Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nuelin SA 250 mg Prolonged-release Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged-release tablet contains 250 mg theophylline.

Excipient with known effect:
Each tablet also contains 200 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release tablet
White, circular, biconvex tablet with breakline, 11 mm in diameter, marked ‘NLS 250’ on one side and ‘3M’ on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Nuelin is indicated for the prophylaxis and treatment of reversible bronchospasm in asthma, bronchitis and emphysema.

Theophylline is well established in the treatment of bronchospasm. It also has anti-inflammatory effects which may be of benefit to patients with asthma.

4.2 Posology and method of administration

Adults: A starting dose of 175 mg twice daily or 5 mg/kg/day is recommended. If well tolerated this may be increased to 350 mg twice daily or 10 mg/kg/day. Adults weighing less than 60 kg may require a lower maintenance dose (e.g. 250 mg twice daily) and those weighing over 80 kg (lean body mass) may require more. The dose should not exceed 750 mg if serum theophylline monitoring is not to be carried out.

Children: Nuelin SA 250 tablets are not recommended for use in children under 12 years of age.

Regular monitoring of plasma concentrations is highly recommended. If plasma monitoring is not undertaken the maximum dose should not exceed 20 mg/kg/day, or 700 mg, whichever is the lesser.

Elderly: Elderly patients may require lower doses due to reduced theophylline clearance.

If adverse effects are experienced the dose should be reduced immediately to a level at which they no longer occur.

Dose increases should be made, if required, at intervals of not less than three days until optimum clinical response is achieved. The peak serum theophylline level should not exceed 20 microgram/ml and steady state levels should not exceed 15 microgram/ml.

Overweight patients: Theophylline does not distribute into fat. Dosage calculations should be based on lean body mass.

Patients vary in their response to xanthines and it is necessary to titrate doses individually using serum concentrations as a guide. Steady state concentrations are generally reached 3 - 4 days after dose adjustment. If a satisfactory clinical response is not achieved, serum theophylline should be measured 10 - 12 hours after the last dose.

The peak serum theophylline concentration (4 - 6 hours post dose) must not exceed 20 microgram/ml.

4.3 Contraindications

Hypersensitivity to theophylline or other xanthines.

Patients with cystic fibrosis may require lower dose because of reduced liver function. Patients being treated with theophylline should not receive electroconvulsive therapy (ECT).

4.4 Special warnings and precautions for use

Use with caution in patients with insomnia, cardiac arrhythmias, peptic ulcer, hyperthyroidism and severe hypertension.

Smoking and alcohol consumption may increase theophylline clearance and increased doses of theophylline are therefore required. In patients with cardiac failure, hepatic dysfunction/disease and fever the reverse is true and these patients may require a reduced dosage. Epilepsy may become uncontrolled.

It is not recommended that the product be used concurrently with non-specific adrenergic agonists, especially adrenaline and ephedrine, or with glucagons or other xanthine drugs as these will potentiate the effects of theophylline.

Xanthines can potentiate hypokalaemia resulting from beta-2-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.

Herbal preparations containing St. John’s Wort (*Hypericum perforatum*) should not be used while taking Nuelin SA 250 due to the risk of decreased plasma concentrations and reduced clinical effects of Nuelin SA 250 (see 4.5 Interactions).

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine, allopurinol, corticosteroids, frusemide, isoprenaline, oral contraceptives, thiabendazole, quinolone antibiotics, diltiazem, verapamil, ciprofloxacin, erythromycin or other macrolide antibiotics delay the elimination of theophylline. A reduction of the theophylline dosage is recommended. Phenytoin, carbamazepine, barbiturates, rifampicin, sulphinpyrazone increase theophylline clearance and therefore the theophylline dosage may need to be increased.

Theophylline can increase lithium excretion.

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.

Plasma concentrations of theophylline can be reduced by concomitant use of the herbal preparation St John’s Wort (*Hypericum perforatum*). This is due to induction of drug metabolising enzymes by St. John’s Wort. Herbal preparations containing St. John’s Wort should therefore not be combined with Nuelin SA 250. The inducing effect may persist for at least 2 weeks after cessation of treatment with St. John’s Wort. If a patient is already taking St. John’s Wort check theophylline levels and stop St. John’s Wort.

The dose of theophylline may need adjusting.

4.6 Fertility, pregnancy and lactation

There is inadequate evidence of safety of the drug in human pregnancy but it has been in wide use for many years without apparent ill consequence; there is evidence of harmful effects in pregnancy in animals. Theophylline crosses the placenta and may result in potentially dangerous serum theophylline concentrations in the foetus. Nuelin should not be given during pregnancy unless considered essential by the physician.

Theophylline is excreted in breast milk and has been shown to cause irritability in infants. It is therefore recommended that the mother nurses her infant just prior to taking her next dose, when plasma theophylline levels are expected to be low.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

The following adverse reactions may occur: nausea, vomiting, dyspepsia, abdominal pain, headache, dizziness, dermatitis/rash, tremor, tachycardia, palpitations, dysrhythmia, vascular collapse, agitation, nervousness and convulsions. These are a result of the pharmacological activity of the drug.

4.9 Overdose

Over 3g could be serious in an adult (40mg/kg in a child). The fatal dose may be as little as 4.5g in an adult (60 mg/kg in a child), but is generally higher.

Symptoms:
Warning: serious features may develop as long as 12 hours after overdosage with sustained release formulations.

Alimentary features:
Nausea, vomiting (which is often severe), epigastric pain and haematemesis. Consider pancreatitis if abdominal pain persists.

Neurological features:
Restlessness, hypertonia, exaggerated limb reflexes and convulsions.
Coma may develop in very severe cases.

Cardiovascular features:
Sinus tachycardia is common. Ectopic beats and supraventricular and ventricular tachycardia may follow.

Metabolic features:
Hypokalaemia due to shift of potassium from plasma into cells is common, can develop rapidly and may be severe. Hyperglycaemia, hypomagnesaemia and metabolic acidosis may also occur. Rhabdomyolysis may also occur

Management:

Activated charcoal or gastric lavage should be considered if a significant overdose has been ingested within 1-2 hours. Repeated doses of activated charcoal given by mouth can enhance theophylline elimination. Measure the plasma potassium concentration urgently, repeat frequently and correct hypokalaemia. BEWARE! If large amounts of potassium have been given, serious hyperkalaemia may develop during recovery. If plasma potassium is low then the plasma magnesium concentration should be measured as soon as possible.

In the treatment of ventricular arrhythmias, proconvulsant antiarrhythmic agents such as lignocaine (lidocaine) should be avoided because of risk of causing or exacerbating seizures.

Measure the plasma theophylline concentration regularly when severe poisoning is suspected, until concentrations are falling. Vomiting should be treated with an antiemetic such as metoclopramide or ondansetron.

Tachycardia with an adequate cardiac output is best left untreated. Beta-blockers may be given in extreme cases but not if the patient is asthmatic. Control isolated convulsions with intravenous diazepam. Exclude hypokalaemia as a cause.

Haemoperfusion is probably only of value on acute overdose, before the onset of major complications.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Theophylline directly relaxes smooth muscle thus acting mainly as a bronchodilator and vasodilator. The drug also possesses other actions typical of the xanthine derivatives - coronary vasodilator, diuretic, cardiac stimulant, cerebral stimulant and skeletal muscle stimulant.

5.2 Pharmacokinetic properties

It has been established that the xanthines, which include theophylline, are readily absorbed after oral, rectal or parenteral administration and this is well documented in published literature.

Theophylline is excreted in the urine as metabolites, mainly 1,3-dimethyluric acid and 3-methylxanthine, and about 10% is excreted unchanged.

Plasma half-lives ranging from 3 to 9 hours and therapeutic plasma concentrations from about 5 to 20 microgram per ml have been reported.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate
Cellulose acetate phthalate
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 30ºC.

6.5 Nature and contents of container

Nuelin SA tablets are supplied in UPVC blister packs. Each pack contains 60 tablets.

The UPVC pack comprises:

i) 250 micron clear rigid UPVC
ii) 20 micron hard temper aluminium foil coated for sealing to UPVC.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Meda Health Sales Ireland Limited,
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8 MARKETING AUTHORISATION NUMBER

PA 1332/20/2

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