DESIZON®

zonisamide

20 mg/ml oral suspension

NEW: The first UK licensed oral liquid formulation of zonisamide[1]

High concentration, low volume oral suspension

- Age-appropriate formulation for children aged 6 years and above
- Ability-appropriate formulation for adults with swallowing difficulties

Convenient dosing

- Once or twice a day administration
- The only formulation of zonisamide licensed for feeding tube administration
- Can be taken with or without food

Convenient presentation

- 250mg bottle with calibrated 10ml oral dosing syringe and bung
- 3 year shelf life

Indicated for: Monotherapy in the treatment of partial seizures, with or without secondary generalisation, in adults with newly diagnosed epilepsy.

Adjunctive therapy in the treatment of partial seizures, with or without secondary generalization, in adults, adolescents and children aged six years and above.

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Special warnings and precautions for use of Desizon 20mg/ml oral suspension: (refer to SmPC)[1]

Heat stroke and dehydration

Preventing overheating and dehydration in children

Desizon can cause children to sweat less and overheat and if the child is not treated this can lead to brain damage and death. Children are most at risk especially in hot weather.

When a child is taking Desizon:

- The child should stay cool especially in hot weather
- The child must avoid heavy exercise especially when the weather is hot
- The child must drink plenty of cold water
- The child must not take any of these medicines: carbonic anhydrase inhibitors (like topiramate and acetazolamide), and anticholinergic agents (like clomipramine, hydroxyzine, diphenhydramine, haloperidol, imipramine and oxybutynin)

IF ANY OF THE FOLLOWING OCCUR, THE CHILD NEEDS URGENT MEDICAL ATTENTION:

The skin feels very hot with little or no sweating, or the child becomes confused or has muscle cramps, or the child's heartbeat or breathing become rapid.

- Take the child to a cool, shaded place
- Keep the child's skin cool with water
- Give the child cold water to drink

Unexplained rash

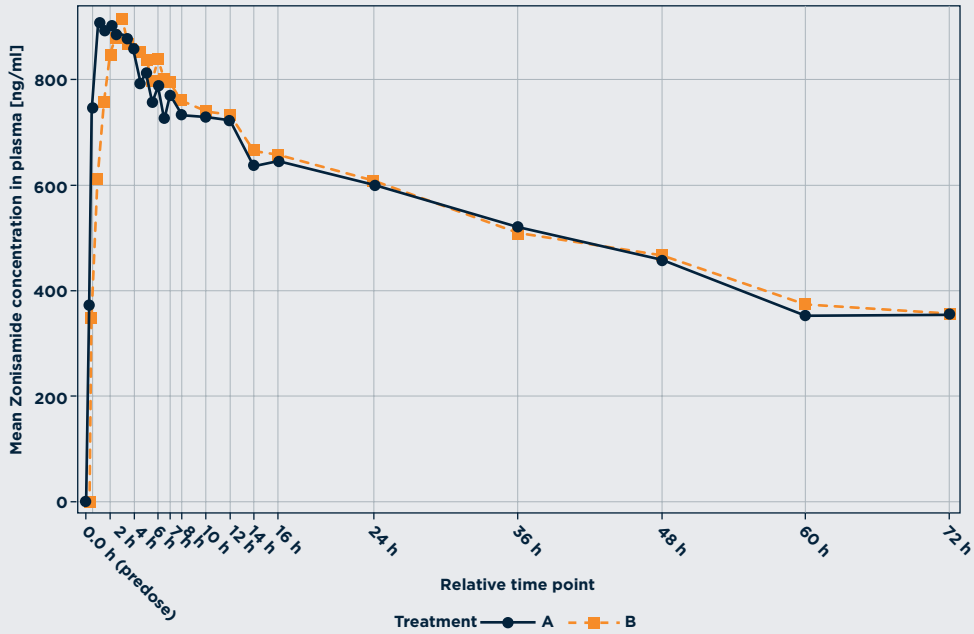
Serious rashes occur in association with Desizon 20mg/ml oral suspension therapy, including cases of Stevens-Johnson syndrome.

Weight loss

Desizon 20mg/ml oral suspension may cause weight loss. A dietary supplement or increased food intake may be considered if the patient is losing weight or is underweight whilst on this medication. If substantial undesirable weight loss occurs, discontinuation of Desizon should be considered. Weight loss is potentially more serious in children.

Desizon 20mg/ml oral suspension is bioequivalent to the leading brand[2]

Geometric mean zonisamide concentration in plasma – time profile (linear)



- **Desizon 20mg/ml oral suspension is bioequivalent to Zonegran Capsules**
- **Zonisamide Half Life is 60 hours, allowing Once Daily Administration**

- **Once Daily Administration has been shown in Neurology to improve compliance:[3]**
  - *"Each increase in dose frequency (one, two, three, or four doses daily) increased the likelihood of a seizure after missed dose by 36%"[3]*
- **Desizon 20mg/ml oral suspension is free from sorbitol and maltitol[1] which are known to cause GI side effects and reduced efficacy[4,5]**

To guarantee the correct Desizon 20mg/ml oral suspension prescription:

- **Rx Desizon 20mg/ml oral suspension**
- **Remember to prescribe by brand to ensure ongoing supply of the licensed medicine**

BECAUSE FORMULATION MATTERS

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high concentration • low volume

Desizon 20mg/ml oral suspension dosage and titration guide for adults[1]

New patients

Treatment Regimen	Titration Phase			Usual Maintenance Dose
Monotherapy • Newly diagnosed adult patients	**Week 1 + 2** 100mg (5ml) once a day	**Week 3 + 4** 200mg (10ml) once a day	**Week 5 + 6** 300mg (15ml) once a day	300mg (15ml) once a day*
Adjunctive therapy • with CYP3A4-inducing agents (see section 4.5)	**Week 1** 50mg/day (2.5ml/day) in two divided doses (2x 1.25ml/day)	**Week 2** 100mg/day (5ml/day) in two divided doses (2x 2.5ml/day)	**Week 3 to 5** Increase at weekly intervals in increments of 100mg (5ml)	300 to 500mg per day once a day (15 to 25ml/day) or two divided doses (2x 7.5 to 2x 12.5ml/day)
Adjunctive therapy • without CYP3A4-inducing agents; or with renal or hepatic impairment	**Week 1 + 2** 50mg/day (2.5ml/day) in two divided doses (2x 1.25ml/day)	**Week 3 + 4** 100mg/day (5ml/day) in two divided doses (2x 2.5ml/day)	**Week 5 to 10** Increase at two-weekly intervals in increments of up to 100mg (5ml)	300 to 500mg per day once a day (15 to 25ml/day) or two divided doses (2x 7.5 to 2x 12.5ml/day). Some patients may respond to lower doses.

If a higher dose is required: increase at two weekly intervals in increments of 100mg (5ml) up to a maximum of 500mg (25ml).

Existing patients currently on a different formulation of zonisamide

Converting patients currently taking a different formulation of zonisamide to Desizon 20mg/ml oral suspension:

- **Dose of Desizon in mls = current daily dose of zonisamide in mgs/20**
- **Example: A patient currently on a maintenance dose of 300mg/day zonisamide would need 300/20 = 15mls Desizon 20mg/ml oral suspension**

Desizon 20mg/ml oral suspension dosage and titration guide for paediatric use (children from 6 years and above)[1]

Dose recommendations for children aged 6 and above with a body weight of 20-40kg

	Initial Dose	Maintenance Dose
20kg	20mg/day = 1ml/day	120 – 160mg/day = 6 – 8ml/day
25kg	25mg/day = 1.25ml/day	150 – 200mg/day = 7.5 – 10ml/day
30kg	30mg/day = 1.5ml/day	180 – 240mg/day = 9 – 12ml/day
35kg	35mg/day = 1.75ml/day	210 – 280mg/day = 10.5 – 14ml/day
40kg	40mg/day = 2ml/day	240 – 320mg/day = 12 – 16ml/day

Dose based on 1mg/kg/day (0.05ml/kg body weight) starting dose.
Weekly increments of 1mg/kg/day (0.05ml/kg body weight) – with CYP3A4-inducing agents.
Fortnightly increments of 1mg/kg/day (0.05ml/kg body weight – without CYP3A4-inducing agents.
For existing patients, dose of Desizon 20mg/ml oral suspension in mls = total current daily dose of zonisamide in mgs/20
e.g. a 30kg child on a maintenance dose of 200mgs zonisamide will need 200/20 = 10mls Desizon 20mg/ml oral suspension/day.

Age appropriate oral liquid volumes[6,7]

Age	Max acceptable volume[7]	Age	Max acceptable volume[6]
0-3	5ml	2-5	5ml
5-12	10ml	6-12	10ml

- **Desizon 20mg/ml oral suspension is formulated as an age-appropriate formulation that facilitates use of an acceptable volume for children in a single daily dose**

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Desizon® (zonisamide) Prescribing Information.
Always consult the Summary of Product Characteristics (SmPC) before prescribing Desizon®.
Zonisamide available as Desizon® 20 mg/ml oral suspension. **Indications**: Monotherapy: Partial seizures with or without secondary generalisation in adults with newly diagnosed epilepsy. Adjunctive therapy: Partial seizures with or without secondary generalisation in adults, adolescents and children aged 6 years and above. **Dosage:** Dosage escalation and maintenance required. May be taken as monotherapy or added to existing therapy in adults. If discontinuation required, withdraw gradually. *Monotherapy*: Adults: Starting dose 100 mg (5 ml) od increasing to 200 mg (10 ml) od after 2 weeks and 300 mg (15 ml) after 4 weeks. Dose can be increased at 2 weekly intervals in increments of 100 mg (5 ml) to a maximum of 500 mg (25 ml) once a day. *Adjunctive therapy with CYP3A4 inducing agents*: Initial dose 50 mg (2.5 ml) per day in 2 divided doses to 100 mg (5 ml) per day in 2 divided doses at 2 weeks. Dose can be increased at weekly intervals in increments of 100 mg (5 ml) to up to 500 mg (25 ml) per day, once daily or in 2 divided doses. *Adjunctive therapy with renal or hepatic impairment*: Initial dose 50 mg (2.5 ml) per day in 2 divided doses for first 2 weeks to 100 mg (5 ml) per day in 2 divided doses at 4 weeks. Dose can be increased at 2 weekly intervals in increments of 100 mg (5 ml) to up to 500 mg (25 ml) per day, once a day or in 2 divided doses. *Paediatric Population >6 years*: Must be added to the existing therapy. *Adjunctive therapy with CYP3A4 inducing agents with 20 kg to 55 kg body weight*: 1 mg (0.05 ml)/kg/day od with increase at weekly intervals to up to 8 mg/kg/day (0.4 ml/kg/day) od. *Adjunctive therapy with CYP3A4 inducing agents >55 kg body weight*: 300 to 500 mg/day (15 ml to 25 ml/day) od *Adjunctive therapy without CYP3A4 inducing agents*: 1 mg (0.05 ml)/kg/day od with increase at 2 weekly intervals to up to 8 mg/kg/day (0.4 ml/kg/day) od to a maintenance dose of 500 mg/day (25 ml/day) od. Elderly: Caution should be exercised at initiation in elderly patients as there is limited information on the use in these patients. Renal impairment: Caution must be exercised in renal impairment, limited information on use in such patients and a slower titration might be required (see SmPC). Hepatic impairment: Use in patients with hepatic impairment has not been studied, use in patients with severe hepatic impairment is not recommended. **Administration:** Shake the bottle well before use. Oral suspension may be swallowed directly from oral syringe followed by glass of water or may be diluted in water or juice. See SmPC for administration via a feeding tube. Contraindications: Hypersensitivity to active substance, sodium methyl p-hydroxybenzoate (E219), sodium propyl p-hydroxybenzoate (E217), sulphonamides or to any of the excipients. **Special warnings and precautions for use (see SmPC**). The warnings and precautions mentioned are also applicable to adolescent and paediatric patients. Serious rashes including Stevens-Johnson syndrome. Gradual dose reduction required to reduce possibility of withdrawal seizures, sulphonamide reactions, acute myopia and secondary angle closure glaucoma: caution should be used when treating patients with history of eye increased levels of hepatobiliary parameters, suicidal ideation and behaviour have been reported: monitor patients for signs and consider treatment. Discontinuation to be considered in cases of pancreatitis, rhabdomyolysis. Advise patients/carers to seek medical advice if signs emerge; weight loss might be experienced.

Preventing overheating and dehydration in children: Desizon can cause children to sweat less and overheat and if not treated this can lead to brain damage and death. Most at risk in hot weather. When taking Desizon, children should stay cool and avoid heavy exercise in hot weather, drink plenty of cold water. Following medicines must not be taken: carbonic anhydrase inhibitors (like topiramate and acetazolamide), and anticholinergic agents (like clomipramine, hydroxyzine, diphenhydramine, haloperidol, imipramine and oxybutynin). If skin feels very hot with little or no sweating, or the child becomes confused or has muscle cramps, or the child's heartbeat or breathing become rapid, take the child to a cool place, cool skin with water, give cold water to drink and seek immediate medical attention.

Interactions: Caution in using carbonic anhydrase inhibitors in adults and should not be used as co-medication in paediatric population. Caution is advised in patients on P-gp substrate medications. **Effects on ability to drive and use machines**: No studies have been performed, however caution must be exercised during activities requiring high degree of alertness. **Pregnancy/ lactation**: Women of childbearing potential: Women must use effective contraception during treatment and for one month after discontinuation. Avoid sudden discontinuation. Pregnancy: Must not be used during pregnancy unless clearly necessary and if potential benefit is considered to justify risk to the foetus. Lactation: Excreted in breast milk therefore not recommended and breast feeding must not be resumed until one month after therapy completion. **Side effects (see SmPC for full list)**: *Very common*: Anorexia, agitation, irritability, confusional state, depression, ataxia, dizziness, memory impairment, somnolence, diplopia, decreased bicarbonate. *Common*: Ecchymosis, hypersensitivity, lability, anxiety, insomnia, psychotic disorder, bradyphrenia, disturbance in attention, nystagmus, paraesthesia, speech disorder, tremor, abdominal pain, constipation, diarrhoea, dyspepsia, nausea, rash, pruritis, alopecia, nephrolithiasis, fatigue, influenza like illness, pyrexia, oedema peripheral, weight decreased. *Uncommon*: Pneumonia, urinary tract infection, hypokalaemia, anger, aggression, suicidal ideation, suicide attempt, convulsion, vomiting, cholecystitis, Cholithiasis, calcus urinary. *Rare:* Agranulocytosis, aplastic anaemia, leucocytosis, leucopoenia, lymphadenopathy, pancytopenia, thrombocytopenia, drug induced hypersensitivity syndrome, drug rash with eosinophilia and systemic symptoms, metabolic acidosis, renal tubular acidosis, hallucination, amnesia, coma, grand mal seizure, myasthenic syndrome, neuroleptic malignant syndrome, status epilepticus, angle closure glaucoma, eye pain, myopia, vision blurred, visual acuity reduced, dyspnoea, pneumonia, aspiration respiratory disorder, hypersensitivity type pneumonitis, pancreatitis, hepatocellular damage, anhidrosis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, rhabdomyolysis, hydronephrosis, renal failure, urine abnormality, blood creatine phosphokinase, blood creatinine, blood urea increased, liver function tests abnormal, heat stroke. **Pack sizes and NHS price:** 20 mg/ml oral suspension. Pack size 250 ml £181.90 [PL14040/0036]; **Legal category:** POM. **Marketing Authorisation Holder:** Desitin Arzneimittel GmbH, Weg beim Jaeger 214, 22335 Hamburg, Germany. **Prepared:** 21 Apr 2020**.** For further on Desizon® please contact Medical Information on MedInfo@desitin.co.uk.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Adverse events should also be reported to Desitin Pharma Limited on MedInfo@desitin.co.uk.

References
1. Desizon SmPC.
2. Data on file.
3. Cramer *et al.* The relationship between poor medication compliance and seizures, *Epilepsy and Behavior* 2002; **2**: 338-342.
4. Arthur & Burgess How to identify and manage 'problem'excipients in medicines for children.
5. Shankar R *et al.* Person centred and patient focused approaches to drug administration in people with epilepsy (PWE) and intellectual disability (LD). Poster presentation Istanbul. Data on file.
6. Mistry P and Batchelor on behalf of SPaeDD-UK project. Evidence of acceptability of oral paediatric medicines: a review. *J Pharmacol* 2017; **69**(4): 361-376.
7. Nunn T EMA Workshop on Paediatric Formulations II, 8 Nov 2011.http//www.ema.europa.eu/docs/en_GB/ document _library/Presentation/2012/01/WC500121603.pdf (last accessed May 2020).

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