

Section 3 - Summary of Product Characteristics

Product Summary

1 Trade Name of the Medicinal Product

PHENOBARBITAL TABLETS BP 30mg

2 Qualitative and Quantitative Composition

Each tablet contains 30mg Phenobarbital PhEur.

3 Pharmaceutical Form

White uncoated tablets.

Clinical Particulars

4.1 Therapeutic Indications

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

4.2 Posology and Method of Administration

Adults: 60-300mg at night.

Child: 5-10mg/kg daily

Elderly: No specific dosage recommendations.

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 porphyria.
- severe respiratory depression.
- severe renal or hepatic impairment.

4.4 Special Warnings and Precautions for Use

Care should be taken when prescribing phenobarbital in the following situations:

- young, debilitated or senile patients.
- renal impairment.
- existing liver disease.
- respiratory depression (avoid if severe).
- history of asthma - hypersensitivity reactions such as bronchospasm more likely.

- 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.
- severe anaemia - may be complicated by barbiturate induced respiratory depression.
- diabetes mellitus.
- hyperactivity - may be exacerbated.
- 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 Interactions with other Medicaments and other forms of Interaction

The following drug interactions should be considered when prescribing phenobarbital:

- Phenobarbital may induce liver microsomal enzymes, increasing the rate of metabolism of certain drugs. The serum concentrations of the following drugs may be reduced: coumarin anticoagulants, anti-epileptic drugs (such as phenytoin, carbamazepine, sodium valproate, lamotrigine), tricyclic antidepressants, mianserin, phenothiazines, systemic steroids including oral contraceptives, (which may lead to contraceptive failure), fenoprofen, phenylbutazone, griseofluvin, rifampicin, chloramphenicol, doxycycline, metronidazole, ciclosporin, theophylline, digitoxin, calcium channel antagonists (especially felodipine, verapamil, nimodipine and nifedipine - may require an increase in dosage), antiarrhythmics (disopyramide and quinidine), paracetamol, mexiletine.
- The metabolism of thyroxine is accelerated by phenobarbital. Prescribers should be alert for changes in thyroid status if barbiturates are added or withdrawn from patients being treated for hypothyroidism.
- Increased sedative effects may occur with phenytoin and sodium valproate.
- Vitamin D requirements may increase.
- Antipsychotics and antidepressant may antagonise anticonvulsant effects (seizure threshold lowered).
- Carbonic anhydrase inhibitors may enhance the risk of barbiturate induced osteomalacia.
- Methylphenidate - concurrent use may increase serum concentration of phenobarbital.
- Concurrent administration with alcohol may lead to an additive CNS depressant effect. This effect is likely with concurrent administration with other CNS depressants.
- Phenobarbital may interfere with some laboratory tests including metyrapone test, phenolamine tests and serum bilirubin estimation.
- 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

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. Following parenteral administration fetal blood concentration approaches maternal blood concentration. Barbiturates have been shown to cause an increased incidence of fetal abnormalities. The use of phenobarbital in pregnancy, especially the first and third trimesters should be avoided unless considered essential. Neonatal bleeding may occur and prophylactic treatment with vitamin K₁ for mother before delivery (as well as for neonate) is recommended. Patients taking phenobarbital should be adequately supplemented with folic acid before conception and during pregnancy.

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 effected before undertaking any potentially hazardous tasks.

4.8 Undesirable Effects

Phenobarbital treatment may cause the following undesirable effects:

Effects on CNS - mental depression, paradoxical reactions (unusual excitement), hallucinations, memory and cognitive impairment, hyperactivity, behavioural disturbances, drowsiness, lethargy, ataxia, nystagmus.

Effects on lungs - respiratory depression.

Effects on skin - allergic skin reactions (maculopapular morbilliform or scarlatiniform rashes), other skin reactions such as exfoliative dermatitis, erythema multiforme, toxic epidermal necrosis or Stevens-Johnson syndrome are rare.

Effects on blood - megaloblastic anaemia (due to folate deficiency), agranulocytosis, thrombocytopenia.

Other effects - hepatitis, cholestasis, osteomalacia, rickets, hypotension.

4.9 Overdose

Symptoms - drowsiness, coma, respiratory depression, hypotension and hypothermia. Duration and depth of cerebral depression varies with the dose and tolerance of the patient.

Treatment - supportive measures may be sufficient if symptoms are mild. If within four hours of ingestion gastric aspiration or lavage may be beneficial to 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 severe barbiturate poisoning who fail to improve, or who deteriorate despite good supportive care.

Pharmacological Properties

5.1 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 reuptake into synaptosomes. These additional biochemical actions may contribute towards the anticonvulsant effects of the drug.

5.2 Pharmacokinetic properties

Phenobarbital is readily absorbed from the gastrointestinal tract after oral dosage and onset of action is within 30 minutes. Plasma half life is extended, and can be up to 100 hours in adults.

5.3 Preclinical safety data

Not applicable.

Pharmaceutical Particulars

6.1 List of excipients

Also contains lactose, magnesium stearate, maize starch.

6.2 Incompatibilities

Incompatible with macrogol.

6.3 Shelf-life

Shelf-life

Three years from the date of manufacture (polypropylene tablet containers).

Two years from the date of manufacture (blisters & amber glass bottles).

Shelf-life after dilution/reconstitution

Not applicable.

Shelf-life after first opening

Not applicable.

6.4 Special precautions for storage

Store below 25°C in a dry place.

6.5 Nature and contents of container

The product containers are rigid injection moulded polypropylene or injection blow-moulded polyethylene tablet containers with polyfoam wad or polyethylene ullage filler and snap-on

polyethylene lids; in case any supply difficulties should arise the alternative is amber glass bottles with screw caps and polyfoam wad or cotton wool.

The product may also be supplied in blister packs in cartons:

- a) Carton: Printed carton manufactured from white folding box board.
- b) Blister pack: (i) 250µm white rigid PVC. (ii) Surface printed 20µm hard temper aluminium foil with 5-7g/M² PVC and PVdC compatible heat seal lacquer on the reverse side.

Pack sizes: 28s, 30s, 56s, 60s, 84s, 90s, 100s, 112s, 120s, 168s, 180s, 250s, 500s, 1000s

6.6 Instructions for use/handling

Not applicable.

Administrative Data

7 MARKETING AUTHORISATION HOLDER

Name or style and permanent address of registered place of business of the holder of the Marketing Authorisation:

Actavis UK Limited
(Trading style: Actavis)
Whiddon Valley
BARNSTAPLE
N Devon EX32 8NS

8 Marketing Authorisation Number

PL 0142/0418

9 Date of First Authorisation/Renewal of Authorisation

29.11.96
Renewed: 03.02.02

10 DATE OF REVISION OF THE TEXT

May 2007