial respiration if individual(s) are not breathing and call emergency medical service. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.
Protection of First-Aiders:	Use personal protective equipment (see section 8).
Signs and Symptoms:	Ingestion of this material may cause effects similar to those seen in clinical use including dry mouth, drowsiness, headache, dizziness, nausea, vomiting, weakness, anxiety, and dilated pupils. Cases of severe overdose may lead to respiratory depression, hypotension, coma, convulsions, cardiac arrhythmia, and tachycardia.
Medical Conditions Aggravated by Exposure:	Note determined.
Notes to Physician:	Treat supportively and symptomatically.

5. FIREFIGHTING MEASURES

Suitable Extinguishing Media:	Use water, carbon dioxide, dry chemical or water spray.
Unsuitable Extinguishing Media:	Do not use water jet as an extinguisher, as this will spread the fire.

Specific Hazards Arising from the Chemical

Hazardous Combustion Products:	No data available.
Other Specific Hazards:	Closed containers may explode from the heat of fire.
Special Protective Equipment and Precautions for Firefighters:	Wear self-contained breathing apparatus and full and protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions: Use personal protective equipment recommended in Section 8 of this document and isolate the hazard area.

Personal Protective Equipment: For personal protection see section 8.

Methods for Cleaning Up: Absorb with inert material. Recover product and place in an appropriate container for disposal in accordance with local, state and federal regulations. Wipe working area surfaces to dryness, and then wash with soap and water.

Environmental Precautions: Contain material and prevent release to basements, confined spaces, waterways or soil.

Reference to Other Sections: Refer to Sections 8, 12 and 13 for further information.

7. HANDLING AND STORAGE

Precautions for Safe Handling: In the US, Butorphanol is Schedule IV controlled substance. Appropriate training and procedures may be required during the routine handling of this product. Handle in accordance with product label and/or product insert information. Handle in accordance with good industrial hygiene and safety practices.

Conditions for Safe Storage, Including Any Incompatibilities: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Protect from light. Store away from oxidizing agents and acids.

Specific End Use: Pharmaceutical drug product.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Occupational Exposure Guidelines:

Ingredient	Type	Value
Butorphanol Tartrate	TWA	2 mcg/m^3

TWA: Time Weighted Average.

Engineering Controls: Engineering controls should be used as the primary means to control exposures.

Respiratory Protection: Where respirators are deemed necessary to reduce or control occupational exposures, use NIOSH-approved respiratory protection and have an effective respirator program in place (applicable U.S. regulation OSHA 29 CFR 1910.134).

Eyes Protection:	Avoid contact with eyes. Face shields or goggles may be required if splash potential exists or if corrosive materials are present. Approved eye protection (e.g., bearing the ANSI Z87 or CSA stamp) is preferred. Maintain eyewash facilities in the work area.
Hand Protection:	Wear chemically compatible gloves for handling solutions and ensure that the glove material is protective against the solvent being used. Use handling practices that minimize direct hand contact. Employees who are sensitive to natural rubber (latex) should use nitrile or other synthetic non-latex gloves. Use of powdered latex gloves should be avoided due to the risk of latex allergy.
Skin Protection:	Wear protective laboratory coat, apron, or disposable garment when working with large quantities.
General Hygiene Considerations:	Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment to remove contaminants.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State/Color:	Clear, colorless solution.
Odor:	No data available.
Odor Threshold:	No data available.
pH:	No data available.
Melting Point:	No data available.
Freezing Point:	No data available.
Boiling Point:	No data available.
Flash Point:	No data available.
Evaporation Rate:	No data available.
Flammability (solid, gas):	No data available.
Flammability Limit - Lower:	No data available.
Flammability Limit - Upper:	No data available.
Vapor Pressure:	No data available.
Vapor Density:	No data available.
Relative Density:	No data available.
Solubility(ies):	Soluble in water.
Partition Coefficient (n-octanol/water):	No data available.
Auto-Ignition Temperature:	No data available.
Decomposition Temperature:	No data available.
Viscosity:	No data available.

10. STABILITY AND REACTIVITY

Reactivity:	The product is stable and non-reactive under normal conditions of use, storage and transport.
Chemical Stability:	Stable under recommended storage conditions.

Possibility of Hazardous Reactions: No dangerous reaction known under conditions of normal use.

Conditions to Avoid (e.g., static discharge, shock, or vibration): Contact with incompatible materials.

Incompatible Materials: Strong oxidizing agents.

Hazardous Decomposition Products: No hazardous decomposition products are known. May include products of carbon, nitrogen and hydrogen chloride.

11. TOXICOLOGICAL INFORMATION

Information on the Likely Routes of Exposure

Inhalation: Under normal conditions of intended use, this material is not expected to be an inhalation hazard.

Ingestion: May be harmful if swallowed.

Skin Contact: May cause mild skin irritation.

Eye Contact: May cause eye irritation.

Symptoms Related to the Physical, Chemical and Toxicological Characteristics: See Section 4. To the best of our knowledge, the chemical, physical and toxicological properties have not been thoroughly investigated.

Delayed and Immediate Effects of Exposure: No data available.

Acute Toxicity

Not fully established. This product is a mixture that has not been fully tested as a whole. Information provided herein is derived from the approved product insert and/or supplier SDS for active ingredients.

Ingredient	Species	Route	Test Type	Dosage
Butorphanol Tartrate	Rat	Oral	LD_{50}	350 mg/kg
	Mouse	Oral	LD_{50}	395 mg/kg
	Monkey	Oral	LD_{50}	50 mg/kg

Irritation / Sensitization

Ingredient	Study Type	Species	Severity
No data available	No data available	No data available	No data available

Repeated Dose Toxicity

Ingredient	Duration	Species	Route	Dosage	Test Type	Target Organ
No data available	No data available	No data available	No data available	No data available	No data available	No data available

Reproduction and Developmental Toxicity

Ingredient	Study Type	Species	Route	Dosage	Test Type	Effect(s)
Butorphanol Tartrate	Reproductivity Study	Rabbit	Not specified	10 mg/kg	Not specified	Not teratogenic
	Reproductivity Study	Rat	Not specified	25 mg/kg/day	Not specified	Not teratogenic; no adverse reproductive effects
	Reproductivity Study	Rat	Not specified	5 mg/day	Not specified	Fetotoxic but not teratogenic

Genetic Toxicity

Ingredient	Study Type	Cell Type / Organism	Result
Butorphanol Tartrate	Genotoxicity study	E. coli	Negative
	Genotoxicity assays	Salmonella typhimurium	Negative
	Unscheduled DNA synthesis and repair assays	Human fibroblast cells	Negative

Aspiration Hazard: No data available.

Toxicokinetics/Metabolism: No data available.

Target Organ Effects: Based on clinical use, possible target organs include the central nervous system, cardiovascular system, respiratory system, and the gastrointestinal system.

Systemic Effects: No data available.

Reproductive Effects: Studies performed in mice and rabbits revealed no evidence of impaired fertility or harm to the fetus due to butorphanol tartrate. In the female rat, parenteral administration was associated with increased nervousness and decreased care for the newborn, resulting in a decreased survival rate of the newborn. The nervousness was see only in the rat species.

Carcinogenicity: Two-year carcinogenicity studies were conducted in mice (up to 2 mg/kg/day via oral gavage) and rats given butorphanol tartrate in the diet up to 60 mg/kg/day. There was no evidence of treatment-related carcinogenicity in either species in these studies.

Mutagenicity: Butorphanol was not genotoxic in S. typhimurium or E. coli assays or in unscheduled DNA synthesis and repair assays conducted in cultured human fibroblast cells.

National Toxicology Program (NTP): Not considered to be a carcinogen.

International Agency for Research on Cancer (IARC): Not considered to be a carcinogen.

Occupational Safety and Health Administration (OSHA): Not considered to be a carcinogen.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity

Ingredient	Species	Test Type	Dosage	Duration
No data available	No data available	No data available	No data available	No data available

Terrestrial Toxicity: No data available.
Persistence and Degradability: No data available.
Bioaccumulative Potential: No data available.
Mobility in Soil: No data available.
Mobility in Environment: No data available.
Other Adverse Effects: No data available.

13. DISPOSAL CONSIDERATIONS

Do not empty into drains; dispose of this material and its container in a safe way. Dispose of all waste in accordance with Federal, State and Local regulations.

14. TRANSPORT INFORMATION

Department of Transportation (DOT): Not regulated as a hazardous material.

UN Proper Shipping Name	UN Number	Transport Hazard Class	Packing Group
Not applicable	Not applicable	Not applicable	Not applicable

International Air Transport Association (IATA): Not regulated as a dangerous good.

UN Proper Shipping Name	UN Number	Transport Hazard Class	Packing Group
Not applicable	Not applicable	Not applicable	Not applicable

International Maritime Dangerous Good (IMDG): Not regulated as a dangerous good.

UN Proper Shipping Name	UN Number	Transport Hazard Class	Packing Group
Not applicable	Not applicable	Not applicable	Not applicable

15. REGULATORY INFORMATION

US FEDERAL REGULATIONS

Toxic Substance Control Act (TSCA):

Ingredient	Inventory
Butorphanol Tartrate	No

CERCLA Hazardous Substance:

Ingredient	Reportable Quantity
Not applicable	Not applicable

EPCRA Extremely Hazardous Substances and Toxic Chemicals:

Ingredient	Section 302	Section 313
Not applicable	Not applicable	Not applicable

U.S. STATE RIGHT-TO-KNOW REGULATIONS

Ingredient	New Jersey	Pennsylvania	Massachusetts
Butorphanol Tartrate	Not listed	Not listed	Not listed

California Proposition 65: This product does not contain any chemicals known to State of California to cause cancer, birth defects, or any other reproductive harm.

16. OTHER INFORMATION

The vial stopper contains dry natural rubber.

See footer of this document for Revision Date and Revision Number.

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