ELIXOPHYLLIN®
ELIXIR
(Theophylline Oral Solution, USP)
(THEOPHYLLINE ANHYDROUS)

Each 15 mL (tablespoonful) contains 80 mg theophylline anhydrous.

Alcohol 20%.

Dosage: Should be individualized. See package insert.

Store at controlled room temperature 15º–30º C (59º–86º F).

Dispense in a tight, light-resistant container. Avoid exposure to excessive heat.

Mfg. by:
Nostrum Laboratories, Inc.
Bryan, OH 43506

NDC 70408-644-34

16 OUNCES (473 mL)

Each 15 mL (tablespoonful) contains 80 mg theophylline anhydrous.

Alcohol 20%.

Dosage: Should be individualized. See package insert.

Store at controlled room temperature 15º–30º C (59º–86º F).

Dispense in a tight, light-resistant container. Avoid exposure to excessive heat.

Mfg. by:
Nostrum Laboratories, Inc.
Bryan, OH 43506

NDC 70408-644-34

16 OUNCES (473 mL)
**ELIXOPHYLLIN Elixir**

(Theophylline Oral Solution, USP)

**Rx Only**

**DESCRIPTION**

Theophylline is a methylxanthine structurally classified as a methylxanthine. It is a white, odorless, crystalline powder with a bitter taste. Amorphous theophylline has the chemical class formula 3,7-Dimethyl-1,3,7-dihydro-1H-purine-2,6-dione. Theophylline has been shown to be effective in the management of various bronchospastic conditions including asthma, chronic bronchitis, bronchitis associated with emphysema, and bronchitis due to smoking, chronic obstructive pulmonary disease, bronchitis due to chronic bronchitis, and asthma due to chronic obstructive pulmonary disease.

**PHARMACODYNAMIC PROPERTIES**

100% increase

Increases theophylline clearance by

May lower theophylline seizure

Similar to diazepam.

Note:

- Sepsis with multi-organ failure 0.47 (0.19-1.9) 18.8 (6.3-24.1)
- Liver disease – cirrhosis 0.31** (0.1-0.7) 32** (10-56)
- COPD - 0.54 (0.44-0.64) 11 (9.4-12.6)
- otherwise healthy non-smoking asthmatics 0.65 (0.27-1.03) 8.7 (6.1-12.8)
- 13-15 years 0.9 (0.48-1.3) NR†

**Teens**

13-15 years 0.9 (0.48-1.3) NR†

**Race**

60% increase

**Gender**

Men 0.9 (0.62-1.5)

Women 1.3 (0.92-1.9)

**DOSAGE AND ADMINISTRATION**

**Contraindications**

**Warnings**

100% increase. Beta-2 blocking

190% increase

**Drug Interactions**

**Side Effects**

**Common Side Effects**

**Rare**

- Agitation
- Anemia
- Arthralgia
- AST/ALT/LFT increases
- AST/ALT/LFT decreases
- Ataxia
- Bradycardia
- Decreased uric acid
- Diarrhea
- Dizziness
- Dyspnea
- Ectopic atrial contractions
- Ectopic ventricular contractions
- ECG changes
- Edema
- Emotional lability
- Exfoliative dermatitis
- Fluid retention
- Flu-like symptoms
- Gastroesophageal reflux disease
- Gastrointestinal bleeding
- Gastrointestinal perforation
- Headache
- Hemorrhage
- Hiccups
- Impotence
- Infusion site reactions
- Intrahepatic cholestasis
- Itching
- Jaundice
- Leg cramps
- Malignant hyperthermia
- Myalgia
- Nausea
- Nerve damage
- Nervousness
- Nocturnal somnolence
- Nocturnal sweating
- Oliguria
- Palpitations
- Pneumonia
- Pneumothorax
- Pruritus
- Purpura
- Quincke’s edema
- Rhabdomyolysis
- Reticulocytosis
- Respiratory distress
- Seizures
- Skin rash
- Sudden death
- Syncope
- Tachycardia
- Tachypnea
- Thrombocytopenia
- Urinary retention
- Urticaria
- Vomiting
- Weight loss

**Precautions**

**Special Populations**

**Special Populations (See Table I for mean clearance and half-life values)**

**Overview**

Serum Concentration-Effect Relationship:

**Clinical Pharmacology**

Theophylline is a methylxanthine structurally classified as a methylxanthine. It is a white, odorless, crystalline powder with a bitter taste. Amorphous theophylline has the chemical class formula 3,7-Dimethyl-1,3,7-dihydro-1H-purine-2,6-dione. Theophylline has been shown to be effective in the management of various bronchospastic conditions including asthma, chronic bronchitis, bronchitis associated with emphysema, and bronchitis due to smoking, chronic obstructive pulmonary disease, bronchitis due to chronic bronchitis, and asthma due to chronic obstructive pulmonary disease.

**Mechanism of Action:**

Theophylline does not directly activate the adenosine receptors but instead may exert its therapeutic effects through the inhibition of adenosine receptors. Adenosine receptors are known to be involved in the regulation of bronchodilation, and theophylline has been shown to inhibit the actions of adenosine on these receptors. The inhibition of adenosine may lead to increased airway patency and improved bronchodilation, which is beneficial in the treatment of asthma.

**Indications and Usage:**

Theophylline is indicated for the treatment of bronchial asthma or chronic bronchitis in patients 18 years of age and older. It is also indicated for use in the management of bronchitis associated with emphysema in patients 18 years of age and older.

**Contraindications:**

Theophylline is contraindicated in patients with a history of hypersensitivity to theophylline or other components in the product.

**Warnings:**

Theophylline is contraindicated in patients with a history of hypersensitivity to theophylline or other components in the product.

**Precautions:**

**Special Populations (See Table I for mean clearance and half-life values)**

Serum Concentration-Effect Relationship:

Theophylline is rapidly and completely absorbed after oral administration in solution or immediate- release tablets. Theophylline does not undergo any appreciable systemic extraction during absorption. Theophylline has a half-life of 3 to 6 hours in normal volunteers and is reduced in patients with severe cardiac disease or hepatic insufficiency. Serum theophylline concentrations are also affected by factors such as age, weight, gender, and concurrent medications. The clearance of theophylline is decreased by 50% or more in patients with hepatic insufficiency and end-stage renal disease, no dosage adjustment is required in adults and children with severe hepatic impairment and no dosage adjustment is required in patients with end-stage renal disease. In patients with chronic asthma, including patients with severe asthma requiring inhaled corticosteroids, theophylline clearance is decreased by 50% or more in patients with severe hepatic impairment and no dosage adjustment is required in patients with end-stage renal disease. In patients with chronic asthma, including patients with severe asthma requiring inhaled corticosteroids, theophylline clearance is decreased by 50% or more in patients with severe hepatic impairment and no dosage adjustment is required in patients with end-stage renal disease.

**Contraindications:**

Theophylline is contraindicated in patients with a history of hypersensitivity to theophylline or other components in the product.

**Warnings:**

Theophylline is contraindicated in patients with a history of hypersensitivity to theophylline or other components in the product.

**Precautions:**

**Special Populations (See Table I for mean clearance and half-life values)**

Serum Concentration-Effect Relationship:

Theophylline is rapidly and completely absorbed after oral administration in solution or immediate-release tablets. Theophylline does not undergo any appreciable systemic extraction during absorption. Theophylline has a half-life of 3 to 6 hours in normal volunteers and is reduced in patients with severe cardiac disease or hepatic insufficiency. Serum theophylline concentrations are also affected by factors such as age, weight, gender, and concurrent medications. The clearance of theophylline is decreased by 50% or more in patients with hepatic insufficiency and end-stage renal disease, no dosage adjustment is required in adults and children with severe hepatic impairment and no dosage adjustment is required in patients with end-stage renal disease. In patients with chronic asthma, including patients with severe asthma requiring inhaled corticosteroids, theophylline clearance is decreased by 50% or more in patients with severe hepatic impairment and no dosage adjustment is required in patients with end-stage renal disease. In patients with chronic asthma, including patients with severe asthma requiring inhaled corticosteroids, theophylline clearance is decreased by 50% or more in patients with severe hepatic impairment and no dosage adjustment is required in patients with end-stage renal disease.

**Contraindications:**

Theophylline is contraindicated in patients with a history of hypersensitivity to theophylline or other components in the product.

**Warnings:**

Theophylline is contraindicated in patients with a history of hypersensitivity to theophylline or other components in the product.

**Precautions:**

**Special Populations (See Table I for mean clearance and half-life values)**

Serum Concentration-Effect Relationship:

Theophylline is rapidly and completely absorbed after oral administration in solution or immediate-release tablets. Theophylline does not undergo any appreciable systemic extraction during absorption. Theophylline has a half-life of 3 to 6 hours in normal volunteers and is reduced in patients with severe cardiac disease or hepatic insufficiency. Serum theophylline concentrations are also affected by factors such as age, weight, gender, and concurrent medications. The clearance of theophylline is decreased by 50% or more in patients with hepatic insufficiency and end-stage renal disease, no dosage adjustment is required in adults and children with severe hepatic impairment and no dosage adjustment is required in patients with end-stage renal disease. In patients with chronic asthma, including patients with severe asthma requiring inhaled corticosteroids, theophylline clearance is decreased by 50% or more in patients with severe hepatic impairment and no dosage adjustment is required in patients with end-stage renal disease. In patients with chronic asthma, including patients with severe asthma requiring inhaled corticosteroids, theophylline clearance is decreased by 50% or more in patients with severe hepatic impairment and no dosage adjustment is required in patients with end-stage renal disease.
The Effect of Other Drugs on Theophylline Serum Concentration Measurements:

- Methadone: Clinical studies have shown that methadone administered concomitantly with theophylline does not alter plasma theophylline concentrations.
- Antiarrhythmics: Theophylline plasma concentrations may be increased by concomitant use of disopyramide or lidocaine.
- Oral contraceptives: The effects of oral contraceptives on theophylline disposition are not known.
- Acetylsalicylic acid (ASA): Small increases in theophylline peak plasma concentration. (ASA has no significant effect on theophylline steady state plasma concentration).
- Probenecid: Theophylline plasma concentrations are increased in patients on long-term treatment with probenecid.
- Mannitol: Theophylline clearance is increased by mannitol administration.
- Prilocaine: Prilocaine administration has no significant effect on theophylline steady state plasma concentration.

Carcinogenesis, Mutagenesis, and Impairment of Fertility:

No evidence of carcinogenicity has been observed in mice and rats treated with theophylline at increased doses, and the drug has been shown to be non-mutagenic in several in vitro and in vivo tests. It has been shown to have no effect on fertility in rats and mice.

Pregnancy:

Data are insufficient to evaluate the risk of teratogenicity in humans. It is not known whether theophylline is excreted in human milk. Because of its potential for serious adverse reactions in nursing infants, it is not recommended to use the drug in lactating women.

Pediatric Use:

The safety and efficacy of theophylline have been established in patients with asthma and bronchitis aged 12 months or older. Use in children under 12 months is not recommended due to the lack of adequate studies in this age group.

Elderly Patients:

Theophylline is generally well tolerated in elderly patients, but they may be more sensitive to the effects of overdosage. The dosage of theophylline should be selected with caution in elderly patients, and dosage adjustments may be required. Elderly patients are at significantly greater risk of experiencing serious toxicity from theophylline overdose compared to younger adults.

Pediatric:

The safety and efficacy of theophylline in children have not been established. Use in children under 12 months is not recommended due to the lack of adequate studies in this age group.

Drug Interactions:

- Theophylline and other drugs that are eliminated by renal clearance (e.g., probenecid, angiotensin-converting enzyme inhibitors) may interact if theophylline plasma concentrations are monitored.
- Theophylline may increase the serum concentrations of warfarin, and patients receiving warfarin should be monitored for evidence of increased anticoagulant activity.
- Theophylline may decrease the serum concentrations of digoxin, and patients receiving digoxin should be monitored for evidence of decreased digitalis optical activity.

Adverse Reactions:

- Theophylline is generally well tolerated, but adverse reactions such as nausea, vomiting, diarrhea, and abdominal discomfort are common. These reactions are generally dose-related and may be reduced by starting at a lower dose and gradually increasing it.
- Severe adverse reactions such as seizures, hemodynamic compromise, and respiratory depression are rare.

Dosage and Administration:

- The dose of theophylline should be individualized for each patient based on the patient's age, weight, renal function, and other factors.
- The most effective route of administration is oral, as theophylline is well absorbed orally and has a short half-life. Intravenous administration should be reserved for life-threatening overdosage.
- Theophylline may be administered continuously through a nasogastric tube in conjunction with appropriate measures to enhance theophylline clearance (e.g., a neonate where dialysis may not be technically feasible).
- Measurement of serum theophylline concentrations should be performed to guide dosage adjustments.

Table VI. Dosage adjustment guided by serum theophylline concentration.

- Theophylline dosage should be adjusted based on serum theophylline concentrations measured at 2-hour intervals until a steady state is achieved.
- Theophylline concentration should be measured immediately upon presentation, 2-4 hours later, and then at sufficient intervals, to guide dosage adjustments.

Contraindications:

- Theophylline is contraindicated in patients with known hypersensitivity to the drug, or those with severe hepatic or renal disease.
- Theophylline should be used with caution in patients with bronchial asthma or other obstructive lung disease, as it may exacerbate bronchial hyperresponsiveness.
- Theophylline should be used with caution in patients with cardiac disease, as it may cause arrhythmias.
- Theophylline should be used with caution in patients with a history of seizures, as it may cause seizures.
- Theophylline should be used with caution in patients with a history of psychiatric illness, as it may cause agitation or excitement.

Precautions:

- Theophylline should be used with caution in patients with a history of psychiatric illness, as it may cause agitation or excitement.
- Theophylline should be used with caution in patients with a history of respiratory compromise, as it may cause bronchospasm.
- Theophylline should be used with caution in patients with a history of cardiac disease, as it may cause arrhythmias.
- Theophylline should be used with caution in patients with a history of gastrointestinal disease, as it may cause gastrointestinal disturbances.
- Theophylline should be used with caution in patients with a history of allergic reactions, as it may cause allergic reactions.

Nursing Mothers:

- No data are available to evaluate the effects of theophylline on milk production in breastfeeding mothers. It is not known whether theophylline is excreted in human milk.

Pediatric:

- The safety and efficacy of theophylline in children have not been established. Use in children under 12 months is not recommended due to the lack of adequate studies in this age group.
- The most effective route of administration is oral, as theophylline is well absorbed orally and has a short half-life. Intravenous administration should be reserved for life-threatening overdosage.
- Theophylline may be administered continuously through a nasogastric tube in conjunction with appropriate measures to enhance theophylline clearance (e.g., a neonate where dialysis may not be technically feasible).