

## **Product Summary**

### **1. Trade Name of the Medicinal Product**

Aminophylline injection B.P. 500 mg /2 ml.

### **2. Qualitative and Quantitative Composition**

Each 2 ml of solution contains Aminophylline Hydrate B.P. 500 mg equivalent to 479.45mg aminophylline.

### **3. Pharmaceutical Form**

Clear, sterile solution for injection, intended for parenteral administration to human beings.

## **Clinical Particulars**

### **4.1 Therapeutic Indications**

Aminophylline is a complex of theophylline and ethylenediamine and is given for its theophylline activity to relax smooth muscle and to relieve bronchial spasm.

Aminophylline injection is indicated for relief of bronchospasm associated with asthma and in chronic obstructive pulmonary disease.

### **4.2 Posology and Method of Administration**

Aminophylline Injection B.P. 500mg/2ml is for deep intramuscular injection.

Adults:

For adult patients, including the elderly, a single dose of 500mg (2ml) may be administered by deep intramuscular injection.

Children:

Aminophylline Injection (intramuscular) 500mg in 2ml is not suitable for use in children.

For maintenance therapy, Aminophylline Injection (intravenous) 250mg in 10ml can be administered via larger volume infusion solutions, rate-regulated to deliver the required amount of drug each hour.

Therapeutic plasma concentrations of theophylline are considered to be in the range of 5 to 20mcg/ml and levels above 20mcg/ml are more likely to be associated with toxic effects. There is marked interpatient variation in the

dosage required to achieve plasma levels of theophylline that are within the desired therapeutic range.

During therapy, patients should be monitored carefully for signs of toxicity and, where possible, the serum theophylline levels should also be monitored.

### **4.3 Contra-indications**

Aminophylline should not be administered to patients with a known hypersensitivity to the xanthine group of drugs.

### **4.4 Special Warnings and Precautions for Use**

Elderly patients, or those with cardiac or hepatic disease should be monitored carefully for signs of theophylline toxicity. Children are particularly susceptible to the effects of theophylline and care is required when administering aminophylline to children.

There have been reports of seizures in children with theophylline plasma levels within the accepted therapeutic range. Alternative treatment should be considered in patients with a history of seizure activity and, if Aminophylline Injection is used in such patients, they should be carefully observed for possible signs of central stimulation.

Because the mean half-life of theophylline is shorter in smokers than in non-smokers, the former group may require larger doses of aminophylline.

To reduce the undesirable stimulating effects of aminophylline on the central nervous and cardiovascular systems, intravenous administration of the drug should be slow and should not exceed a rate of 25 mg/min.

Methylxanthines may increase gastric acidity and care should be taken when they are used in patients with a history of peptic ulceration.

Aminophylline should not be administered concurrently with other xanthine medications.

The label shall contain the following statements:-

Protect from light.

Store below 25°C.

If only part used discard the remaining solution.

Discard the ampoule if the contents are discoloured.

#### **4.5 Interactions with other Medicaments and other forms of Interaction**

Increased serum levels of theophylline have been reported in patients who were also taking cimetidine, erythromycin, ciprofloxacin, allopurinol, thiabendazole, diltiazem or oral contraceptives. Factors such as viral infection or cardiac failure can also reduce theophylline clearance. There is an increased likelihood of toxicity occurring if ephedrine or other sympathomimetic agents are given concomitantly with aminophylline.

The concomitant use of theophylline and fluvoxamine should usually be avoided. Where this is not possible, patients should have their theophylline dose halved and plasma theophylline should be monitored closely. Factors such as cardiac failure or viral infection, including infection with influenza virus, can also reduce theophylline clearance.

Smoking can increase clearance of theophylline, as can carbamazepine, phenytoin, rifampicin and sulphinpyrazone.

Xanthines can potentiate hypokalaemia resulting from beta<sub>2</sub> agonist therapy, steroids, diuretics and hypoxia. Particular caution is advised in severe asthma. It is recommended that serum potassium levels are monitored in such situations.

#### **4.6 Pregnancy and Lactation**

As with other drugs, aminophylline should only be used during pregnancy if considered essential by the physician. Theophylline crosses the placenta and is secreted into breast milk.

#### **4.7 Effects on Ability to Drive and Use Machines**

Nil.

#### **4.8 Undesirable Effects**

Aminophylline may cause gastro-intestinal irritation, with nausea, vomiting and abdominal pain. Symptoms of central nervous system stimulation may occur, including insomnia, restlessness and anxiety. Theophylline can precipitate cardiac arrhythmias and hypotension may follow intravenous injection, particularly if the injection is too rapid. Allergic reactions to aminophylline may occur.

## **4.9 Overdose**

Signs of overdosage may include gastrointestinal disturbances such as nausea and vomiting, manifestations of central nervous system stimulation including headache, restlessness and muscle twitching, and cardiovascular reactions such as palpitation and hypotension.

There is no specific antidote and treatment is supportive and symptomatic. Aminophylline therapy should be discontinued.

Metabolic disturbances, especially hypokalaemia, should be corrected immediately. Intravenous fluids, oxygen and other supportive measures should be administered to correct hypotension, dehydration and acid-base imbalance. Sympathomimetic agents should be avoided. Diazepam may be administered intravenously to control convulsions. A patent airway should be maintained and artificial respiration may be required for respiratory depression.

Theophylline is dialyzable; charcoal haemoperfusion and haemodialysis should be considered in cases of severe toxicity.

Serial plasma-theophylline concentrations should be measured until a decreasing trend to levels below 20mcg/ml has been demonstrated.

## **Pharmacological Properties**

### **5.1 Pharmacodynamic Properties**

Aminophylline is a complex of theophylline and ethylenediamine and is given for its theophylline activity to relax smooth muscle and to relieve bronchial spasm.

Theophylline is a smooth muscle relaxant and it relaxes the smooth muscle of the bronchial airways. Other actions of theophylline include cardiac stimulation, CNS stimulation, decreased peripheral vascular resistance and diuresis.

### **5.2 Pharmacokinetic Properties**

Theophylline is approximately 60% bound to plasma proteins but binding is decreased to about 40% in neonates and in adults with hepatic disease. The drug is widely distributed and it crosses the placenta and passes into breast milk.

Theophylline is metabolised in the liver and the metabolites are excreted in the urine. In adults, about 10% of a dose of theophylline is excreted unchanged in the urine. There is considerable inter-individual variation in the rate of hepatic metabolism of theophylline, resulting in large variations in clearance, serum concentrations and half-lives. Cigarette smoking increases theophylline clearance and shortens its serum half-life.

### **5.3 Preclinical Safety Data**

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

## **Pharmaceutical Particulars**

### **6.1 List of Excipients**

Ethylenediamine Ph. Eur.  
Water for Injections B.P.

### **6.2 Incompatibilities**

Incompatibility has been reported with chlorpromazine, clindamycin, corticotrophin, dimenhydrinate, doxorubicin, erythromycin gluceptate, hydralazine hydrochloride, hydroxyzine hydrochloride, opioid analgesics, oxytetracycline hydrochloride, phenytoin sodium, procaine hydrochloride, prochlorperazine salts, promazine hydrochloride, promethazine hydrochloride, sulphafurazole diethanolamine and vancomycin hydrochloride.

### **6.3 Shelf Life**

Unopened : 3 years (36 months)  
After reconstitution: not applicable.  
After first opening : not applicable\*

\*If only part of an ampoule is used, discard the remaining solution.

### **6.4 Special Precautions for Storage**

Protect from light.  
Store below 25°C.

### **6.5 Nature and Contents of Container**

2ml, clear glass ampoules, glass type 1 Ph. Eur. borosilicate glass presented in cardboard cartons to contain 10 x 2ml ampoules.

### **6.6 Instruction for Use/Handling**

For deep intramuscular injection.  
Use as directed by the physician.  
Keep out of reach of children.  
If only part used, discard the remaining solution.  
Discard the ampoule if the contents are discoloured.

### **Administrative Data**

7. Marketing Authorisation Holder

Antigen International Ltd.,  
Roscrea,  
Co. Tipperary,  
Ireland.

8. **Marketing Authorisation Number**

PL 2848/5939R.

9 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE  
AUTHORISATION**

13/03/2009

10 **DATE OF REVISION OF THE TEXT**

13/03/2009