

•THEOPHYLLINE tab

**Class:** Phosphodiesterase Enzyme Inhibitor, Nonselective

**Indications:**

Treatment of symptoms and reversible airway obstruction due to chronic asthma, or other chronic lung diseases

**Note:** The Global Initiative for Asthma Guidelines (2009) and the National Heart, Lung and Blood Institute Guidelines (2007) do not recommend oral theophylline as a long-term control medication for asthma in children  $\leq 5$  years of age; use has been shown to be effective as an add-on (but not preferred) agent in older children and adults with severe asthma treated with inhaled or oral glucocorticoids. The guidelines do not recommend theophylline for the treatment of exacerbations of asthma.

The Global Initiative for Chronic Obstructive Lung Disease Guidelines (2013) suggest that while higher doses of slow release formulations of theophylline have been proven to be effective for use in COPD, it is not a preferred agent due to its potential for toxicity.

**Available dosage form in the hospital:**

-THEOPHYLLINE 300MG TAB

-THEOPHYLLINE 200MG TAB

**Dosage:** Doses should be individualized based on steady-state serum concentrations and ideal body weight.

**-Acute symptoms: Loading dose: Oral, I.V.:**

- Asthma exacerbations:* While theophylline may be considered for relief of asthma symptoms, the role of treating exacerbations is not supported by current practice.
- COPD treatment:* Theophylline is currently considered second-line intravenous therapy in the emergency department or hospital setting when there is inadequate or insufficient response to short acting bronchodilators (Global Initiative for COPD Guidelines, 2013).
- **If no theophylline received within the previous 24 hours:** 4.6 mg/kg loading dose (~5.8 mg/kg hydrous aminophylline) I.V. or 5 mg/kg orally. Loading dose intended to achieve a serum level of approximately 10 mcg/ml; loading doses should be given intravenously (preferred) or with a rapidly absorbed oral product (not an extended-release product). **Note:** On the average, for every 1 mg/kg theophylline given, blood levels will rise 2 mcg/ml.
- **If theophylline has been administered in the previous 24 hours:** A loading dose is not recommended without obtaining a serum theophylline concentration. The loading dose should be calculated as follows:

$$\text{Dose} = (\text{desired serum theophylline concentration} - \text{measured serum theophylline concentration}) (V_d)$$

**-Acute symptoms: Maintenance dose: I.V.: Note:** To achieve a target concentration of 10 mcg/ml unless otherwise noted. Lower initial doses may be required in patients with reduced theophylline clearance. Dosage should be adjusted according to serum level measurements during the first 12- to 24-hour period.

- Adults 16-60 years (otherwise healthy, nonsmokers): 0.4 mg/kg/hour; maximum: 900 mg/day unless serum levels indicate need for larger dose.
- Adults >60 years: 0.3 mg/kg/hour; maximum: 400 mg/day unless serum levels indicate need for larger dose.

**-Treatment of chronic conditions:** With newer guidelines suggesting lower therapeutic theophylline ranges, it is unlikely that doses larger than >10 mg/kg/day will be required in children  $\geq 1$  year of age.

- Oral solution: Initial dose: 300 mg/day administered in divided doses every 6-8 hours; Maintenance: 400-600 mg/day (maximum: 600 mg/day) .
- Oral extended release formulations: Initial dose: 300-400 mg once daily; Maintenance: 400-600 mg once daily (maximum: 600 mg/day).

**-Dosage adjustment after serum theophylline measurement:**

Asthma: Within normal limits: Adults: 5-15 mcg/ml: Maintain dosage if tolerated. Recheck serum theophylline concentration at 24-hour intervals (for acute I.V. dosing) or at 6- to 12-month intervals (for oral dosing). Finer adjustments in dosage may be needed for some patients. If levels  $\geq 15$  mcg/ml, consider 10% dose reduction to improve safety margin.

**Note:** Recheck serum theophylline levels after 3 days when using oral dosing, or after 12 hours (children) or 24 hours (adults) when dosing intravenously. Patients maintained with oral therapy may be reassessed at 6- to 12-month intervals.

**Geriatric**

-Acute symptoms: Adults >60 years:

- Loading dose: Oral, I.V.: Refer to adult dosing.
- Maintenance dose: I.V.: 0.3 mg/kg/hour; maximum 400 mg/day unless serum levels indicate need for larger dose

-Chronic conditions: Oral: Adults >60 years: Do not exceed a dose of 400 mg/day

-Cardiac decompensation, cor pulmonale, hepatic dysfunction, sepsis with multiorgan failure, shock: Refer to adult dosing.

**Renal Impairment**

Oral: I.V.:

No dosage adjustment necessary.

### **Hepatic Impairment:**

Oral: No dosage adjustment provided in manufacturer's labeling. However, dose reduction and frequent monitoring of serum theophylline concentration are required in patients with decreased hepatic function (eg, cirrhosis, acute hepatitis, cholestasis).

I.V.: Initial: 0.25 mg/kg/hour; maximum daily dose: 400 mg daily unless serum concentrations indicate need for larger dose. Use with caution and monitor serum theophylline concentrations frequently.

### **Dosing: Obesity**

Use ideal body weight for obese patients.

### **Common side effect:**

Frequency not defined. Adverse events observed at therapeutic serum levels:

- Cardiovascular: Flutter, tachycardia
- Central nervous system: Headache, hyperactivity (children), insomnia, restlessness, seizures, status epilepticus (nonconvulsive)
- Endocrine & metabolic: Hypercalcemia (with concomitant hyperthyroid disease)
- Gastrointestinal: Nausea, reflux or ulcer aggravation, vomiting
- Genitourinary: Difficulty urinating (elderly males with prostatism)
- Neuromuscular & skeletal: Tremor
- Renal: Diuresis (transient)

**Pregnancy Risk Factor: C**