1.3.1.1 Proposed Professional Information

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

SEDABARB

2. QUALITATIVE AND QUANTITAIVE COMPOSITION

Each tablet contains:

Phenobarbitone 30 mg

Contains sugar: Lactose monohydrate 17,9 mg per tablet

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet

White normal biconvex tablet, with a breakline on one side, 5,5 mm in diameter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SEDABARB is indicated for the prophylactic treatment of epilepsy of a convulsive type and as a general sedative.

4.2 Posology and method of administration

For Epilepsy - 1 tablet morning and at night.

For Hypnotic - 1 tablet to be taken one hour before bedtime.

For Sedative - 1 tablet to be taken three times a day.

4.3 Contraindications

SEDABARB is contraindicated in patients with:

- Hypersensitivity to barbiturates, in cases of acute intermittent porphyria, in severe hepatic or renal function impairment and in hyperkinetic children or to any of the excipients in listed in section 6.1.
- Patients with acute intermittent porphyria.

4.4 Special warnings and precautions for use

- Prolonged use of **SEDABARB** may lead to dependence of the barbiturate - alcohol type.
- Abrupt withdrawal of **SEDABARB** may result in a severe abstinence syndrome, which includes grand mal seizures and delirium. Withdrawal of **SEDABARB** in these cases should be cautious and gradual.
- Tolerance to the hypnotic effects of **SEDABARB** may also occur after prolonged administration.
- **SEDABARB** should be administered cautiously to the elderly; reduced dosage should be employed until tolerance is assessed.
- It should be used with care in patients with impaired hepatic or renal function.
- Care is needed when **SEDABARB** is given to patients with severe respiratory insufficiency.
- Contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucosegalactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

The effects of **SEDABARB** is enhanced by concurrent administration of other sedatives, monoamine oxidase inhibitors, and some tranquillisers, and may be enhanced by anticholinesterases, sodium valproate, sulphonylurea antidiabetics, and tricyclic antidepressants. The concomitant administration of **SEDABARB** and alcohol may produce very serious respiratory depression and a lowering of the lethal dose of **SEDABARB.**

The effects of other depressants of the central nervous system such as anaesthetics,

antihistamines and narcotic analgesics may also be enhanced by barbiturates.

The effects of phenothiazines may be initially enhanced and subsequently diminished. The effects of **SEDABARB** may be diminished by rendering the urine alkaline and possibly by reserpine and folic acid.

SEDABARB may also enhance the activity of methotrexate, cyclophosphamide, and sulphonylureas, as well as the toxic effects of tricyclic antidepressants.

SEDABARB increases the rate of metabolism of many medicines by induction of metabolising enzymes in liver microsomes. This may result in a reduction in activity. Medicines affected include carbamazepine, coumarin anticoagulants, doxycycline, folic acid, phenylbutazone, phenazone, phenytoin, corticosteroids and other steroid hormones, cyclosporin, metronidazole, quinidine, theophyllin, tricyclic antidepressants, oral contraceptives. The activity of griseofulvin may be reduced if it is given by mouth with **SEDABARB**.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception

Phenobarbitone should not be used in women of childbearing potential unless the potential benefit is judged to outweigh the risks following careful consideration of alternative suitable treatment options.

A pregnancy test to rule out pregnancy should be considered prior to commencing treatment with phenobarbitone in women of childbearing potential.

Women of childbearing potential should use highly effective contraception during treatment with phenobarbitone and for 2 months after the last dose. Due to enzyme induction, phenobarbitone may result in a failure of the therapeutic effect of oral contraceptive drugs containing oestrogen and/or progesterone. Women of childbearing potential should be advised to use other contraceptive methods while on treatment with phenobarbitone, e.g. two complementary forms of contraception including a barrier method, oral contraceptive containing higher doses of estrogen, or a non-hormonal intrauterine device (see section 4.5).

Women of childbearing potential should be informed of and understand the risk of potential harm to the foetus associated with phenobarbitone use during pregnancy and the importance of planning a pregnancy.

Women planning a pregnancy should be advised to consult in advance with her physician so that specialist medical advice can be provided and appropriate other treatment options can be discussed prior to conception and before contraception is discontinued.

Antiepileptic treatment should be reviewed regularly and especially when a woman is planning to become pregnant.

Women of childbearing potential should be counselled to contact her doctor immediately if she becomes pregnant or thinks she may be pregnant while on treatment with phenobarbitone.

Pregnancy

Risk related to antiepileptic medicinal products in general

Medical advice regarding the potential risks to a fetus caused by both seizures and antiepileptic treatment should be given to all women of childbearing potential taking antiepileptic treatment, and especially to women planning pregnancy and women who are pregnant. Antiepileptic treatment should be reviewed regularly and especially when a woman is planning to become pregnant. In pregnant women being treated for epilepsy, sudden discontinuation of antiepileptic drug (AED) therapy should be avoided as this may lead to breakthrough seizures that could have serious consequences for the woman and the unborn child. As a general principle, monotherapy is preferred for treating epilepsy in pregnancy whenever possible because therapy with multiple AEDs appear to be associated with a higher risk of congenital malformations than monotherapy, depending on the associated AEDs.

Risk related to phenobarbitone

Phenobarbitone 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.

Phenobarbitone therapy in epileptic pregnant women presents a risk to the fetus in terms of major and minor congenital defects including congenital craniofacial and cardiac defects, digital abnormalities and, less commonly, cleft lip and palate.

Studies in women with epilepsy who were exposed to phenobarbitone during pregnancy identified a frequency of major malformations of 6-7 % in their offspring compared to the background rate in the general population of 2-3 %. Studies have found the risk of congenital malformations following in-utero exposure to phenobarbitone to be dose-dependent, however, no dose has been found to be without risk. Therefore, the lowest effective dose should be used.

Adverse effects on neurobehavioral development have also been reported. Studies investigating neurodevelopmental effects of prenatally administered phenobarbitone were mostly small in numbers; however, significant negative effects on neurodevelopment and IQ were found following in utero and postnatal exposure.

Data from a registry study suggest an increase in the risk of infants born small for gestational age or with reduced body length to women with epilepsy who were exposed to phenobarbitone during pregnancy compared to women exposed to lamotrigine monotherapy during pregnancy.

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.

Patients taking phenobarbitone should be adequately supplemented with folic acid before conception and during pregnancy (see section 4.5).

Breast-feeding

Phenobarbitone 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

SEDABARB causes drowsiness and patients receiving it should not drive vehicles or operate machinery where loss of concentration could lead to injury.

4.8 Undesirable effects

System Organ Class	**Frequency Unknown**
Musculoskeletal and connective tissue disorders:	Ataxia
Psychiatric disorders:	Paradoxical excitement, disorientation, restlessness, mental confusion and depression.
Nervous system disorders:	Nystagmus, hyperexcitability may occur in children, dizziness
Respiratory disorders:	Severe respiratory insufficiency and respiratory depression
Hepato-bilary	Hepatitis and cholestasis
Skin and subcutaneous tissue disorders:	Skin rashes, maculopapular, scarlatiniform, purpura, exfoliative dermatitis, erythema multiforme (the Stevens-Johnson Syndrome), toxic epidermal necrolysis.
General disorders and administration site conditions	Impaired hepatic or renal function, irritability

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Barbiturate overdosage is a frequent cause of acute poisoning and death; the toxic effects of overdosage include prolonged coma, respiratory depression; and cardiovascular depression, with hypotension and shock leading to renal failure. Absent bowel sounds are a sign of severe poisoning, their return sometimes heralding further absorption of any remaining barbiturate in the gastro-intestinal tract, with resultant relapse. Hypothermia is common, with associated pyrexia during recovery. Characteristic erythematous or haemorrhagic blisters (bullae) may occur. Death is usually due to respiratory and circulatory failure. The aim in treating poisoning with Sedabarb is to prevent further absorption. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 <u>Pharmacodynamic properties</u>

SEDABARB is a long-acting barbiturate.

5.2 Pharmacokinetic properties

- Like other barbiturates phenobarbitone is readily absorbed from the gastrointestinal tract, although it is relatively lipid-insoluble; peak concentrations occur about 2 hours after oral doses and within 4 hours of intramuscular doses.
- Phenobarbitone is about 45 to 60 % bound to plasma proteins and is only partly metabolised in the liver. About 25 % of a dose is excreted in the urine unchanged at normal urinary pH.
- The plasma half-life is about 75 to 120 hours in adults but is greatly prolonged in neonates, and shorter (about 21 to 7 5 hours) in children.

- Phenobarbitone kinetics show considerable interindividual variation. Monitoring of plasma concentrations has been performed as an aid in assessing control and the therapeutic range of plasma-phenobarbitone has been quoted *as* 15 to 40 micrograms/mL or around 60 to 180 micromoles/litre.
- Phenobarbitone crosses the placental hairier and is distributed into breast milk.
- The pharmacokinetics of phenobarbitone are affected if given with other antiepileptics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Flowlac 100
- Magnesium stearate
- Microcrystalline cellulose
- Sodium starch glycolate

6.1 Incompatibilities

Not applicable

6.3 Shelf life

100, 500, 5000, 1000 and 5000: 24 Months

Patient ready packs: 15 months

6.4 Special precautions for storage

Keep in a cool, dry place, at or below 25 ^{o}C.

6.5 Nature and contents of container

Amber PVC containers of 100, 500, 1000 and 5000 tablets.

White polypropylene securitainers of 42, 100 and 1000 tablets.

Patient ready packs of different pack sizes.

6.6 Special precautions for disposal and other handling

Return all unused or expired medicines to your pharmacist for safe disposal.

Do not dispose of unused medicines in drains sewage systems (e.g. toilets)

7 HOLDER OF CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICALS (PTY) LTD

14 LAUTRE ROAD

STORMILL EXT. 1

ROODEPOORT

1724

SOUTH AFRICA

8 REGISTRATION NUMBER(S)

E/2.3/107 (South Africa)

B9315035 (Botswana)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19 June 1974

10 DATE OF REVISON OF THE TEXT

07 November 2022