SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Phenobarbital Tablets BP 30 mg.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 30 mg Phenobarbital PhEur.

3. PHARMACEUTICAL FORM

Tablets for oral use.

Appearance: White, circular, biconvex tablet.

4.1. Therapeutic indications

Phenobarbital tablets are indicated for the management of all forms of epilepsy except absence seizures.

4.2. Posology and Method of Administration

Adults and the elderly: 60 - 180 mg daily at night.

Caution must be exercised in the treatment of elderly patients with careful monitoring of their condition.

Children: 5 - 8 mg per kg bodyweight daily.

Administration: Oral; the tablets should be swallowed with water.

4.3 Contra-Indications

1. Known hypersensitivity to barbiturates.
2. Hypersensitivity to any of the ingredients in this medicine.
3. Acute intermittent porphyria.
4. Severe respiratory depression.
5. Severe impairment of renal and hepatic function.

4.4. Special Warnings and Special Precautions for Use

Phenobarbital should be used with caution in the young, debilitated or senile patients and those with renal impairment, existing liver disease or respiratory depression (should be avoided if severe).

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

Avoid sudden withdrawal to prevent rebound seizures.

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. A meta-analysis of randomised placebo controlled trials of anti-epileptic drugs has also shown a small increased risk of suicidial ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increase risk for Phenobarbital.
Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.

Phenobarbital should be used with caution in the young, elderly, debilitated or senile patients and those with renal impairment, existing liver disease or respiratory depression (should be avoided if severe), pregnancy and breast-feeding and porphyria.

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

Avoid sudden withdrawal to prevent rebound seizures.

This product contains lactose. 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

Phenobarbital may induce liver microsomal enzymes and the rate of metabolism of certain drugs can be increased and serum concentrations of the following drugs may be reduced: coumarin anticoagulants, phenytoin, carbamazepine, clonazepam, an active metabolite of oxcarbazepine, tigabine, doxycycline, metronidazole, haloperidol, lopinavir, montelukast, toremifene, ethosuximide, gestrinone, tibolone, tropisetron, lamotrigine, phenylbutazone, systemic corticosteroids including oral contraceptives (which may lead to contraceptive failure), griseofulvin, mianserin, rifampicin, phenothiazines, tricyclic antidepressants, chloramphenicol, cyclosporin, calcium channel antagonists (especially felodipine, verapamil, isradipine and probably nicardipine, nimodipine and nifedipine – may require an increase in dosage, and other dihydropyridines, and diltiazem which may require an increase in dosage), theophylline, anti-virals (e.g. indinavir and saquinavir), anti-arrhythmics (e.g. disopyramide and quinidine), digitoxin and high doses of folic acid.

Vitamin D requirements may be increased.

Antagonism of the anticonvulsant effect of Phenobarbital (convulsive threshold lowered) can occur when taken with antipsychotic and antidepressant drugs.

The plasma concentration of Phenobarbital may possibly be reduced by folic acid and folinic acid.

Increased sedative effects may occur with phenytoin and sodium valproate. Concomitant administration of phenobarbital and other anti-epileptics may increase the toxicity of phenobarbital without a corresponding increase in the anti-epileptic effect.

Concurrent administration with alcohol may lead to an additive CNS depressant effect.

Phenobarbital has been shown to accelerate the metabolism of levothyroxine and liothyronine. Prescribers should be alert for changes in thyroid status if barbiturates are added or withdrawn from patients being treated for hypothyroidism.

The effect of phenobarbital can be reduced by concomitant use of the herbal remedy St John's wort *(Hypericum perforatum).*

4.6. Pregnancy and lactation

The use of phenobarbital in pregnancy, especially the first and third trimesters should be avoided unless it is considered to be essential. Phenobarbital can cross the placental barrier and there is an increased risk of teratogenicity. Neonatal bleeding may occur and prophylactic treatment with vitamin K1 for the mother before delivery (as well as for the neonate) is recommended.

Patients taking phenobarbital should be adequately supplemented with folic acid before conception and during pregnancy to counteract the risk of neural tube defects.

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 or operating machinery. If patients are affected they should not drive or operate machinery.

4.8. Undesirable effects

Memory and cognitive impairment in the elderly, hyperactivity and behavioural disturbance in children. Drowsiness, lethargy, mental depression. Ataxia, nystagmus and respiratory depression. Megaloblastic anaemia (due to folate deficiency). Hepatitis, cholestasis and osteomalacia have been associated with barbiturate administration.

Hypersensitivity reactions occur in a small proportion of patients; skin reactions are reported in 1 to 3% of patients receiving phenobarbital, and are most commonly maculopapular, morbilliform or scarlatiniform rashes. Severe reactions such as exfoliative dermatitis, erythema multiforme and toxic epidermal necrolysis are extremely rare.

4.9. Overdose

Drowsiness, coma, respiratory depression, hypotension and hypothermia. The duration and depth of cerebral depression varies with the dose and tolerance of the patient. Supportive measures alone may be sufficient if symptoms are mild. If within four hours of ingestion, gastric aspiration or lavage may be of benefit in adults. The prime objective of treatment is to maintain vital functions while the majority of the drug is metabolised by hepatic enzymes. Given normal renal function, forced alkaline diuresis (maintaining the urinary

pH at approximately 8 by intravenous infusion) may enhance the excretion of the drug from the kidneys. Charcoal haemoperfusion is the treatment of choice for the majority of patients with very severe barbiturate poisoning who fail to improve, or who deteriorate despite good supportive care.

5.1. Pharmacodynamic properties

Pharmacodynamic group: (antiepileptics, barbiturates and derivatives)
ATC Code: N03 AA02

The barbiturates reversibly depress the activity of all excitable tissues. The CNS is extremely sensitive and when barbiturates are given in sedative or hypnotic doses there is little effect on skeletal, cardiac or smooth muscle. The ability of phenobarbital to exert maximum anticonvulsant action at doses below those required for hypnosis, determine its clinical use as an anti-epileptic. It limits the spread of seizure and elevates the seizure threshold. Although a precise relationship between the therapeutic results and concentration in blood plasma does not exist, plasma concentrations of 10 to 25µg/ml are usually recommended for the control of epilepsy; 150µg/ml is the minimum for prophylaxis against febrile convulsions.

5.2. Pharmacokinetic Properties

Oral absorption of phenobarbital is complete but somewhat slow, peak concentrations in plasma occur several hours after a single dose. It is 40 to 60% bound to plasma proteins and bound to a similar extent in tissues including the brain. By the oral route the rate determining step in absorption from the empty stomach is dissolution and dispersal of the drug in the gastrointestinal tract. Absorption takes place mainly from the intestine. The volume of distribution is approximately 0.5 litres per kilogram. The plasma half-life of phenobarbital is about 100 hours in adults, somewhat longer in neonates while it is shorter and more variable in children. The pKa of phenobarbital is 7.3 and up to 25% of a dose is eliminated by pH dependent renal excretion of the unchanged drug. The amount excreted increases with increased alkalinity of the urine. The remainder is inactivated by hepatic microsomal enzymes. Although the drug competes with other weak acids for binding to plasma albumin the only clinically important displacement is that of thyroxine. The absorption of dicumarol and griseofulvin are decreased by phenobarbital.

5.3. Preclinical safety data

Preclinical information has not been included because the safety profile of Phenobarbital has been established after many years of clinical use. Please refer to section 4.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Maize starch, lactose monohydrate, sodium laurilsulfate, sodium starch glycollate, magnesium stearate, stearic acid.

6.2. Incompatibilities

No incompatibilities stated.

6.3. Shelf Life

3 years.

6.4. Special Precautions for Storage

Do not store above 25°C.
Keep the container tightly closed.
Store in the original container.

6.5. Nature and Content of Container

Polypropylene tubes with low density polyethylene caps.

Pack sizes: 28 and 1,000 tablets.

6.6. Instructions for Use, Handling and Disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Limited
Waterford Road
Clonmel
Co. Tipperary
Ireland

8. MARKETING AUTHORISATION NUMBER

PL 00790/0024

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17/12/2008

10 DATE OF REVISION OF THE TEXT

06/05/2009