CAFFEINE AND SODIUM BENZOATE- caffeine and sodium benzoate injection, solution
American Regent, Inc.

Disclaimer: This drug has not been found by FDA to be safe and effective, and this labeling has not been approved by FDA. For further information about unapproved drugs, click here.

CAFFEINE AND SODIUM BENZOATE INJECTION, USP

Rx Only

DESCRIPTION

Caffeine and Sodium Benzoate Injection, USP is a clear, sterile, nonpyrogenic, solution of Caffeine Alkaloid.

Each mL contains: Caffeine (anhydrous) 125 mg; Sodium Benzoate (added to increase the solubility of Caffeine) 125 mg; Water for Injection, USP q.s. pH (range 6.5 to 8.5) adjusted with Hydrochloric Acid and/or Sodium Hydroxide. For intramuscular or slow intravenous administration only.

CLINICAL PHARMACOLOGY

Caffeine is pharmacologically similar to the other xanthine drugs, such as theobromine and theophylline; however, these three agents differ in the intensity of their actions on various structures. Caffeine's CNS and skeletal muscle effects are greater than those of the other xanthines. In all other areas, theophylline has greater activity than caffeine, although some studies report that caffeine has greater diuretic effect than theobromine. The increased levels of intracellular cyclic-AMP mediate most of caffeine's pharmacologic actions. Caffeine competitively inhibits phosphodiesterase, the enzyme that degrades cyclic 3'- 5' adenosine monophosphate. Caffeine stimulates all levels of the CNS. Caffeine's cortical effects are milder and of shorter duration than those of the amphetamines. In slightly larger doses, caffeine stimulates medullary vagal, vasomotor and respiratory centers, promoting bradycardia, vasoconstriction, and increased respiratory rate.

Caffeine produces a positive inotropic effect of the myocardium and a positive chronotropic effect at the sinoatrial node, causing transient increases in heart rate, force of contraction, cardiac output and heart work. In doses greater than 250 mg, the centrally mediated vagal effects of caffeine may be masked by increased sinus rates; tachycardia, extrasystoles, or other major ventricular arrhythmias may result.

Caffeine constricts cerebral vasculature. In contrast, the drug directly dilates peripheral blood vessels, decreasing peripheral vascular resistance. The effect of this decrease in peripheral vascular resistance (and possibly that of vagal cardiac stimulation) on blood pressure is offset by increased cardiac output (and possibly stimulation of the medullary vasomotor area). The overall effect of caffeine on heart rate and blood pressure depends on whether CNS or peripheral effects predominate. Therapeutic doses of

caffeine increase blood pressure only slightly.

Caffeine stimulates voluntary skeletal muscle, increasing the force of contraction and decreasing muscular fatigue. The drug also stimulates gastric acid secretion from parietal cells. Caffeine increases renal blood flow and glomerular filtration rate and decreases proximal tubular reabsorption of sodium and water, resulting in mild diuresis.

Caffeine stimulates glycogenolysis and lipolysis, but increase in blood glucose and in plasma lipids are insignificant in normal patients. Tolerance may develop to the diuretic, cardiovascular, and CNS effects of caffeine.

Pharmacokinetics

Caffeine is rapidly distributed throughout the body tissues, readily crossing the placenta and blood-brain barrier. Approximately 17% of the drug is bound to plasma proteins. Caffeine has approximately a half-life ($T_{½}$) of 3-4 hours in adults. In adults, the drug is rapidly metabolized in the liver to 1-methyluric acid, 1-methylxanthine and 7-methylxanthine. Caffeine and its metabolites are excreted primarily by the kidneys.

INDICATIONS AND USAGE

Caffeine and Sodium Benzoate Injection has been used in conjunction with supportive measure to treat respiratory depression associated with overdosage with CNS depressant drugs (e.g., narcotic analgesics, alcohol). However, because of questionable benefit and transient action, most authorities believe caffeine and other analeptics should not be used in these conditions and recommend other supportive therapy.

CONTRAINDICATIONS

None known.

PRECAUTIONS

Large doses of caffeine may produce headache, excitement, agitation, a condition resembling anxiety neurosis, scintillating scotoma, hyperesthesia, tinnitus, muscle tremors or twitches, diuresis, tachycardia, extrasystoles, and other cardiac arrhythmias. Further CNS depression may occur when already depressed patients are too vigorously treated with Caffeine and Sodium Benzoate Injection.

Caffeine and other xanthines may enhance the cardiac inotropic effects of ß-adrenergic stimulating agents. Caffeine has also been reported to increase its own metabolism and that of other drugs, including phenobarbital and aspirin. Caffeine produces false-positive elevations of serum urate as measured by the Bittner method. The drug also produces slight increases in urine levels of vanilamandelic acid (VMA), catecholamines, and 5-hydrocyindoleacetic acid. Because high urine levels of VMA or catecholamines may result in false-positive diagnosis of pheochromocytoma or neuroblastoma, caffeine intake should be avoided during tests for these disorders.

Pregnancy

Teratogenic Effects

Pregnancy Category C. Animal reproduction studies have not been conducted with Caffeine and Sodium Benzoate Injection. It is also not known whether Caffeine and Sodium Benzoate Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Caffeine and Sodium Benzoate Injection should be given to a pregnant woman only if clearly needed.

OVERDOSAGE

Acute toxicity involving caffeine has been reported rarely. Mild delirium, insomnia, diuresis, dehydration, and fever commonly occur with overdosage. More serious symptoms of overdosage include cardiac arrhythmias and clonic-tonic convulsions. In adults, IV doses of 57 mg/kg of body weight and oral doses of 18.50 grams have been fatal. In one 5-year-old patient, death occurred following oral ingestion of approximately 3 grams of caffeine. Convulsions may be treated with IV administration of diazepam or a barbiturate such as pentobarbital sodium.

DOSAGE AND ADMINISTRATION

Caffeine and Sodium Benzoate Injection may be administered by intramuscular or slow intravenous injection.

Some clinicians suggest that when used as a mild CNS stimulant to overcome fatigue, oral doses of 100-200 mg of anhydrous caffeine are required. One manufacturer recommends that citrated caffeine be administered orally in dosages of 65-325 mg (about 32-162 mg of anhydrous caffeine) 3 times daily. Another manufacturer recommends an oral dosage of 250 mg of anhydrous caffeine in an extended-release formulation once daily, but warns that the drug should not be administered less than 6 hours before retiring.

Analeptic use of caffeine is strongly discouraged by most clinicians. However, the manufacturer of Caffeine and Sodium Benzoate Injection recommends intramuscular, or in emergency respiratory failure, intravenous injection of 500 mg of the drug (about 250 mg of anhydrous caffeine) or a maximum single dose of 1 gram (about 500 mg of anhydrous caffeine) for the treatment of respiratory depression associated with overdosage of CNS depressants, including narcotic analgesics and alcohol, and with electric shock.

The usual dose is 0.5 g (7 ½ grains) as frequently as directed by the physician. The maximum safe dose is 0.5 g and the total dose in 24 hours should rarely exceed 2.5 g.

Parenteral drug products should be inspected visually for particulate matter prior to administration whenever solution and container permit.

HOW SUPPLIED

Caffeine and Sodium Benzoate Injection, USP 250 mg/mL

NDC 0517-2502-10 2 mL Single Dose Vials Packed in boxes of 10.

Store at 20°-25°C (68°-77°F); excursions permitted to 15°-30"C (59°-86°F) (See USP Controlled Room Temperature).

AMERICAN REGENT, INC.
SHIRLEY, NY 11967

IN2502

Rev. 11/05

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Container Label

NDC 0517-2502-01

Rx Only

Caffeine and Sodium Benzoate Injection, USP

250 mg/mL (125 mg/mL Caffeine)

For IM or Slow IV Use

2 mL Single-Dose Vial

Discard Unused Portion

Carton Labeling

NDC 0517-2502-10

Rx Only

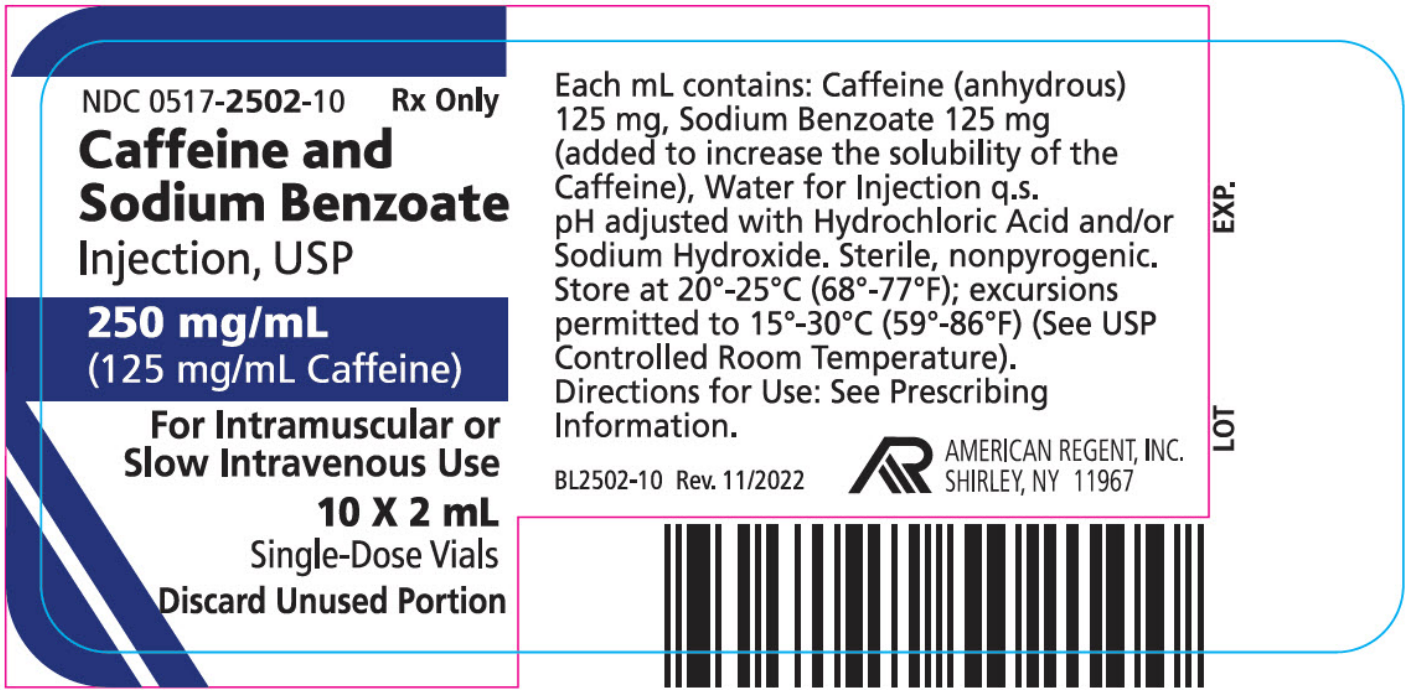
Caffeine and Sodium Benzoate Injection, USP

250 mg/mL (125 mg/mL Caffeine)

For Intramuscular or Slow Intravenous Use

10 X 2 mL Single-Dose Vials

Discard Unused Portion



Serialization Label

CAFFEINE AND SODIUM BENZOATE

caffeine and sodium benzoate injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0517-2502
Route of Administration	INTRAMUSCULAR, INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
CAFFEINE (UNII: 3G6A5W338E) (CAFFEINE - UNII:3G6A5W338E)	CAFFEINE	125 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM BENZOATE (UNII: OJ245FE5EU)	125 mg in 1 mL
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0517-2502-10	10 in 1 BOX	02/01/1993	
1	NDC:0517-2502-01	2 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
unapproved drug other		02/01/1993	

Labeler - American Regent, Inc. (002033710)

Establishment

Name	Address	ID/FEI	Business Operations
American Regent, Inc.		002033710	analysis(0517-2502) , manufacture(0517-2502)

Revised: 12/2019 American Regent, Inc.