

OSPOLOT®
(SULTHIAME) TABLETS

1 NAME OF THE MEDICINE

Sulthiame

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ospolot film-coated tablets contain 50 mg or 200 mg of sulthiame.

Excipients of known effect: sugars as lactose.

For the full list of excipients, see Section 6.1 List of Excipients.

3 PHARMACEUTICAL FORM

Ospolot 50 mg tablets are white film-coated round tablets, debossed "50" on one side and plain on the reverse side.

Ospolot 200 mg tablets are white film-coated round tablets debossed "200" on one side and scored on the reverse side.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Ospolot is indicated as an anticonvulsant for behavioural disorders associated with epilepsy; hyperkinetic behaviour; temporal lobe epilepsy; myoclonic seizures; grand mal attacks; Jacksonian seizures.

4.2 DOSE AND METHOD OF ADMINISTRATION

Caution should be used when establishing dosage in the presence of renal or hepatic impairment.

Treatment should start with a low dosage which is gradually increased until clinical response is satisfactory. This may require four weeks. Ospolot tablets should preferably be swallowed whole with a little fluid after meals.

Adults

Initially 100 mg twice daily or 50 mg three times daily (optimum: 200 mg three times daily).

Children

Initially 3-5 mg/kg daily in equal divided doses (optimum: 10-15 mg/kg daily in equal divided doses).

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4.3 CONTRAINDICATIONS

Ospolot may not be used in cases of

- known hypersensitivity to sulthiame, other sulfonamides or to any of the excipients listed in Section 6.1 List of Excipients.

Sulthiame should not be used in patients with

- known acute porphyria
- hyperthyroidism or arterial hypertension.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Ospolot should be administered to patients with a history of psychiatric disorders or impaired renal function only with adequate monitoring. Sulthiame is predominantly renally excreted.

Suicidal behaviour and ideation

Antiepileptic drugs, including sulthiame, increase the risk of suicidal thoughts or behaviour in patients taking these drugs for any indication. Patients treated with any antiepileptic drug (AED) for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behaviour, and/or any unusual changes in mood or behaviour.

Pooled analyses of 199 placebo-controlled clinical trials (mono- and injunctive therapy) of 11 different AEDs showed that patients randomised to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% CI:1.2, 2.7) of suicidal thinking or behaviour compared to patients randomised on placebo. In these trials, which had a median treatment duration of 12 weeks, the estimated incidence rate of suicidal behaviour or ideation among 27,863 AED-treated patients was 0.43%, compared to 0.23% among 16,029 placebo-treated patients, representing an increase of approximately one case of suicidal thinking or behaviour for every 530 patients treated. There were four suicides in drug-treated patients in the trials and none in placebo-treated patients, but the number is too small to allow any conclusion about drug effect on suicide.

The increased risk of suicidal thoughts or behaviour with AEDs was observed as early as one week after starting drug treatment with AEDs and persisted for the duration of treatment assessed. Because most trials included in the analysis did not extend beyond 24 weeks, the risk of suicidal thoughts could not be assessed.

The risk of suicidal thoughts or behaviour was generally consistent among drugs in the data analysed. The finding of increased risk with AEDs of varying mechanisms of action and across a range of indications suggests that the risk applies to all AEDs used for any indication. The risk did not vary substantially by age (5 - 100 years) in the clinical trials analysed. Table 1 shows absolute and relative risk by indication for all evaluated AEDs.

Table 1: Risk by indication for antiepileptic drugs in the pooled analysis

Indication	Placebo patients with events/1000 patients	Drug patients with events/1000 patients	Relative Risk: Incidence of events in Drug patients/ incidence in Placebo patients	Risk Difference: Additional Drug patients with events per 1000 patients
Epilepsy	1.0	3.4	3.5	2.4
Psychiatric	5.7	8.5	1.5	2.9
Other	1.0	1.8	1.9	0.9
Total	2.4	4.3	1.8	1.9

The relative risk for suicidal thoughts or behaviour was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar for the epilepsy and psychiatric indications.

Anyone considering prescribing sulthiame or any other AED must balance this risk with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behaviour. Should suicidal thoughts and behaviour emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behaviour and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behaviour, or the emergence of suicidal thoughts, behaviour, or thoughts about self-harm. Behaviours of concern should be reported immediately to the treating doctor.

The patients, their caregivers, and families should be instructed to consult the attending doctor immediately if fever, sore throat, allergic skin reactions with lymph node swelling and / or flu-like symptoms occur during treatment with Ospolot. Progressive thrombocytopenias or leukopenias that are accompanied by clinical symptoms, such as fever or sore throat, require interruption of treatment. In cases of severe allergic reactions, Ospolot must be discontinued immediately. Treatment should also be interrupted if a lasting increase in creatinine occurs. The blood count, liver enzymes and urine should be checked regularly.

Patients with rare hereditary problems of galactose intolerance, lactase deficiency or glucose-galactose malabsorption should not take Ospolot.

Use in hepatic impairment

See Section 4.2 Dose and Method of Administration.

Use in renal impairment

Ospolot should be administered to patients with a history of impaired renal function only with adequate monitoring. Sulthiame is predominantly renally excreted.

Use in the elderly

No data available.

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Paediatric use

See Section 4.2 Dose and Method of Administration, Children.

Effects on laboratory tests

Sulthiame may interfere with the estimation of barbiturates in laboratory tests on blood.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Alcohol: Alcohol must not be consumed during treatment. As sulthiame is a sulfonamide derivative, it can theoretically have a similar effect as that of Disulfiram. These symptoms include a very unpleasant, although generally self-limiting systemic reaction caused by vasodilatation, with pulsating headache, respiratory depression, nausea, vomiting, tachycardia, hypotension, amblyopia, confusion, shock reactions, arrhythmias, loss of consciousness and seizures. The degree and duration of these symptoms can vary to a great extent.

Primidone: The concomitant use of sulthiame and primidone may lead to severe side-effects, especially in children, including dizziness, unstable gait, drowsiness and psychotic reactions.

Phenytoin: The addition of sulthiame to pre-existing phenytoin therapy is shown to be followed by a rise in the serum levels of phenytoin. It has been suggested that this may be due either to inhibition by sulthiame of the hydroxylation of phenytoin or to displacement of phenytoin from a storage site by sulthiame. Phenytoin dosage may need to be reduced when sulthiame is added. This combination requires especially strict monitoring and frequent controls of phenytoin plasma levels, particularly in the case of impaired renal function.

Phenobarbitone: Sulthiame may also induce a rise in the serum level of phenobarbitone.

Carbamazepine: There are indications that sulthiame serum levels may decrease if carbamazepine is taken concomitantly.

Lamotrigine: In combination with lamotrigine, an elevation of lamotrigine levels in the blood has also been observed in individual cases. Therefore, lamotrigine levels should be checked more frequently at the beginning of such a treatment.

Carboanhydrase-Inhibitors: Concomitant use of sulthiame and other carbonic anhydrase inhibitors (e.g. topiramate, acetazolamide) may increase the risk of undesirable effects due to carbonic anhydrase inhibition.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

Ospolot is Pregnancy Category D- *Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects.*

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The risk of a mother with epilepsy giving birth to a baby with an abnormality is about three times that of the normal population. Some of this risk is due to the anticonvulsant drugs taken. Mothers taking more than one anticonvulsant drug might have a higher risk of having a baby with a malformation than mothers taking one drug. There is a lack of data permitting any statement that women taking sulthiame are at any different risk of having a baby with an abnormality from women taking other anticonvulsants. Overall, the risk of having an abnormal child is far outweighed by the dangers to the mother and fetus of uncontrolled convulsions. If administered during pregnancy the dose of sulthiame must be kept as low as possible, particularly between days 20 and 40 of gestation.

Use in lactation

It is not known whether sulthiame is excreted in breast milk or whether it has a harmful effect on the newborn. Therefore, it is not recommended for breastfeeding mothers, unless the expected benefits outweigh any potential risk.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The following frequency categories are used for the evaluation of adverse effects:

Very common	($\geq 1/10$)
Common	($\geq 1/100$ to $< 1/10$)
Uncommon	($\geq 1/1,000$ to $< 1/100$)
Rare	($\geq 1/10,000$ to $< 1/1,000$)
Very rare	($< 1/10,000$)
Not known	(frequency cannot be estimated from the available data)

Metabolism and nutrition disorders

Very common: anorexia

Common: weight loss

Psychiatric disorders

Uncommon: hallucinations, anxiety, lack of drive, psychic changes, depression, behavioural anomaly

Nervous system disorders

Common: ataxia, paraesthesias in the extremities and in the face (dose dependent), dizziness (giddiness)

Uncommon: headache, myasthenic phenomena, grand-mal status, increased seizure activity, drooling, insomnia

Not known: polyneuritis

Eye disorders

Common: double vision

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Cardiac disorders

Common: stenocardia, tachycardia

Respiratory, thoracic and mediastinal disorders

Very common: hyperpnoea, dyspnoea

Common: tachypnoea, singultus

Gastrointestinal disorders

Very common: gastric complaints (in about 10% of patients)

Uncommon: abdominal pain, nausea

Hepatobiliary disorders

Not known: hepatotoxic reactions, increase of liver enzymes

Skin and subcutaneous disorders

Uncommon: Stevens-Johnson syndrome

Not Known: Rash, Lyell's syndrome

Musculoskeletal and connective tissue disorders

Uncommon: joint pain

Renal and urinary disorders

Not known: acute renal failure

Blood and lymphatic system disorders

Uncommon: leucopenia

In one case, administration of Ospolot led to progressive weakness of the limbs, hypersalivation, slurred speech, increasing drowsiness up to coma. The symptoms abated within hours of Ospolot being discontinued.

Sulthiame is a carbonic anhydrase inhibitor. Therefore, undesirable effects of carbonic anhydrase inhibition, such as renal stone formation, metabolic acidosis, haemodilution and changes in serum electrolyte values, cannot be excluded during administration of sulthiame.

Disturbances in calcium and Vitamin D metabolism have been occasionally reported in association with long-term anticonvulsant therapy.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Clinical features have included vomiting, hypotension, headache, vertigo, ataxia, metabolic acidosis with hyperpnoea and catatonic state.

There is no specific antidote. Treatment consists of general supportive measures including intravenous fluids. The urine should be rendered alkaline to prevent crystalluria; forced alkaline diuresis may promote elimination of sulthiame.

There is no information on the applicability of dialysis.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

The structure of sulthiame is distinct from that of other anticonvulsants. It is a cyclic sulfonamide derivative without antimicrobial activity.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

No data available.

Distribution

No data available.

Metabolism

No data available.

Excretion

No data available.

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5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The excipients in Ospolot tablets are maize starch, lactose monohydrate, purified talc, colloidal anhydrous silica, gelatin, magnesium stearate, hypromellose, macrogol 4000 and titanium dioxide.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG)¹. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

The Ospolot 50 mg tablets and Ospolot 200 mg tablets are supplied in HDPE bottles with a PP child resistant cap (200 tablets/bottle).

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical name: 4-(Tetrahydro-2H-1,2-thiazin-2-yl)benzenesulfonamide- S,S-dioxide.

The molecular weight of the compound is 290.4. The molecular formula is C₁₀H₁₄N₂O₄S₂.

The structure of sulthiame is distinct from that of other anticonvulsants. It is a cyclic sulfonamide derivative without antimicrobial activity.

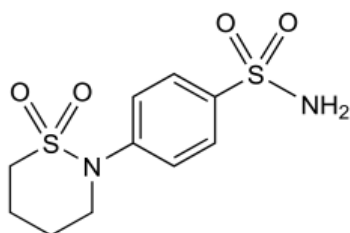
¹ AUST R 18847, AUST R 18848

PRODUCT INFORMATION

Ospolot®



Chemical structure



CAS number

61-56-3

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 - Prescription Only Medicine

8 SPONSOR

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Telephone: 1800 720 020

9 DATE OF FIRST APPROVAL

8 Oct 1991

10 DATE OF REVISION

01 Jun 2022

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
Title	Minor editorial update – From 'tablet' to 'tablets'.
4.3	Minor editorial update – From 'sulphonamides' to 'sulfonamides'.
4.5	Minor editorial update – From 'sulphonamide' to 'sulfonamide'.
4.8	Minor editorial update – From 'behavioral' to 'behavioural'.
5.1	Minor editorial update – From 'sulphonamide' to 'sulfonamide'.
6.5	Included 'PP child resistant cap'. Deleted Phebra product Code.

² Ospolot, Phebra and the Phi symbol are trademarks of Phebra Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia.