Aminophylline

Introduction: Aminophylline Injection is a sterile, nonpyrogenic solution of Aminophylline in water for injection. Aminophylline (dihydrate) is approximately 79% of anhydrous aminophylline by weight. Aminophylline Injection is administered by slow intravenous injection or diluted and administered by intravenous infusion.

Mechanism of action: Causes bronchodilatation, diuresis, CNS and cardiac stimulation, and gastric acid secretion by blocking phosphodiesterase which increases tissue concentrations of cyclic adenine monophosphate (cAMP) which in turn promotes catecholamine stimulation of lipolysis, glycogenolysis, and gluconeogenesis and induces release of epinephrine from adrenal medulla cells.

Pharmacology:
Absorption: Oral: Dosage form dependent
Distribution: 0.45 L/kg based on ideal body weight
Protein binding: 40%, primarily to albumin
Metabolism: Children >1 year and Adults: Hepatic; involves CYP1A2, 2E1 and 3A4; forms active metabolites (caffeine and 3-methylxanthine)
Half-life elimination: Highly variable and dependent upon age, liver function, cardiac function, lung disease, and smoking history
Excretion: Urine Children >3 months and Adults: 10% unchanged
Indications: Intravenous aminophylline is indicated as an adjunct to inhaled beta-2 selective agonists and systemically administered corticosteroids for the treatment of acute exacerbations of the symptoms and reversible airflow obstruction associated with asthma and other chronic lung diseases, e.g., emphysema and chronic bronchitis.
Dosage: ***Treatment of acute bronchospasm***: I.V.: Loading dose (in Patient's not currently receiving theophylline or aminophylline): 6 mg/kg (based on aminophylline) administered I.V. over 20-30 minutes; administration rate should not exceed 25 mg/minute (aminophylline)
Approximate I.V. maintenance dosages are based upon **continuous infusions**; bolus dosing (often used in children <6 months of age) may be determined by multiplying the hourly infusion rate by 24 hours and dividing by the desired number of doses/day
6 weeks to 6 months: 0.5 mg/kg/hour
6 months to 1 year: 0.6-0.7 mg/kg/hour
1-9 years: 1 mg/kg/hour
9-16 years and smokers: 0.8 mg/kg/hour
Adults, nonsmoking: 0.5 mg/kg/hour
Older patients and patients with cor pulmonale: 0.3 mg/kg/hour
Patients with congestive heart failure: 0.1-0.2 mg/kg/hour
Side effects: Intravenous aminophylline is indicated as an adjunct to inhaled beta-2 selective agonists and systemically administered corticosteroids for the treatment of acute exacerbations of the symptoms and reversible airflow obstruction associated with asthma and other chronic lung diseases, e.g., emphysema and chronic bronchitis.

Precautions:

General: Careful consideration of the various interacting drugs and physiologic conditions that can alter aminophylline clearance and require dosage adjustment should occur prior to initiation of aminophylline therapy and prior to increases in aminophylline dose

Monitoring Serum Aminophylline Concentrations: Serum aminophylline concentration measurements are readily available and should be used to determine whether the dosage is appropriate. Specifically, the serum aminophylline concentration should be measured as follows:

- Before making a dose increase to determine whether the serum concentration is sub-therapeutic in a patient who continues to be symptomatic.
- Whenever signs or symptoms of aminophylline toxicity are present.
- Whenever there is a new illness, worsening of an existing concurrent illness or a change in the patient's treatment regimen that may alter aminophylline clearance (e.g., fever >102°F sustained for ≥ 24 hours, hepatitis, or drugs listed in are added or discontinued).

Pregnancy: **CATEGORY C:** There are no adequate and well controlled studies in pregnant women.

Nursing Mothers: Aminophylline is excreted into breast milk and may cause irritability or other signs of mild toxicity in nursing human infants. The concentration of aminophylline in breast milk is about equivalent to the maternal serum concentration. Serious adverse effects in the infant are unlikely unless the mother has toxic serum aminophylline concentrations.

Pediatric Use: Aminophylline is safe and effective for the approved indications in children. The constant infusion rate of intravenous aminophylline must be selected with caution in children since the rate of aminophylline clearance is highly variable across the age range of neonates to adolescents. Due to the immaturity of aminophylline metabolic pathways in children under the age of one year, particular attention to dosage selection and frequent monitoring of serum aminophylline concentrations are required when aminophylline is prescribed to children in this age group.

Geriatric Use: Elderly patients are at significantly greater risk of experiencing serious toxicity from aminophylline than younger patients due to pharmacokinetic and pharmacodynamic changes associated with aging. Aminophylline clearance is reduced in patients greater than 60 years of age, resulting in increased serum aminophylline concentrations in response to a given aminophylline infusion rate. Protein binding may be decreased in the elderly resulting in a larger proportion of the total serum aminophylline concentration in the pharmacologically active unbound form. Elderly patients also appear to be more sensitive to the toxic effects of aminophylline after chronic overdosage than younger patients. For these reasons, the maximum infusion rate of aminophylline in patients greater than 60 years of age ordinarily should not exceed 17 mg/hr (21 mg/hr as Aminophylline) unless the patient continues to be symptomatic and the steady state serum aminophylline concentration is <10 mcg/mL. Aminophylline infusion rates greater than 17 mg/hr (21 mg/hr as Aminophylline) should be prescribed with caution in elderly patients.

Contraindications: Hypersensitivity to aminophylline, ethylenediamine, or any component of the formulation

How supplied: Customized As Per Request.