Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ospolot 20 mg/ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml oral suspension contains 20 mg sulthiame.

Excipients with known effect:
Each ml contains 2,3 mg of sodiummethyl parahydroxybenzoate (E219) and 0,6 mg of sodium propyl parahydroxybenzoate (E217), 0,0026 mg of fructose, 0,0024 mg of glucose, 0,0005 mg of sucrose and 0,000004 mg of sulphur dioxide (E220).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension

White suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For treatment of SeLECTS (Self-Limited Epilepsy with Centrotemporal Spikes) (former Rolandic epilepsy) in children and adolescents aged 3 years and abovenon responder/intolerant to other treatments or without other therapeutic alternatives.

4.2 Posology and method of administration

Ospolot should be initiated and supervised by physicians with experience in the treatment of epilepsy.

Posology
The dose must be established and monitored by the doctor on an individual basis. The maintenance dose is about 5 to 10 mg per kg body weight and day. It should be built up step-wise (tapered in) over a one-week period. Due to the short half-life of sulthiame, the daily dose should as far as possible be spread over three single doses (see tables 1 and 2 with dosing examples). If the daily dose is spread over the day in this way, constant plasma levels are to be expected after five to six days. Therapeutic plasma concentrations of sulthiame have not yet been determined.
Ospolot oral suspension and Ospolot film-coated tablets may be interchanged at equal doses. A control of plasma levels should be considered when switching from tablets to oral suspension.
A switch from another medicinal product or from combination treatment should be done gradually.

The oral suspension is the preferred formulation for use in infants, children and adolescents weighing 12 kg or more (age group 3 and above). For dosing examples, refer to tables 1 and 2, however, the titration must be carried out on an individual basis.

Table 1

Patient-Weight	Build-up dose: **2.5 mg* sulthiame per kg per day**	
	Single dose (given 3 x daily)	**Total daily dose**
12 - 18 kg	**0.5 – 0.75 ml** (equivalent to 10 – 15 mg sulthiame)	1.5 – 2.25 ml (equivalent to 30 – 45 mg sulthiame)
18 - 24 kg	**0.75 -1.0 ml** (equivalent to 15 – 20 mg sulthiame)	2.25 – 3.0 ml (equivalent to 45 – 60 mg sulthiame)
24 - 30 kg	**1.0 -1.25 ml** (equivalent to 20 – 25 mg sulthiame)	3.0 – 3.75 ml (equivalent to 60 – 75 mg sulthiame)
30 - 36 kg	**1.25 – 1.5 ml**	3.75 – 4.5 ml

	(equivalent to 25 – 30 mg sulthiame)	(equivalent to 75 – 90 mg sulthiame)
36 – and above	**1.5 ml and above** (equivalent to 30 mg sulthiame and above)	4.5 and above (equivalent to 90 mg sulthiame and above)

*1 ml Ospolot oral suspension contains 20 mg sulthiame => 0.25 ml = 5 mg sulthiame

Table 2

Patient-Weight	Maintenance dose: **5 mg* sulthiame per kg per day**	
	Single dose **(given 3 x daily)**	**Total daily dose**
12 - 18 kg	**1.0 – 1.5 ml** (equivalent to 20 – 30 mg sulthiame)	3.0 – 4.5 ml (equivalent to 60 – 90 mg sulthiame)
18 - 24 kg	**1.5 -2.0 ml** (equivalent to 30 – 40 mg sulthiame)	4.5 – 6.0 ml (equivalent to 90 – 120 mg sulthiame)
24 - 30 kg	2**.0 -2.5 ml** (equivalent to 40 – 50 mg sulthiame)	6.0 – 7.5 ml (equivalent to 120 – 150 mg sulthiame)
30 - 36 kg	**2.5 – 3.0 ml** (equivalent to 50 – 60 mg sulthiame)	7.5 – 9.0 ml (equivalent to 150 – 180 mg sulthiame)
36 – and above	**3.0 ml and above** (equivalent to 60 mg sulthiame and above)	9.0 and above (equivalent to 180 mg sulthiame and above)

*1 ml Ospolot oral suspension contains 20 mg sulthiame => 0.25 ml = 5 mg sulthiame

Note: Forsingle doses of 10 ml or more tablets may be used.

Duration of treatment
Ospolot should not be discontinued abruptly. A paediatric neurologist experienced in treating epilepsy should decide on the duration of treatment and discontinuation on an individual basis.
If therapy is not successful, treatment with sulthiame should be discontinued after about one to two months.

Patients with renal impairment
Use in patients with renal impairment has not been studied. Caution must be exercised in treating patients with renal impairment and a slower titration may be required. Since sulthiame and its metabolites are excreted renally, it should be discontinued in patients who develop acute renal failure or where a clinically significant sustained increase in serum creatinine is observed.

Patients with hepatic impairment
Use in patients with hepatic impairment has not been studied. Therefore, use in patients with severe hepatic impairment is not recommended. Caution must be exercised in treating patients with mild to moderate hepatic impairment, and a slower titration of Ospolot may be required.

Method of administration
Ospolot is for oral use.
Before taking Ospolot, the bottle should be shaken very well (at least once for 30 seconds) and the dose prepared immediately afterwards (to avoid sedimentation). The oral suspension may be swallowed directly from the oral syringe, or taken promptly after mixing preferable with a small volume of water, alternatively with orange juice, milk, yoghurt or wheat porridge.
When taking the oral suspension directly from the oral syringe, the patient should drink some water, juice or milk immediately afterwards due to the bitter taste of sulthiame.
Carbonated beverages or hot food should not be taken with the suspension to avoid eructation or slowed swallowing. Ospolot may be taken with or without food, preferably the patient should not change the way to take Ospolot during therapy (see section 5.2).

The oral suspension may also be administered via a feeding tube that should be rinsed with minimum 15 ml of water immediately after administration. If this method of administration is used, the dose should be prepared as described above immediately before administration

4.3 Contraindications

- Hypersensitivity to the active substance, other sulphonamides or to any of the excipients listed in section 6.
- hyperthyroidism
- known acute porphyria

- arterial hypertension

4.4 Special warnings and precautions for use

Sulthiame should not be administered, or only administered with special caution
- in patients with impaired renal function
- in patients with a history of psychiatric disorders.

Laboratory monitoring
It is recommendable to monitor the blood count, liver enzymes and renal function parameters before treatment with Ospolot, then at weekly intervals in the first month of treatment, and thereafter at monthly intervals. After six months of treatment, two to four checks per year are sufficient.

Note:
Treatment should be interrupted if a lasting increase in creatinine occurs.

Hypersensitivity reactions:
The patient respectively the parents 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. In cases of severe allergic reactions Ospolot must be discontinued immediately.

Progressive thrombocytopenias or leukopenias that are accompanied by clinical symptoms require discontinuation of Ospolot.

Suicidal ideation and suicidal behaviour
Suicidal ideation and behaviour have been reported in patients treated with antiepileptic medicinal products in several indications. A meta-analysis of randomised placebo controlled trials of anti-epileptic medicinal products has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for sulthiame.

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.

Excipients
Sodium methyl parahydroxybenzoate (E219) and sodium propyl parahydroxybenzoate (E217) may cause allergic reactions (possibly delayed).

Sulphur dioxide (E 220) may rarely cause severe hypersensitivity reactions and bronchospasm.

This medicine contains glucose, sucrose and 0,0026 mg fructose in each ml.
Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.
Glucose, Fructose and sucrose may be harmful to the teeth.

This medicinal product contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

Influence of other medicinal products on sulthiame

Primidon
If sulthiame is combined with primidone, the intensity of undesirable effects of sulthiame may increase; especially in children, dizziness, unstable gait and drowsiness may occur.

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

Influence of sulthiame on other medicinal products

Phenytoin
If sulthiame is combined with phenytoin, the plasma levels of phenytoin can be markedly elevated. This combination requires especially strict monitoring and frequent controls of phenytoin plasma levels, particularly in the case of impaired renal function.

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 (see also section 4.8).

Alcohol
During treatment with sulthiame, the patient should abstain from alcohol. Sulthiame, as a sulphonamide derivative, theoretically may have an effect similar to 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.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of sulthiame in pregnant women. Animal studies are insufficient with respect to reproductive toxicity, but revealed embryotoxic effects (see section 5.3). Administration of antiepileptics during pregnancy has been generally associated with an increased risk for malformations, which may be increased if different antiepileptics are combined. Therefore, Ospolot is not recommended during pregnancy and in women of childbearing potential not using contraception.
In case of pregnancy, the lowest seizure-controlling dose of Ospolot should be administered, if possible, as monotherapy. Prenatal diagnostic measures for early detection of malformations (high-resolution ultrasound and alpha-fetoprotein determination) are recommended. In no case treatment with antiepileptics should be discontinued without medical consent, as uncontrolled seizures can have serious consequences for both the mother and the unborn child.

Breastfeeding
It is unknown whether sulthiame/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. Ospolot should not be used during breast-feeding.

Fertility
There are no data on the effects of sulthiame on fertility.

4.7 Effects on ability to drive and use machines

Even when used as directed, this medicinal product can affect reactions to such an extent - especially at the start of treatment - that the ability to drive a vehicle or use machines may be impaired. This applies to a greater extent in combination with alcohol (see section 4.5 Alcohol).

4.8 Undesirable effects

The following frequency categories are used for the evaluation of undesirable effects:
Very common ³ 1/10)
Common ³ 1/100 to < 1/10)
Uncommon ³ 1/1 000 to < 1/100)
Rare ³ 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
Common: weight loss, lack of appetite

Psychiatric disorders

Uncommon: hallucinations, anxiety, lack of drive
Not known: depressive mood/depression, personality change and behavioural anomaly (e.g. aggressiveness, irritability, mood swings), cognitive impairment

Nervous system disorders
Common: paraesthesias in the extremities and in the face*, dizziness, headache
Uncommon: myasthenic phenomena, grand-mal status, increased seizure activity
Not known: polyneuritis

Eye disorders
Common: double vision
Not known: visual impairment, that may be significant

Cardiac disorders
Common: stenocardia, tachycardia

Respiratory, thoracic and mediastinal disorders
Common: tachypnoea*, hyperpnoea*, dyspnoea, singultus

Gastrointestinal disorders
Very common: gastric complaints like e.g. nausea, vomiting (in about 10% of patients)
Not known: diarrhoea

Hepatobiliary disorders
Not known: hepatotoxic reactions, increase of liver enzymes

Skin and subcutaneous disorders
Not known: Stevens-Johnson syndrome, TEN (toxic epidermal necrolysis)

Musculoskeletal and connective tissue disorders
Uncommon: joint pain

Renal and urinary disorders
Not known: acute renal failure

*Dose-dependent, if necessary the dose has to be adapted.

One patient with long-standing refractory epilepsia experienced progressive weakness of the limbs, hypersalivation, slurred speech, increasing drowsiness up to coma. The symptoms abated within hours of sulthiame being discontinued.

Sulthiame is a carbonic anhydrase inhibitor. Therefore, undesirable effects of carbonic anhydrase inhibition, such as renal stone formation, metabolic acidosis, tiredness/exhaustion, haemodilution and changes in serum electrolyte values (e.g. hypocalcaemia), may occur during administration of sulthiame (see also section 4.5).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via the national reporting system listed in Appendix V.

4.9 Overdose

Symptoms of intoxication
Headache, dizziness, ataxia, impaired consciousness, metabolic acidosis, crystals in the urine. Sulthiame has a low toxicity. Overdoses of 4 to 5 g sulthiame have been survived. The intake of about 20 g sulthiame by adults with the intention of committing suicide was fatal in one case. In another case, a *restitutio ad integrum* was achieved.

Treatment of intoxications

A specific antidote is not known. The standard measures (gastric lavage and active charcoal) for minimising absorption and for maintaining vital functions should be taken. Sodium bicarbonate can be infused to treat acidosis. Alkalising diuretic therapy is recommended for preventing renal damage and crystalluria.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other Antiepileptics
ATC code: N03AX03

Sulthiame belongs to the group of carbonic anhydrase inhibitors and displays an anticonvulsant effect in the electroconvulsion test (rat and mouse) and in the convulsion test with pentamethylene tetrazole (mouse). There is limited evidence from controlled clinical trials on the efficacy and safety of this medicinal product. Sulthiame is a sulphonamide derivative, and its exact mechanism of action is not known.

5.2 Pharmacokinetic properties

Sulthiame pharmacokinetics were not systematically investigated in different age categories in children and adolescents.

Absorption
After oral administration, sulthiame is rapidly and completely absorbed, predominantly from the upper section of the small intestine. Peak plasma concentrations are measured after 1 - 5 hours.
In a single dose pharmacokinetic study with 16 probands, the influence of food intake on the absorption of Ospolot 200 mg tablets was examined. The results show that intake of Ospolot with food leads to a moderately reduced bioavailability of sulthiame.

Distribution
About 29% of the active substance is bound to plasma proteins.

Elimination
80 to 90% is eliminated with the urine and 10 to 20% with the faeces after biliary secretion. Within 24 hours, 32% of the administered dose is excreted unchanged via the kidneys. In a single dose pharmacokinetic study with 16 healthy adult probands, a half-life of approximately 12 h was determined. Based on published pharmacokinetic studies, a shorter half-life is assumed in children.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity.

Mutagenic and carcinogenic potential
Sulthiame did not show any mutagenic potential *in vitro* and *in vivo* . Long-term carcinogenicity studies have not been conducted.

Reproductive toxicity
The reproductive toxicity of sulthiame was insufficiently investigated. In an embryotoxicity study on rats, embryotoxic effects were noted at the lowest tested dose (30 mg/kg/day). Studies regarding effects on fertility and peri- and postnatal development of the off-spring are lacking.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium methyl parahydroxybenzoate (E219)
sodium propyl parahydroxybenzoate (E217)
sucralose (E955)
docusate sodium
xanthan gum (E415)
sodium dihydrogen phosphate dihydrate (E339)

dipotassium phosphate (E340)
strawberry flavour (containing Acacia E414)
sweetness Modulator Flavour (containing fructose, glucose, sucrose, sulphur dioxide (E220))
masking flavour (containing Sucralose E955, Maltodextrin (potatoe))
phosphoric acid 85% (E338) (for pH adjustment)
purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

After first opening: 3 months

6.4 Special precautions for storage

This medicinal productdoes not require any special storage conditions.

6.5 Nature and contents of container

200 ml or 250 ml oral suspension in an amber glass bottle (type III) with a child resistant closure (polypropylene) in a cardboard box also containing a 10 ml oral syringe, graduated every 0.25 ml (HDPE, polypropylene) and an adapter for the oral syringe (LDPE).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Administration through enteral feeding tubes:

- feasible enteral tube sizes: CH/FR 4.5 – 12
- Ospolot shows no tendencies for tube blocking

7 MARKETING AUTHORISATION HOLDER

Desitin Arzneimittel GmbH
Weg beim Jager 214
Hamburg
22335
Germany

8 MARKETING AUTHORISATION NUMBER

PA0815/005/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th October 2024

10 DATE OF REVISION OF THE TEXT

March 2025