

ATROPINE SULFATE- atropine sulfate injection, solution

Amneal Pharmaceuticals LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ATROPINE SULFATE INJECTION safely and effectively. See full prescribing information for ATROPINE SULFATE INJECTION.

ATROPINE SULFATE injection, for intravenous use
Initial U.S. Approval: 1960

INDICATIONS AND USAGE

Atropine is a muscarinic antagonist indicated for temporary blockade of severe or life-threatening muscarinic effects. (1)

DOSAGE AND ADMINISTRATION

- For intravenous administration. (2.1)
- Titrate according to heart rate, PR interval, blood pressure and symptoms. (2.1)
- Adult dosage
 - Antisialagogue or for antivagal effects: Initial single dose of 0.5 mg to 1 mg. (2.2)
 - Antidote for organophosphorus or muscarinic mushroom poisoning: Initial single dose of 2 mg to 3 mg, repeated every 20 to 30 minutes. (2.2)
 - Bradycardic cardiac arrest: 1 mg dose, repeated every 3 to 5 minutes if asystole persists. (2.2)
- Patients with Coronary Artery Disease: Limit the total dose to 0.03 mg/kg to 0.04 mg/kg. (2.4)

DOSAGE FORMS AND STRENGTHS

- 0.5 mg/5 mL (0.1 mg/mL) injection in 5 mL single-dose glass syringe. (3)
- 1 mg/10 mL (0.1 mg/mL) injection in 10 mL single-dose glass syringe. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Tachycardia. (5.1)
- Glaucoma. (5.2)
- Pyloric obstruction. (5.3)
- Worsening urinary retention. (5.4)
- Viscid bronchial plugs. (5.5)

ADVERSE REACTIONS

Most adverse reactions are directly related to atropine's antimuscarinic action. Dryness of the mouth, blurred vision, photophobia and tachycardia commonly occur with chronic administration of therapeutic doses. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Mexiletine: Decreases rate of mexiletine absorption. (7.1)

Revised: 1/2024

FULL PRESCRIBING INFORMATION: CONTENTS*
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 General Administration

- 2.2 Adult Dosage
- 2.3 Pediatric Dosage
- 2.4 Dosing in Patients with Coronary Artery Disease

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Tachycardia
- 5.2 Acute Glaucoma
- 5.3 Pyloric Obstruction
- 5.4 Complete Urinary Retention
- 5.5 Viscid Plugs

6 ADVERSE REACTIONS

7 DRUG INTERACTIONS

- 7.1 Mexiletine

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

16 HOW SUPPLIED/STORAGE AND HANDLING

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Atropine sulfate injection is indicated for temporary blockade of severe or life-threatening muscarinic effects, e.g., as an antisialagogue, an antivagal agent, an antidote for organophosphorus or muscarinic mushroom poisoning and to treat bradycardic cardiac arrest.

2 DOSAGE AND ADMINISTRATION

2.1 General Administration

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not administer unless solution is clear and seal is intact. Each syringe is intended for single-

dose only. Discard unused portion.

For intravenous administration.

Titrate based on heart rate, PR interval, blood pressure and symptoms.

2.2 Adult Dosage

Table 1: Recommended Dosage

Use	Dose (adults)	Repeat
Antisialagogue or other anticholinergic	0.5 mg to 1 mg	1 to 2 hours
Organophosphorus or muscarinic mushroom poisoning	2 mg to 3 mg	20 to 30 minutes
Bradyasystolic cardiac arrest	1 mg	3 to 5 minutes; 3 mg maximum total dose

2.3 Pediatric Dosage

Dosing in pediatric populations has not been well studied. Usual initial dose is 0.01 mg/kg to 0.03 mg/kg.

2.4 Dosing in Patients with Coronary Artery Disease

Limit the total dose of atropine sulfate to 0.03 mg/kg to 0.04 mg/kg [see Warnings and Precautions (5.1)].

3 DOSAGE FORMS AND STRENGTHS

Atropine Sulfate Injection USP, **0.5 mg/5 mL (0.1 mg/mL)** is available as a sterile, clear, colorless solution supplied in 5 mL single-dose glass syringe for intravenous administration.

Atropine Sulfate Injection USP, **1 mg/10 mL (0.1 mg/mL)** is available as a sterile, clear, colorless solution supplied in 10 mL single-dose glass syringe for intravenous administration.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Tachycardia

When the recurrent use of atropine is essential in patients with coronary artery disease, the total dose should be restricted to 2 mg to 3 mg (maximum 0.03 mg/kg to 0.04 mg/kg) to avoid the detrimental effects of atropine-induced tachycardia on myocardial oxygen demand.

5.2 Acute Glaucoma

Atropine may precipitate acute glaucoma.

5.3 Pyloric Obstruction

Atropine may convert partial organic pyloric stenosis into complete obstruction.

5.4 Complete Urinary Retention

Atropine may lead to complete urinary retention in patients with prostatic hypertrophy.

5.5 Viscid Plugs

Atropine may cause inspissation of bronchial secretions and formation of viscid plugs in patients with chronic lung disease.

6 ADVERSE REACTIONS

The following adverse reactions have been identified during post-approval use of atropine sulfate. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Most of the side effects of atropine are directly related to its antimuscarinic action. Dryness of the mouth, blurred vision, photophobia and tachycardia commonly occur. Anhidrosis can produce heat intolerance. Constipation and difficulty in micturition may occur in elderly patients. Occasional hypersensitivity reactions have been observed, especially skin rashes which in some instances progressed to exfoliation.

7 DRUG INTERACTIONS

7.1 Mexiletine

Atropine sulfate injection decreased the rate of mexiletine absorption without altering the relative oral bioavailability; this delay in mexiletine absorption was reversed by the combination of atropine and intravenous metoclopramide during pretreatment for anesthesia.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Animal reproduction studies have not been conducted with atropine. It also is not known whether atropine can cause fetal harm when given to a pregnant woman or can affect reproduction capacity.

8.3 Nursing Mothers

Trace amounts of atropine was found in breast milk. The clinical impact of this is not known.

8.4 Pediatric Use

Recommendations for use in pediatric patients are not based on clinical trials.

8.5 Geriatric Use

An evaluation of current literature revealed no clinical experience identifying differences in response between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

10 OVERDOSAGE

Excessive dosing may cause palpitation, dilated pupils, difficulty in swallowing, hot dry skin, thirst, dizziness, restlessness, tremor, fatigue and ataxia. Toxic doses lead to restlessness and excitement, hallucinations, delirium and coma. Depression and circulatory collapse occur only with severe intoxication. In such cases, blood pressure declines and death due to respiratory failure may ensue following paralysis and coma.

The fatal adult dose of atropine is not known. In pediatric populations, 10 mg or less may be fatal.

In the event of toxic overdosage, a short acting barbiturate or diazepam may be given as needed to control marked excitement and convulsions. Large doses for sedation should be avoided because central depressant action may coincide with the depression occurring late in atropine poisoning. Central stimulants are not recommended.

Physostigmine, given as an atropine antidote by slow intravenous injection of 1 mg to 4 mg (0.5 mg to 1 mg in pediatric populations), rapidly abolishes delirium and coma caused by large doses of atropine. Since physostigmine is rapidly destroyed, the patient may again lapse into coma after one to two hours, and repeated doses may be required.

Artificial respiration with oxygen may be necessary. Ice bags and alcohol sponges help to reduce fever, especially in pediatric populations.

Atropine is not removed by dialysis.

11 DESCRIPTION

Atropine sulfate injection, USP is a sterile, nonpyrogenic isotonic solution of atropine sulfate monohydrate in water for injection with sodium chloride sufficient to render the solution isotonic. It is administered parenterally by intravenous injection.

Each milliliter (mL) contains 0.1 mg (adult strength) of atropine sulfate monohydrate equivalent to 0.083 mg (adult strength) of atropine, and sodium chloride, 9 mg. May contain sodium hydroxide and/or sulfuric acid for pH adjustment.

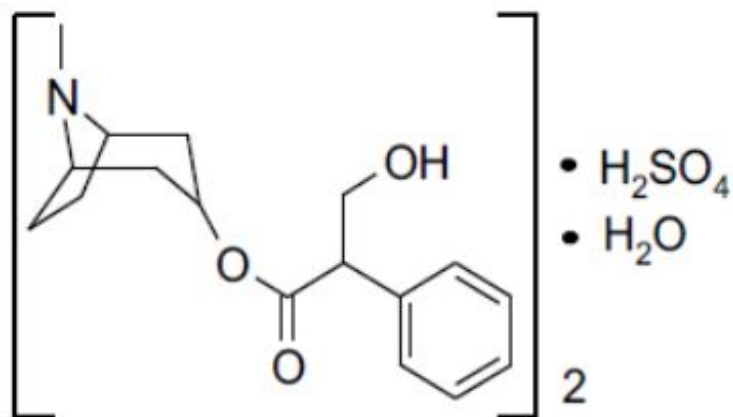
0.308 mOsmol/mL (calc.). pH 3.0 to 6.5.

Sodium chloride added to render the solution isotonic for injection of the active ingredient is present in amounts insufficient to affect serum electrolyte balance of sodium (Na⁺) and chloride (Cl⁻) ions.

The solution contains no bacteriostat, antimicrobial agent or added buffer (except for pH

adjustment) and is intended for use only as a single-dose injection. When smaller doses are required the unused portion should be discarded.

Atropine sulfate, USP is chemically designated 1 α H, 5 α H-tropan-3- α -ol (\pm)-tropate (ester), sulfate (2:1) (salt) monohydrate, (C₁₇H₂₃NO₃)₂ H₂SO₄ H₂O, colorless, almost white to white solid. It is very soluble in water and glacial acetic acid, freely soluble in ethanol (96%) and practically insoluble in diethyl ether. It has the following structural formula:



Atropine, a naturally occurring belladonna alkaloid, is a racemic mixture of equal parts of d- and l-hyocyanine, whose activity is due almost entirely to the levo isomer of the drug.

Sodium chloride, USP is chemically designated NaCl, a white crystalline powder freely soluble in water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Atropine is an antimuscarinic agent since it antagonizes the muscarine-like actions of acetylcholine and other choline esters.

Atropine inhibits the muscarinic actions of acetylcholine on structures innervated by postganglionic cholinergic nerves, and on smooth muscles which respond to endogenous acetylcholine but are not so innervated. As with other antimuscarinic agents, the major action of atropine is a competitive or surmountable antagonism which can be overcome by increasing the concentration of acetylcholine at receptor sites of the effector organ (e.g., by using anticholinesterase agents which inhibit the enzymatic destruction of acetylcholine). The receptors antagonized by atropine are the peripheral structures that are stimulated or inhibited by muscarine (i.e. exocrine glands and smooth and cardiac muscle). Responses to postganglionic cholinergic nerve stimulation also may be inhibited by atropine but this occurs less readily than with responses to injected (exogenous) choline esters.

12.2 Pharmacodynamics

Atropine-induced parasympathetic inhibition may be preceded by a transient phase of stimulation, especially on the heart where small doses first slow the rate before characteristic tachycardia develops due to paralysis of vagal control. Atropine exerts a more potent and prolonged effect on heart, intestine and bronchial muscle than scopolamine, but its action on the iris, ciliary body and certain secretory glands is weaker than that of scopolamine. Unlike the latter, atropine in clinical doses does not depress the central nervous system but may stimulate the medulla and higher cerebral centers. Although mild vagal excitation occurs, the increased respiratory rate and (sometimes) increased depth of respiration produced by atropine are more probably the result of bronchiolar dilatation. Accordingly, atropine is an unreliable respiratory stimulant and large or repeated doses may depress respiration.

Adequate doses of atropine abolish various types of reflex vagal cardiac slowing or asystole. The drug also prevents or abolishes bradycardia or asystole produced by injection of choline esters, anticholinesterase agents or other parasympathomimetic drugs, and cardiac arrest produced by stimulation of the vagus. Atropine also may lessen the degree of partial heart block when vagal activity is an etiologic factor. In some patients with complete heart block, the idioventricular rate may be accelerated by atropine; in others, the rate is stabilized. Occasionally a large dose may cause atrioventricular (A-V) block and nodal rhythm.

Atropine sulfate injection in clinical doses counteracts the peripheral dilatation and abrupt decrease in blood pressure produced by choline esters. However, when given by itself, atropine does not exert a striking or uniform effect on blood vessels or blood pressure. Systemic doses slightly raise systolic and lower diastolic pressures and can produce significant postural hypotension. Such doses also slightly increase cardiac output and decrease central venous pressure. Occasionally, therapeutic doses dilate cutaneous blood vessels, particularly in the "blush" area (atropine flush) and may cause atropine "fever" due to suppression of sweat gland activity in infants and small children.

The effects of intravenous atropine on heart rate (maximum heart rate) and saliva flow (minimum flow) after intravenous administration (rapid, constant infusion over 3 minutes) are delayed by 7 to 8 minutes after drug administration and both effects are non-linearly related to the amount of drug in the peripheral compartment. Changes in plasma atropine levels following intramuscular administration (0.5 mg to 4 mg doses) and heart rate are closely overlapped but the time course of the changes in atropine levels and behavioral impairment indicates that pharmacokinetics is not the primary rate-limiting mechanism for the central nervous system effect of atropine.

12.3 Pharmacokinetics

Atropine disappears rapidly from the blood following injection and is distributed throughout the body. Exercise, both prior to and immediately following intramuscular administration of atropine, significantly increases the absorption of atropine due to increased perfusion in the muscle and significantly decreases the clearance of atropine. The pharmacokinetics of atropine is nonlinear after intravenous administration of 0.5 mg to 4 mg. Atropine's plasma protein binding is about 44% and saturable in the 2 mcg/mL to 20 mcg/mL concentration range. Atropine readily crosses the placental barrier and enters the fetal circulation but is not found in amniotic fluid. Much of the drug is destroyed by enzymatic hydrolysis, particularly in the liver; from 13% to 50% is excreted unchanged in the urine. Traces are found in various secretions, including milk. The major metabolites of atropine are noratropine, atropin-n-oxide, tropine and tropic acid. The

metabolism of atropine is inhibited by organophosphate pesticides.

Specific Populations

The elimination half-life of atropine is more than doubled in children under two years and the elderly (> 65 years old) compared to other age groups. There is no gender effect on the pharmacokinetics and pharmacodynamics (heart rate changes) of atropine.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies have not been performed to evaluate the carcinogenic or mutagenic potential of atropine or its potential to affect fertility adversely.

16 HOW SUPPLIED/STORAGE AND HANDLING

Atropine Sulfate Injection USP, **0.5 mg/5 mL (0.1 mg/mL)** is available as a sterile, clear, colorless solution for intravenous administration and supplied in 5 mL single-dose glass syringe as follows:

	Strength (Concentration)	NDC#	
		Unit of Sale	Each
Atropine Sulfate Injection, USP	0.5 mg/5 mL (0.1 mg/mL)	NDC 70121-1705-7 (package of 10, 5 mL single-dose glass syringes)	NDC 70121-1705-1 (1 syringe in 1 carton)

Atropine Sulfate Injection USP, **1 mg/10 mL (0.1 mg/mL)** is available as a sterile, clear, colorless solution for intravenous administration and supplied in 10 mL single-dose glass syringe as follows:

	Strength (Concentration)	NDC#	
		Unit of Sale	
Atropine Sulfate Injection, USP	1 mg/10 mL (0.1 mg/mL)	NDC 70121-1706-1 (1, 10 mL single-dose glass syringe in 1 carton)	
		NDC 70121-1706-2 (10, 10 mL single-dose glass syringes in 1 carton)	

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Manufactured by:

Amneal Pharmaceuticals Pvt. Ltd.
Parenteral Unit

Ahmedabad 382213, INDIA

Distributed by:

Amneal Pharmaceuticals LLC

Bridgewater, NJ 08807

Rev. 01-2024-01

PRINCIPAL DISPLAY PANEL

NDC 70121-1705-1

Atropine Sulfate Injection USP, 0.5 mg/5 mL (0.1 mg/mL)

Rx only

5 mL Syringe Label

Amneal Pharmaceuticals LLC



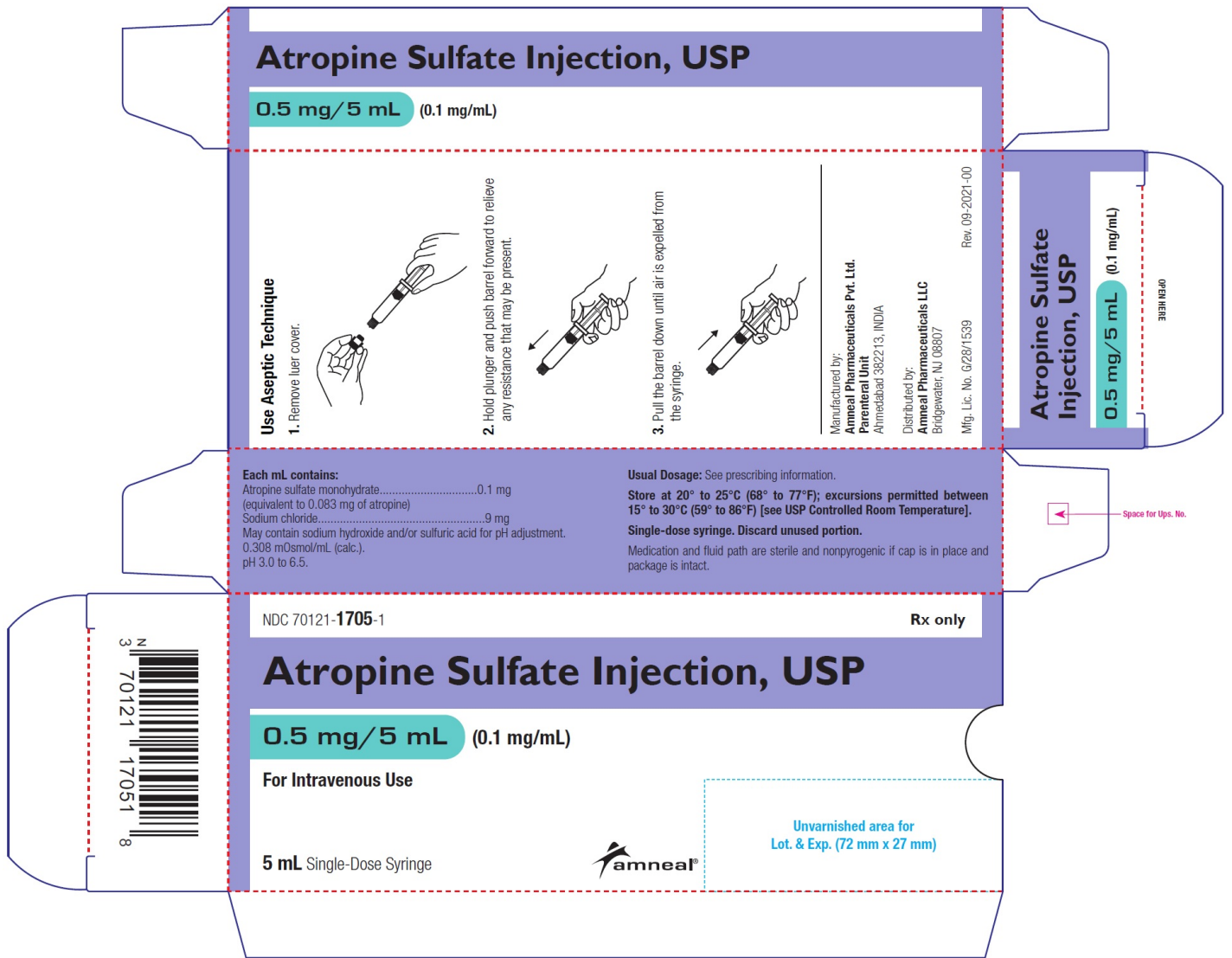
NDC 70121-1705-1

Atropine Sulfate Injection USP, 0.5 mg/5 mL (0.1 mg/mL)

Rx only

Carton Label

Amneal Pharmaceuticals LLC



NDC 70121-1705-7
Atropine Sulfate Injection USP, 0.5 mg/5 mL (0.1 mg/mL)
Rx only
Carton Label (Package of 10 Syringes)
Amneal Pharmaceuticals LLC



NDC 70121-1706-1
Atropine Sulfate Injection USP, 1 mg/10 mL (0.1 mg/mL)
Rx only
10 mL Syringe Label
Amneal Pharmaceuticals LLC



NDC 70121-1706-3
Atropine Sulfate Injection USP, 1 mg/10 mL (0.1 mg/mL)
Rx only
10 mL Tray Label
Amneal Pharmaceuticals LLC

NDC 70121-1706-3

Rx only

Atropine Sulfate Injection, USP

1 mg/10 mL

(0.1 mg/mL)

For Intravenous Use

5 x 10 mL Single-Dose Syringe

Each mL contains:

Atropine sulfate monohydrate.....0.1 mg

(equivalent to 0.083 mg of atropine)

Sodium chloride.....9 mg

May contain sodium hydroxide and/or sulfuric acid
for pH adjustment.

0.308 mOsmol/mL (calc.).

pH 3.0 to 6.5.

Usual Dosage: See prescribing information.

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

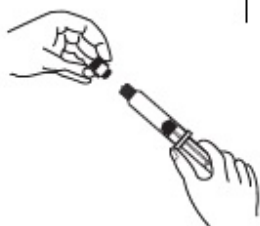
Single-dose syringe. Discard unused portion.

Medication and fluid path are sterile and nonpyrogenic if cap is in place and package is intact.

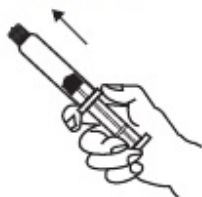
CAUTION: Liquid in glass. Handle with care. Inspect syringe for damage prior to assembly.

Use Aseptic Technique

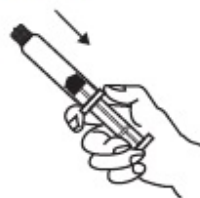
1. Remove luer cover.



2. Hold plunger and push barrel forward to relieve any resistance that may be present.



3. Pull the barrel down until air is expelled from the syringe.



Manufactured by: **Anneal Pharmaceuticals Pvt. Ltd. Parenteral Unit**
Ahmedabad 382213, INDIA

Distributed by: **Anneal Pharmaceuticals LLC**
Bridgewater, NJ 08807

Mfg. Lic. No. G/28/1539

Rev. 01-2024-00



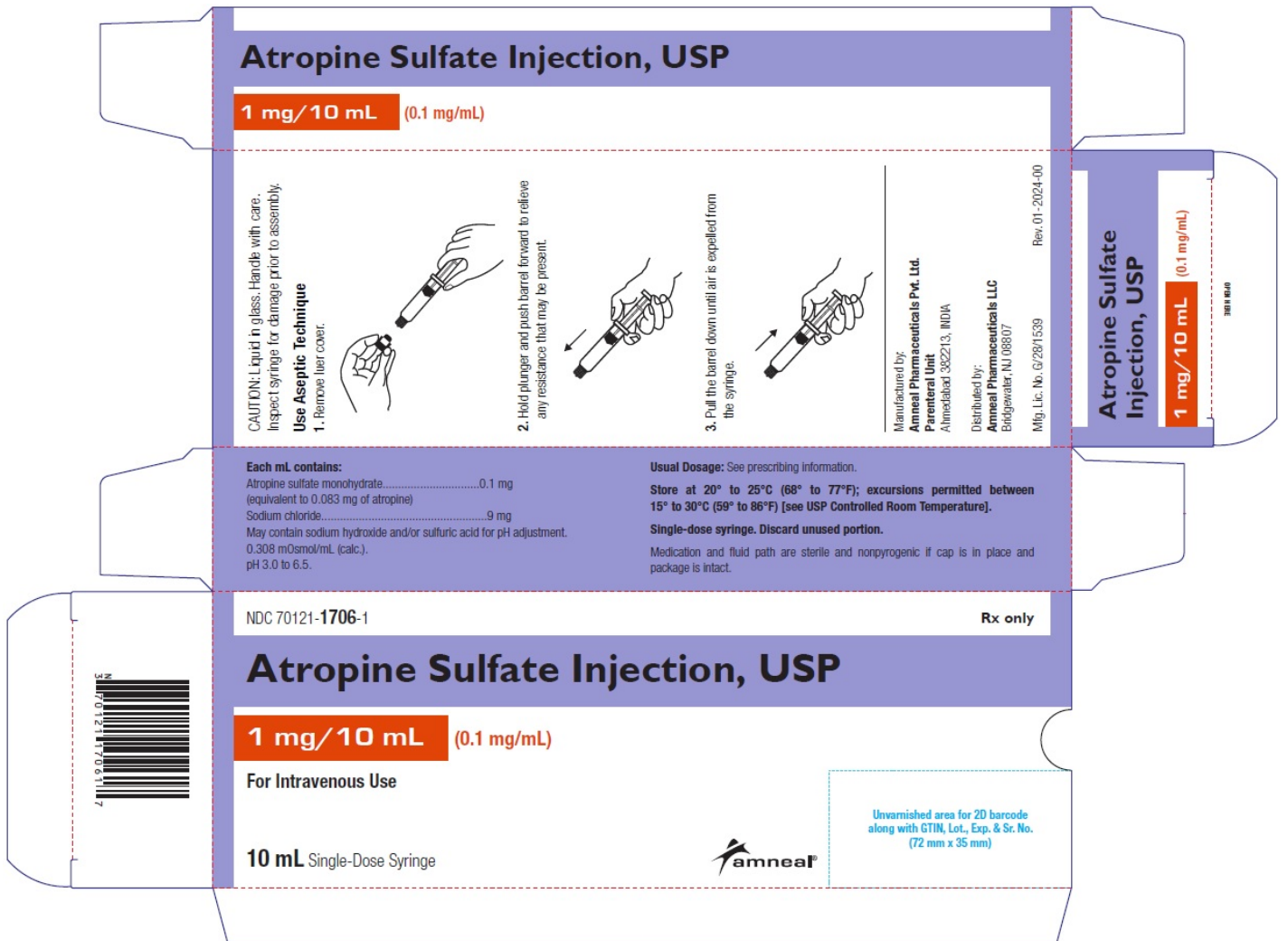
NDC 70121-1706-1

Atropine Sulfate Injection USP, 1 mg/10 mL (0.1 mg/mL)

Rx only

Carton Label

Anneal Pharmaceuticals LLC



NDC 70121-1706-2
Atropine Sulfate Injection USP, 0.5 mg/5 mL (0.1 mg/mL)
Rx only
Carton Label (Package of 10 Syringes)
Amneal Pharmaceuticals LLC

NDC 70121-1706-2

Rx only

Atropine Sulfate Injection, USP

1 mg/10 mL

(0.1 mg/mL)

For Intravenous Use

10 X 10 mL Single-Dose Syringe



Rx only

NDC 70121-1706-2

Atropine Sulfate Injection, USP

1 mg/10 mL

(0.1 mg/mL)

Each mL contains:

Atropine sulfate monohydrate.....0.1 mg
(equivalent to 0.083 mg of atropine)

Sodium chloride.....9 mg

May contain sodium hydroxide and/or sulfuric acid for pH adjustment.
0.308 mOsmol/mL (calc).

pH 3.0 to 6.5.

Usual Dosage: See prescribing information.

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Single-dose syringe. Discard unused portion.

Medication and fluid path are sterile and nonpyrogenic if cap is in place and package is intact.



NDC 70121-1706-2

Rx only

Atropine Sulfate Injection, USP

1 mg/10 mL

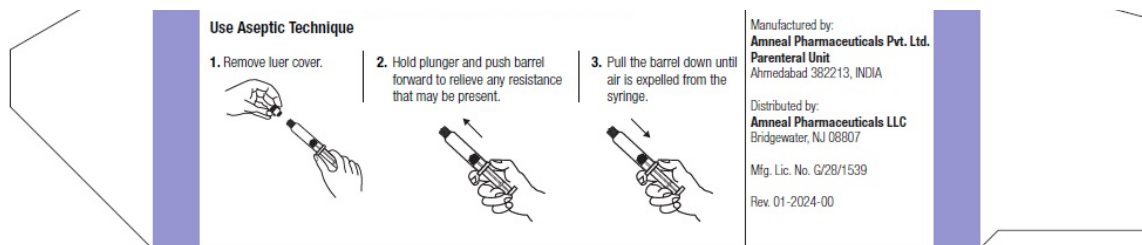
(0.1 mg/mL)

For Intravenous Use

10 X 10 mL Single-Dose Syringe

Unvarnished area for 2D barcode
along with GTIN, Lot., Exp. & Sr. No.
(75 mm x 35 mm)

CAUTION: Liquid in glass. Handle with care. Inspect syringe for damage prior to assembly.



ATROPINE SULFATE

atropine sulfate injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:70121-1705
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ATROPINE SULFATE (UNII: 03J5ZE7KA5) (ATROPINE - UNII:7C0697DR9I)	ATROPINE SULFATE	0.1 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	9 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
SULFURIC ACID (UNII: O40UQP6WCF)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:70121-1705-7	10 in 1 PACKAGE	01/29/2022	
1	NDC:70121-1705-1	1 in 1 CARTON		
1		5 mL in 1 SYRINGE, GLASS; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA215342	01/29/2022	

ATROPINE SULFATE

atropine sulfate injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:70121-1706
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ATROPINE SULFATE (UNII: 03J5ZE7KA5) (ATROPINE - UNII:7C0697DR9I)	ATROPINE SULFATE	0.1 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	9 mg in 1 mL
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
SULFURIC ACID (UNII: O40UQP6WCF)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:70121-1706-1	1 in 1 CARTON	01/09/2024	
1		10 mL in 1 SYRINGE, GLASS; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
2	NDC:70121-1706-2	10 in 1 CARTON	01/09/2024	
2		5 in 1 TRAY		
2		10 mL in 1 SYRINGE, GLASS; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA215342	01/09/2024	

Labeler - Amneal Pharmaceuticals LLC (827748190)

Establishment

Name	Address	ID/FEI	Business Operations
Amneal Pharmaceuticals Private Limited		860156658	analysis(70121-1705, 70121-1706) , manufacture(70121-1705, 70121-1706) , pack(70121-1705, 70121-1706) , sterilize(70121-1705, 70121-1706)

Revised: 1/2024

Amneal Pharmaceuticals LLC