SUMMARY OF PRODUCT CHARACTERISTICS PHENOBARBITAL 30 MG TABLETS

1. Name of the Medicinal Product

Phenobarbital 30 mg Tablets

2. Qualitative and Quantitative Composition

Each tablet contains 30 mg of Phenobarbital BP.

3. Pharmaceutical Form

Uncoated Tablet

White circular, flat bevelled-edge tablet, embossed ‘p’ on One side and ‘30’ on the other side.

4. Clinical Particulars

4.1 Therapeutic Indications

Phenobarbital is recommended for all forms of epilepsy (except absence seizures)

4.2 Posology and Method of administration

Adults: 60-180mg at night

Child: 5-8mg/kg daily

Elderly: Phenobarbital clearance diminishes in the elderly. Therefore the dose of phenobarbital is usually lower in elderly patients.

The dose of phenobarbital should be adjusted to meet the needs of individual patients. This usually requires plasma concentration of 15 to 40 micrograms/ml (65 to 170 micromoles/litre).

Method of Administration-For oral administration

4.3 Contraindications

Phenobarbital should not be given to patients with:

- Known hypersensitivity to phenobarbital, other barbiturates or other ingredients in the tablet
- Acute intermittent porphyia
- Severe respiratory depression
- Severe renal or hepatic impairment.

4.4 Special warnings and precautions for use

Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications.

Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered.

Steven-Johnson syndrome and toxic epidermal necrolysis

Life-threatening cutaneous reactions Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the use of phenobarbital. Patients should be advised of the signs and symptoms and monitored closely for skin reactions.

If symptoms or signs of SJS or TEN (e.g. progressive skin rash often with blisters or mucosal lesions) are present, Phenobarbital treatment should be discontinued.

If the patient has developed SJS or TEN with the use of phenobarbital, phenobarbital must not be re-started in this patient at any time.

Care should be used in the following situations:

• Patients with the rare hereditary problems of galactose intolerance, the lapp lactase deficiency or glucose – galactose malabsorption should not take this medicine
• Respiratory depression (avoid if severe)
• Young, debilitated or senile patients
• Renal impairment
• Existing liver disease
• Sudden withdrawal should be avoided as severe withdrawal syndrome (rebound insomnia, anxiety, tremor, dizziness, nausea, fits and delirium) may be precipitated
• Acute chronic pain – paradoxical excitement may be induced or important symptoms masked.

• Prolonged use may result in dependence of the alcohol-barbiturate type. Care should be taken in treating patients with a history of drug abuse or alcoholism.

4.5 Interaction with other medicinal products and other forms of interaction

Valproate and phenytoin have been reported to cause rises in Phenobarbital (and primidone) concentrations in plasma. The effects of Phenobarbital and other barbiturates are enhanced by other CNS depressants including alcohol. Phenobarbital and other barbiturates may reduce the activity of many drugs by increasing the rate of metabolism through induction of drug-metabolising enzymes in liver microsomes.

4.6 Pregnancy and lactation

Phenobarbital therapy in epileptic pregnant women presents a risk to the fetus in terms of major and minor congenital defects such as congenital craniofacial, digital abnormalities and, less commonly, cleft lip and palate. The risk of teratogenic effects developing appears to be greater if more than one antiepileptic drug is administered. The risk to the mother, however is greater if phenobarbital is withheld and seizure control is lost. The risk: benefit balance, in this case, favours continued use of the drug during pregnancy at the lowest possible level to control seizures.

Patients taking phenobarbital should be adequately supplemented with folic acid before conception and during pregnancy. Folic acid supplementation during pregnancy can help to reduce the risk of neural defects to the infant.

Phenobarbital readily crosses the placenta following oral administration and is distributed throughout fetal tissue, the highest concentrations being found in the placenta, fetal liver and brain. Adverse effects on neurobehavioral development have also been reported.

Haemorrhage at birth and addiction are also a risk. Prophylactic treatment with vitamin K1 for the mother before delivery (as well as the neonate) is recommended, the neonate should be monitored for signs of bleeding.

Phenobarbital is excreted into breast milk and there is a small risk of neonatal sedation. Breast feeding is therefore not advisable.

4.7 Effects on ability to drive and use machines

Phenobarbital may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. Patients should be advised to make sure they are not affected before undertaking any potentially hazardous tasks.

4.8 Undesirable Effects

Blood and the lymphatic system disorders: megaloblastic anaemia (due to folate deficiency), agranulocytosis, thrombocytopenia.

• Metabolism and nutritional disorders: osteomalacia, rickets.

•Psychiatric disorders: paradoxical reaction (unusual excitement), hallucinations, restlessness and confusion in the elderly, mental depression, memory and cognitive impairment, drowsiness, lethargy.

• Nervous system disorders: hyperactivity, behavioural disturbances in children, ataxia, nystagmus.

• Cardiac disorders: hypotension.

• Respiratory disorders: respiratory depression.

• Hepato-bilary: hepatitis, cholestasis.

•Skin and subcutaneous tissue disorders: allergic skin reactions (maculopapular morbilliform or scarlatiniform rashes), other skin reactions such as exfoliative dermatitis, erythema multiforme.

Severe cutaneous adverse reactions (SCARs): Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported.

Frequency: very rare

• General disorders and administration site conditions: antiepileptic hypersensitivity syndrome (features include fever, rash, lymphadenopathy, lymphocytosis, eosinophilia, hematological abnormalities, hepatic and other organ involvement including renal and pulmonary systems which may become life threatening).

5 Overdose

Toxicity varies between patients; tolerance will develop with chronic use. Features of poisoning are to be expected after ingestion of 1g in adults.

Features:

Drowsiness, dysarthria, ataxia, nystagmus and disinhibition. There may also be coma, cardiovascular collapse, cardiac arrest, hypotension, hypotonia, hyporeflexia, hypothermia, hypotension and respiratory depression. Barbiturates decrease gut motility, which may lead to slow onset and worsening of symptoms or cyclical improvement and worsening of symptoms.

Management:

Consider activated charcoal (50g for an adult, 10-15g for a child under 5 years) if more than 10mg/kg body weight of phenobarbital has been ingested within 1 hour, provided the airway can be protected. Repeat dose activated charcoal is the best method of enhancing elimination of phenobarbital in symptomaticpatients. In severe hypotension dopamine or dobutamine can be used. Treat rhabdomyolysis with urinary alkalinistion. Haemodialysis or haemofiltrationmay be required for cases of acute renal or severe hyperkalaemia.

Charcoal haemoperfusion is the treatment of choice for the majority of patients with severe barbiturate poisoning who fail to improve, or who deteriorate despite good supportive care.

6 Pharmacological Properties

6.1 Pharmacodynamic Properties

Phenobarbital is a long-acting barbiturate, which because of its depressant effect on the motor cortex, is used in the treatment of epilepsy.

Phenobarbital has a widespread depressant action on cerebral function. It has sedative effects and has some protective action against all varieties of human partial and generalised epilepsy, with the exception of absence seizures.

Phenobarbital is also effective in preventing seizures in the corresponding experimental animal models of epilepsy. In different studies phenobarbital appears to have had inconsistent effects in suppressing experimental epileptic foci, and epileptic after-discharges, but it inhibits synaptic transmission, at least in the spinal cord. The drug's probable biochemical mechanism of action is through prolonging the opening time of Cl- ion channels in postsynaptic neuronal membranes. This effect causes membrane hyperpolarisation and thus impairs nerve impulse propagation. Phenobarbital also decreases intraneuronal Na+ concentrations, and inhibits Ca2+ influx into depolarised synaptosomes. It raises brain serotonin levels, and inhibits noradrenaline (norepinephrine) reuptake into synaptosomes. These additional biochemical actions may contribute towards the anticonvulsant effects of the drug.

6.2 Pharmacokinetic Properties

Absorption – phenobarbital is readily absorbed from the gastrointestinal tract, although it is relatively lipid – insoluble; peak concentrations are reached in about 2 hours after oral administration.

Distribution – phenobarbital is about 45 to 60% bound to plasma proteins. Phenobarbital crosses the placental barrier and is distributed into breast milk.

Metabolism – the plasma half life is about 75 to 120 hours in adults but is greatly prolonged in neonates, and shorter (about 21 to 75 hours) in children. There is considerable interindividual variation in phenobarbital kinetics. Phenobarbital in only partly metabolised in the liver.

Elimination – about 25% of a dose is excreted in the urine unchanged at normal urinary pH.

6.3 Preclinical safety data

Not applicable.

7 Pharmaceutical Particulars

7.1 List of Excipients

Lactose BP

Maize Starch BP

Potassium Sorbate BP

Purified Water BP

Sodium Lauryl Sulphate BP

Colloidal Anhydrous Silica BP

Magnesium Stearate BP

7.2 Incompatibilities

None

7.3 Shelf life

3 Years

7.4 Special precautions for storage

Store in a dry place below 30°C. Protect from light.

7.5 Nature and contents of container

PVC/ALU blister packing

7.6 Instructions for use, handling and disposal

No special requirements

8 Registrant

Cosmos Limited

9 Manufacturer

Cosmos Limited
Rangwe Road; Off Lunga Lunga, Industrial Area
P.O Box 41433, GPO 00100-Nairobi
Kenya
Telephone: + (254-20) 2519603/4/5, 020 8042200/2/3/4/5
Telefax: +254-020-8096280/1
E-mail: admin@cosmos-pharm.com