SAFETY DATA SHEET

1. Identification

Product Identifier: Fentanyl Citrate Injection, USP CII

Synonyms: N-(1-Phenethyl-4-piperidyl)propionanilide citrate (1:1)

National Drug Code (NDC):
17478-030-02
17478-030-25
17478-030-05
17478-030-55
17478-030-20

Recommended Use: Pharmaceutical.

Company:
Akorn, Inc.
1925 West Field Court, Suite 300
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: Not classifiable.
Symbol(s): None.
Signal Word: None.
Hazard Statement(s): None.

Precautionary Statement(s):

P261	Do not breathing dust/fume/gas/mist/vapours/ spray.
P264	Wash hands thoroughly after handling.
P313	Get medical advice/attention if you feel unwell.
P305 + P351 + P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337 + P313	If eye irritation persists, get medical advice/attention.

Hazards Not Otherwise Classified: Not classifiable.

Supplementary Information: While this material is not classifiable as hazardous under the OSHA standard, this SDS contains valuable information critical to safe handling and proper use of the product. This SDS should be retained and available for employees and other users of this product.

3. Composition/Information on Ingredients

Chemical Name	CAS Number	Synonyms	Chemical Formula	Molecular Weight	Percentage
Fentanyl Citrate	990-73-8	N-(1-Phenethyl-4-piperidyl)propionanilide citrate (1:1)	$C_{22}H_{28}N_2O \cdot C_6H_8O_7$	528.60	0.005%

*The formula also contains Sodium Hydroxide to adjust pH between 4.0 – 7.5.

4. First Aid Measures

Ingestion: Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. In the presence of hypoventilation or apnea, oxygen should be administered and respiration should be assisted or controlled as indicated. A patent airway must be maintained; an oropharyngeal airway or endotracheal tube might be indicated. If depressed respiration is associated with muscular rigidity, an intravenous neuromuscular blocking agent might be required to facilitate assisted or controlled respiration. The patient should be carefully observed for 24 hours; body warmth and adequate fluid intake should be maintained. If hypotension occurs and is severe or persists, the possibility of hypovolemia should be considered and managed with appropriate parenteral fluid therapy. A specific narcotic antagonist such as naloxone should be available for use as indicated to manage respiratory depression. This does not preclude the use of more immediate countermeasures. The duration of respiratory depression following overdosage of fentanyl may be longer than the duration of narcotic antagonist action. Consult the package insert of the individual narcotic antagonists for details about use.

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:	None anticipated from normal handling of this product. In clinical use, adverse effects may include respiratory depression, apnea, muscle rigidity, and bradycardia. Other adverse effects have included hypotension/ hypertension, dizziness, blurred vision, nausea, emesis, laryngospasm and diaphoresis. Local reactions such as rash, erythema, and itching have been reported with transdermal use.
Medical Conditions Aggravated by Exposure:	Not determined.
Notes to Physician:	Treat supportively and symptomatically.

5. Firefighting Measures

Suitable Extinguishing Media:	As with any fire, use extinguishing media appropriate for primary cause of fire such as carbon dioxide, dry chemical extinguishing powder or foam.
Unsuitable Extinguishing Media:	Not determined.

Specific Hazards Arising from the Chemical:

Flammability:	None anticipated for this aqueous product.
Hazardous Combustion Products:	Not determined.
Other Specific Hazards:	Not determined.
Special Protective Equipment/ 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: Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill control procedures. Absorb the liquid with suitable material and clean affected area with soap and water.

Environmental Precautions: No data available.

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, fentanyl citrate is a Schedule C-II 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: No special storage required for hazard control. For product protection, follow storage recommendations noted on the product case label, the primary container label, or the product insert.

Specific End Use: Pharmaceuticals.

8. Exposure Controls/Personal Protection

Occupational Exposure Guidelines:

Common or Chemical Name	Employee Exposure Limits
Fentanyl Citrate	Not established.

Engineering Controls: Engineering controls are normally not needed during the normal use of this product.

Respiratory Protection: Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N95 or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

Eyes Protection:	Not required for the normal use of this product. Safety glasses with side shields are recommended. 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:	Not required for the normal use of this product. Chemically compatible gloves. For handling solutions, 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:	Not required for the normal use of this product. Wear protective laboratory coat, apron, or disposable garment when working with large quantities.

9. Physical and Chemical Properties

Physical State/Color:	Sterile, nonpyrogenic aqueous solution.
Odor:	No data available.
Odor Threshold:	No data available.
pH:	4.0 – 7.5.
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):	No data available.
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:	No data available.
Chemical Stability:	Stable under recommended storage conditions.
Possibility of Hazardous Reactions:	No data available.
Conditions to Avoid (e.g., static discharge, shock, or vibration):	No data available.

Incompatible Materials: No data available.

Hazardous Decomposition Products: Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx) and nitrogen oxides (NOx).

Hazardous Polymerization: Not anticipated to occur with this product.

11. Toxicological Information

Information on the Likely Routes of Exposure:

Occupational Exposure Potential: Information on the absorption of this product via inhalation is not available. When applied dermally as an aqueous solution to the forearm of human volunteers, fentanyl citrate was absorbed through the skin in significant amounts (about 18 %). Avoid liquid aerosol generation and skin contact.

Inhalation: May cause irritation to the respiratory system.

Ingestion: No data available.
Skin Contact: No data available.

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 determined for the product formulation. Information for the active ingredient is as follows:

Compound	Species	Route	Test Type	Dose
Fentanyl Citrate	Rat	Oral	LD_{50}	18 mg/kg
Fentanyl Citrate	Mouse	Oral	LD_{50}	368 mg/kg
Fentanyl Citrate	Rat	Intravenous	LD_{50}	0.99, 3.0 mg/kg
Fentanyl Citrate	Mouse	Intravenous	LD_{50}	10.1 mg/kg
Fentanyl Citrate	Dog	Intravenous	LD_{50}	14 mg/kg
Fentanyl Citrate	Monkey	Intravenous	LD_{50}	0.03 mg/kg

LD_{50}: Dosage that produces 50% mortality.

Acute Toxicity – Dermal: No data available.
Acute Toxicity – Inhalation: No data available.
Corrosivity: No data available.

Dermal Irritation: None anticipated from normal handling of this product.

Eye Irritation:	None anticipated from normal handling of this product. However, inadvertent contact of this product with eyes may produce irritation with redness and tearing.
Dermal or Respiratory Sensitization:	None anticipated from normal handling of this product.
Toxicokinetics/Metabolism:	No data available.
Reproductive Effects:	None anticipated from normal handling of this product. Fentanyl has been reported to impair fertility and to be embryocidal (an increase in resorptions in rats) when given at an intravenous dosage of 30 mcg/kg or at a subcutaneous dosage of 160 mcg/kg for 12 to 21 days. No teratogenic or other adverse fetal effects were noted in offspring when pregnant rats were treated throughout pregnancy with continuous infusions of 10 to 500 mcg/kg/day of fentanyl. Increased frequencies of death and developmental delays were noted in fetuses of pregnant mice given single injections of 14,500-16,000 mcg/kg of fentanyl. The potential effects of fentanyl on male and female fertility were evaluated in rats. In a male fertility study, male rats were given fentanyl via continuous intravenous infusion at dosages of 0, 0.025, 0.1 or 0.4 mg/kg/day for 28 days prior to mating; female rats were not treated. In a female fertility study, female rats were given fentanyl via continuous intravenous infusion at dosages of 0, 0.025, 0.1 or 0.4 mg/kg/day for 14 days prior to mating until day 16 of pregnancy; male rats were not treated. Analysis of fertility parameters in both studies showed that intravenous dosages of fentanyl up to 0.4 mg/kg/day given to either the male or the female alone produced no effects on fertility. In a separate study, a single daily bolus dose of fentanyl was shown to impair fertility in rats when given in intravenous doses of 0.3 times the human dose for a period of 12 days. The potential effects of fentanyl on embryo-fetal development were evaluated in rats, mice, and rabbits. Intravenous administration of fentanyl at dosages of 0, 0.01, or 0.03 mg/kg to female rats from gestation days 6 to 18 suggested evidence of embryotoxicity, and a slight increase in mean delivery time in the 0.03 mg/kg/day group. There was no clear evidence of teratogenicity noted. Pregnant female New Zealand White rabbits were treated with fentanyl at dosages of 0, 0.025, 0.1, 0.4 mg/kg via intravenous infusion from days 6 to day 18 of pregnancy. Fentanyl produced a slight decrease in the body weight of the live fetuses at the high dose, an effect attributed to maternal toxicity. There was no evidence for fentanyl induced adverse effects on embryo-fetal development at doses up to 0.4 mg/kg in this The potential effects of fentanyl on prenatal and postnatal development were examined in rats. Female Wistar rats

	were treated with dosages of 0, 0.025, 0.1, or 0.4 mg/kg/day fentanyl via intravenous infusion from day 6 of pregnancy through 3 weeks of lactation. At the high dose, fentanyl treatment significantly decreased body weight in male and female pups and also decreased survival in pups at day 4. Both the mid-dose and high-dose of fentanyl animals demonstrated alterations in development (delayed incisor eruption and eye opening) and transient behavioral development.
Carcinogenicity:	In a two-year carcinogenicity study conducted in rats, fentanyl was not associated with an increased incidence of tumors at subcutaneous doses up to 33 mcg/kg/day in males or 100 mcg/kg/day in females (0.16 and 0.39 times the human daily exposure obtained via the 100 mcg/hour patch based on AUC0–24h comparison).
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.
Mutagenicity:	There was no evidence of mutagenicity in the Ames Salmonella mutagenicity assay, the primary rat hepatocyte unscheduled DNA synthesis assay, the BALB/c 3T3 transformation test, and the human lymphocyte and CHO chromosomal aberration in-vitro assays.
Aspiration Hazard:	None anticipated from normal handling of this product.
Specific Target Organ Toxicity – Single Exposure:	Not determined.
Specific Target Organ Toxicity – Repeat Exposure:	Based on clinical use, possible target organs include the nervous system, respiratory system, and cardiovascular system.

12. Ecological Information

Ecotoxicity

Aquatic:	No data available.
Terrestrial:	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

Dispose of all waste in accordance with Federal, State and Local regulations.

14. Transport Information

UN Number:	Not applicable.
UN Proper Shipping Name:	Not applicable.
Transport Hazard Class(es):	Not applicable.
Packing Group:	Not applicable.
Department of Transportation:	Not regulated as a hazardous material.
International Air Transport Association (IATA):	Not regulated as a dangerous good.
International Maritime Dangerous Good (IMDG):	Not regulated as a dangerous good.

15. Regulatory Information

US Federal Regulations:

Toxic Substance Control Act (TSCA):	Exempt.
CERCLA Hazardous Substance and Reportable Quantity:	Not listed.
SARA 313:	Not listed.
SARA 302:	Not listed.

State Regulations

California Proposition 65:	Not listed.

16. Other Information

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