Scheduling status

S2

Proprietary name (and dosage form)

Nuelin SA 250

Composition

Each Nuelin SA tablet contains 250 mg theophylline BP (anhydrous) in a slow release formulation.

Pharmacological classification

A 10.2 Bronchodilators

Pharmacological action

At the cellular level, the bronchodilatory effect of theophylline is thought to be due to an inhibition of the enzyme nucleotide phosphodiesterase. This enzyme is responsible for the destruction of cyclic 3,5-AMP. The effects of theophylline on bronchial smooth muscle are similar to those produced by bronchodilatory sympathomimetic amines. This similarity is probably related to their common ability to increase the cyclic 3,5-AMP concentration in the tissues.

Indications

Nuelin SA tablets are indicated for the treatment of bronchospasm.

Contra-indications

No other theophylline therapy should be administered concurrently with Nuelin SA. Theophylline may also reduce the therapeutic effect of lithium. Contra-indicated in individuals who have shown hypersensitivity to aminophylline or other xanthine derivatives.

Warnings

Nuelin SA tablets may be halved but **should not be crushed or chewed**.

Dosage and directions for use

Adults:	One Nuelin SA tablet orally twice daily (i.e. 12 hourly) to be increased gradually to two tablets twice daily (i.e. 12 hourly), if necessary and if tolerated.	
Children:	5 to 8 years:	24 mg/kg/24 hours
	9 to 12 years:	20 mg/kg/24 hours
	13 to 16 years:	18 mg/kg/24 hours

The average maintenance dose is 15 to 18 mg/kg/per day. However, the individual biotransformation varies and it is advisable to monitor theophylline therapy with serum assays of theophylline.

Side effects and special precautions

Side-effects associated with the use of xanthine derivatives include the following: insomnia, headache, nausea, vomiting, diarrhoea, diuresis, tremor, malaise, excitation, anorexia, dizziness, gastro-intestinal irritation, tachycardia and palpitations, reduced exercising ability, excessive sweating, visual disorders, gastro-intestinal bleeding and a metallic taste in the mouth.

Severe overdosage or idiosyncrasy may lead to maniacal behavior, repeated vomiting with extreme thirst, delirium, hyperthermia, and convulsions.

Periodic measurement of theophylline serum levels is recommended to assure maximal benefit without excessive risk. The incidence of toxicity increases at serum levels greater than 20 micrograms/ml.

High theophylline serum levels in association with clinical manifestations of toxicity may result from conventional doses in certain clinical situations such as: patients with lowered body plasma clearances (due to cardiac decompensation); patients with liver dysfunction or chronic obstructive lung disease; patients who are more than 55 years of age. Since status asthmaticus is a medical emergency, a patient who is not rapidly responsive to bronchodilators frequently requires additional appropriate medication.

Use theophylline with caution in patients with severe cardiac disease, arrhythmias, acute myocardial injury, congestive heart failure, cor pulmonale, hypertension, severe hypoxaemia, hyperthyroidism, liver or renal disease, dehydration, and in the elderly.

In patients with a history of peptic ulcer, the disorder may be exacerbated. Theophylline may act as a local gastro-intestinal irritant but gastro-intestinal symptoms are more commonly central and associated with serum concentrations exceeding 20 micrograms/ml.

Factors known to influence body clearance of theophylline include: cigarette smoking (increased clearance), age (decreasing clearance with increasing age), congestive heart failure (decreased clearance), liver disease (decreased clearance), pulmonary oedema (decreased clearance),

concurrent infection (decreased clearance) and concurrent administration of antibiotics e.g. erythromycin. In the presence of any of these factors, the monitoring of theophylline serum levels periodically is advisable. Other circumstances in which monitoring serum levels is advisable include: unexplained poor control of asthmatic signs and symptoms; occurrence of toxic symptoms; the addition or removal of other drugs from the therapeutic regimen that affect the metabolism of theophylline; use of unusually high doses.

Usage in pregnancy: Safe use in pregnancy has not been established.

Usage in nursing mothers: Theophylline should not be used in nursing women.

Known symptoms of overdosage and particulars of its treatment

Symptoms: See side-effects. Hypotension and convulsions may occur.

Treatment: Emergency treatment should be started immediately.

A.	**If overdose is established and seizure has not occurred:**	
	(1)	Induce vomiting mechanically even if emesis has occurred spontaneously. If vomiting is unsuccessful gastric lavage should be performed.
	(2)	Administer activated charcoal followed by a cathartic.

B.	**If overdose is established and seizure has occurred:**	
	(1)	Establish an airway.
	(2)	Administer oxygen.
	(3)	Treat the seizure with intravenous diazepam 0,1 to 0,3 mg/kg up to 10 mg.
	(4)	Monitor vital signs, maintain blood pressure and provide adequate hydration.

C.	**Post-seizure coma:**	
	(1)	Maintain airway and oxygenation.
	(2)	Follow above recommendations to prevent drug absorption , but perform intubation and lavage instead of inducing emesis. Introduce the cathartic and charcoal via a large bore gastric lavage tube.
	(3)	Continue to provide full supportive care and adequate hydration while waiting for the drug to be metabolised. This generally occurs rapidly enough so that consideration of dialysis is not warranted.

D.	General:
	Treatment is symptomatic and supportive. **Stimulants (e.g. Ipecac and analeptic agents) should not be used.**

Intravenous fluids may be required to overcome dehydration, acid-base imbalance and hypotension; the latter may also be treated with vasopressors. Apnoea requires ventilatory support. Hyperpyrexia, especially in children, may be treated with tepid water sponge baths or a hypothermic blanket. Theophylline serum levels should be monitored until they fall below 20 micrograms/ml. After emergency treatment medical monitoring should be continued.

Charcoal haemoperfusion should be considered in patients with severe theophylline intoxication as a possible means of preventing irreversible central nervous system damage.

Identification

White round biconvex tablets - markings N/L and 250.

Presentation

In bottles containing 56, 60 or 1000 tablets.

Storage instructions

Should be stored in tightly closed containers at or below 30 °C

KEEP OUT OF REACH OF CHILDREN

Registration number

P/10.2/54

Name and business address of applicant

iNova Pharmaceuticals (Pty) Limited
15e Riley Road
Bedfordview
South Africa

Date of publication of this package insert

8 October 1985