SAFETY DATA SHEET

Issue Date: 08/14/2023 **Revision Date: N/A** **Revision Number: 01**

1. IDENTIFICATION

Product identifier: Buprenorphine and Naloxone Tablets CIII 2mg, 8 mg
NDC Numbers: 00121-1018-30, 00121-2036-30

Supplier Name and Address:	Pharmaceutical Associates, Inc. 201 Delaware Street Greenville, SC 29605
Telephone number:	(864) 277-7282
Emergency phone number:	CHEMTREC 800-424-9300

Recommended use: Human drug – treatment of opioid dependence
Restrictions on use: Prescription use only.

2. HAZARD(S) IDENTIFICATION

Classification:

Physical	Health
Not hazardous	Respiratory Sensitization Category 1 Reproductive Toxicity Category 2 Effects on or via lactation

Label Elements:
Danger!

Hazard statement(s)
May cause allergy or asthma symptoms or breathing difficulties if inhaled.
Suspected of damaging the unborn child.
May cause harm to breast-fed children.

Precautionary statement(s)
Obtain special instructions before use.
Do not handle until all safety precautions have been read and understood.
Do not breathe dusts.
Avoid contact during pregnancy and while nursing.

Precautionary statement(s)
Wash hands thoroughly after handling.
Do not eat, drink or smoke when using this product.
Wear protective clothing and gloves.
In case of inadequate ventilation, wear respiratory protection.
IF INHALED: remove person to fresh air and keep comfortable for breathing. If experiencing respiratory symptoms: Call a POISON CENTER or doctor.
IF exposed or concerned: Get medical attention.
Store locked up.
Dispose in accordance with local and national regulations.

3. COMPOSITION / INFORMATION ON INGREDIENTS

Chemical name	CAS No.	Amount
Buprenorphine Hydrochloride	53152-21-9	1-10%
Citric Acid	77-92-9	1-<10%

Naloxone Hydrochloride	51481-60-8	0.1-1%
d-Limonene	5989-27-5	0.1-<1%

The exact percentage (concentration) of composition has been withheld as a trade secret.

4. FIRST-AID MEASURES

Inhalation: Remove person to fresh air. If irritation occurs or if experiencing respiratory symptoms, get immediate medical attention.
Skin contact: Remove contaminated clothing. Wash skin with soap and water. If irritation develops, get medical attention. Launder clothing before reuse.
Eye contact: Immediately flush eyes with water while lifting the upper and lower lids. Get medical attention if irritation persists**.**
Ingestion: In the case of unintentional ingestion or overdosage, rinse mouth with water. Do not induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to a person who is unconscious or convulsing. Get medical attention.

Most important symptoms/effects, acute and delayed: May cause mild eye and skin irritation. Swallowing may cause headache, nausea and vomiting, excessive sweating, constipation, signs and symptoms of withdrawal, insomnia, pain and swelling. Inhalation of dust may cause an allergic respiratory reaction with asthma symptoms (wheezing and shortness of breath), respiratory irritation and effects similar to ingestion.

Indication of immediate medical attention and special treatment, if necessary: Medical attention is recommended for unintended ingestion or overdosage. Immediate medical attention is recommended for symptoms of respiratory sensitization.

5. FIRE-FIGHTING MEASURES

Extinguishing media: Use any media that is suitable for the surrounding fire.

Specific hazards arising from the chemical: Product is not classified as flammable or combustible but will burn in a fire.

Special protective equipment and precautions for fire-fighters: Firefighters should wear positive pressure self-contained breathing apparatus and full protective clothing for all fires involving chemicals.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment, and emergency procedures: Wear appropriate protective clothing and equipment as described in Section 8. If tablets are damaged and dust is present, eliminate all ignition sources.

Environmental Precautions: Prevent spill from entering sewers and water courses. Report releases as required by local and national authorities.

Methods and materials for containment and cleaning up: Carefully collect tablets, minimizing the generation of airborne dust. Place in appropriate container for disposal. Clean area thoroughly.

7. HANDLING AND STORAGE

Precautions for safe handling: Avoid the generation of dusts. Avoid contact with eyes, skin and clothing. Wash thoroughly with soap and water after handling.

Conditions for safe storage, including any incompatibilities: Store as indicated on product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Exposure guidelines:

Buprenorphine Hydrochloride	None Established
Citric Acid	None Established
Naloxone Hydrochloride	None Established
d-Limonene	None Established

Appropriate engineering controls: Use with adequate general or local exhaust ventilation to minimize exposure levels.

Individual protection measures:
Respiratory protection: None needed under normal use conditions. If exposures are excessive, a NIOSH approved particulate respirator is recommended. Selection of respiratory protection depends on the contaminant type, form and concentration. Select in accordance with OSHA 1910.134 and good Industrial Hygiene practice.
Skin protection: None required for normal use. Impervious gloves recommended for manufacturing operations.
Eye protection: None required for normal use. Chemical safety goggles recommended for manufacturing operations.
Other: None known.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance (physical state, color, etc.): Solid, Tablet
Odor: None

Odor threshold: Not applicable	**pH:** Not applicable
Melting point/freezing point: Not determined	**Boiling Point:** Not applicable
Flash point: Not applicable	**Evaporation rate:** Not applicable
Flammability (solid, gas): Not flammable	**VOC:** Not applicable
Flammable limits: LEL: Not determined	**UEL:** Not determined
Vapor pressure: Not applicable	**Vapor density:** Not applicable
Relative density: No data available	**Solubility(ies):** Soluble
Partition coefficient: n-octanol/water: Not available	**Auto-ignition temperature:** Not available
Decomposition temperature: Not available	**Viscosity:** Not applicable

10. STABILITY AND REACTIVITY

Reactivity: Not reactive under normal conditions of use.
Chemical stability: Stable.
Possibility of hazardous reactions: None known.

Conditions to avoid: None known.
Incompatible materials: Avoid oxidizing agents.
Hazardous decomposition products: Thermal decomposition may yield carbon oxides and chlorine compounds.

11. TOXICOLOGICAL INFORMATION

Acute effects of exposure:
Inhalation: Inhalation of dust may cause an allergic respiratory reaction with asthma symptoms (wheezing and shortness of breath), respiratory irritation and effects similar to ingestion.
Ingestion: Swallowing may cause headache, nausea and vomiting, excessive sweating, constipation, signs and symptoms of withdrawal, insomnia, pain and swelling.
Skin contact: May cause mild irritation.
Eye contact: May cause mild irritation with redness and tearing.
Chronic Effects: None known.
Sensitization: May cause respiratory sensitization.
Germ Cell Mutagenicity: Components are not classified as germ cell mutagens. 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 (*S. 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. Naloxone was weakly positive in the Ames mutagenicity and in the in vitro human lymphocyte chromosome aberration test but was negative in the in vitro Chinese hamster V79 cell HGPRT mutagenicity assay and in the in vivo rat bone marrow chromosome aberration study.
Reproductive Toxicity: Components are not classified as reproductive toxins. Reproduction studies of buprenorphine in rats demonstrated no evidence of impaired fertility at daily oral doses up to 80 mg/kg/day No definitive drug-related teratogenic effects were observed in rats and rabbits at IM doses up to 30 mg/kg/day. Following oral administration of buprenorphine to rats, dose-related post-implantation losses, evidenced by increases in the numbers of early resorptions with consequent reductions in the numbers of fetuses, were observed at doses of 10 mg/kg/day or greater. Following IM administration in the rat and the rabbit, post-implantation losses, as evidenced by decreases in live fetuses and increases in resorptions, occurred at 30 mg/kg/day. Buprenorphine has been detected in breast milk. Naloxone hydrochloride was administered subcutaneously to rats and mice at doses up to 10 mg/kg/day with no embryotoxic or teratogenic effects. Male and female rats were treated with naloxone at 2 and 10 mg/kg with no effects on fertility.
Carcinogenicity: None of the components are listed as carcinogens or suspected carcinogens by IARC, NTP, or OSHA. 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 for 27 months. As in the buprenorphine/naloxone carcinogenicity study in rat, statistically significant dose-related increases in Leydig cell tumors occurred. In an 86-week study in CD-1 mice, buprenorphine was not carcinogenic at dietary doses up to 100 mg/kg/day.

Acute Toxicity Values: Acute Oral Toxicity Estimate (ATE) calculated: >5000 mg/kg
Buprenorphine Hydrochloride: Oral LD50 >1000 mg/kg
Naloxone Hydrochloride: LD50 oral rat >1000 mg; LD50 oral mouse >1000 mg/kg

12. ECOLOGICAL INFORMATION

Environmental properties have not been fully evaluated. Releases to the environment should be avoided.
Ecotoxicity values: No data available.
Persistence and degradability: No data available.
Bioaccumulative potential: No data available.
Mobility in soil: No data is available.
Other adverse effects: None known.

13. DISPOSAL CONSIDERATIONS

Dispose in accordance with all local, state and federal regulations.

14. TRANSPORT INFORMATION

	UN Number	Proper shipping name	Hazard Class	Packing Group	Environmental Hazard
DOT		Not Regulated			
TDG		Not Regulated			
IMDG		Not Regulated			
IATA		Not Regulated			

Transport in bulk (according to Annex II of MARPOL 73/78 and the IBC Code): Not applicable – product is transported only in packaged form.

Special precautions: None known.

15. REGULATORY INFORMATION

Safety, health, and environmental regulations specific for the product in question.

CERCLA: This product is not subject to CERCLA release reporting. Many states have more stringent release reporting requirements. Report spills as required under federal, state and local regulations.

SARA Hazard Category (311/312): Refer to Section 2 for the OSHA Hazard Classification.

EPA SARA 313: This product contains the following chemicals regulated under SARA Title III, section 313:
None

EPA TSCA Inventory: This product is a drug and not subject to TSCA**.**

California Proposition 65: This product is not known to contain regulated chemicals.

CANADA:
Canadian CEPA: This product is a drug and not subject to CEPA regulations.

16. OTHER INFORMATION

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Disclaimer : The information provided on this SDS is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guide for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered as a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other material or in any process, unless specified in the text.