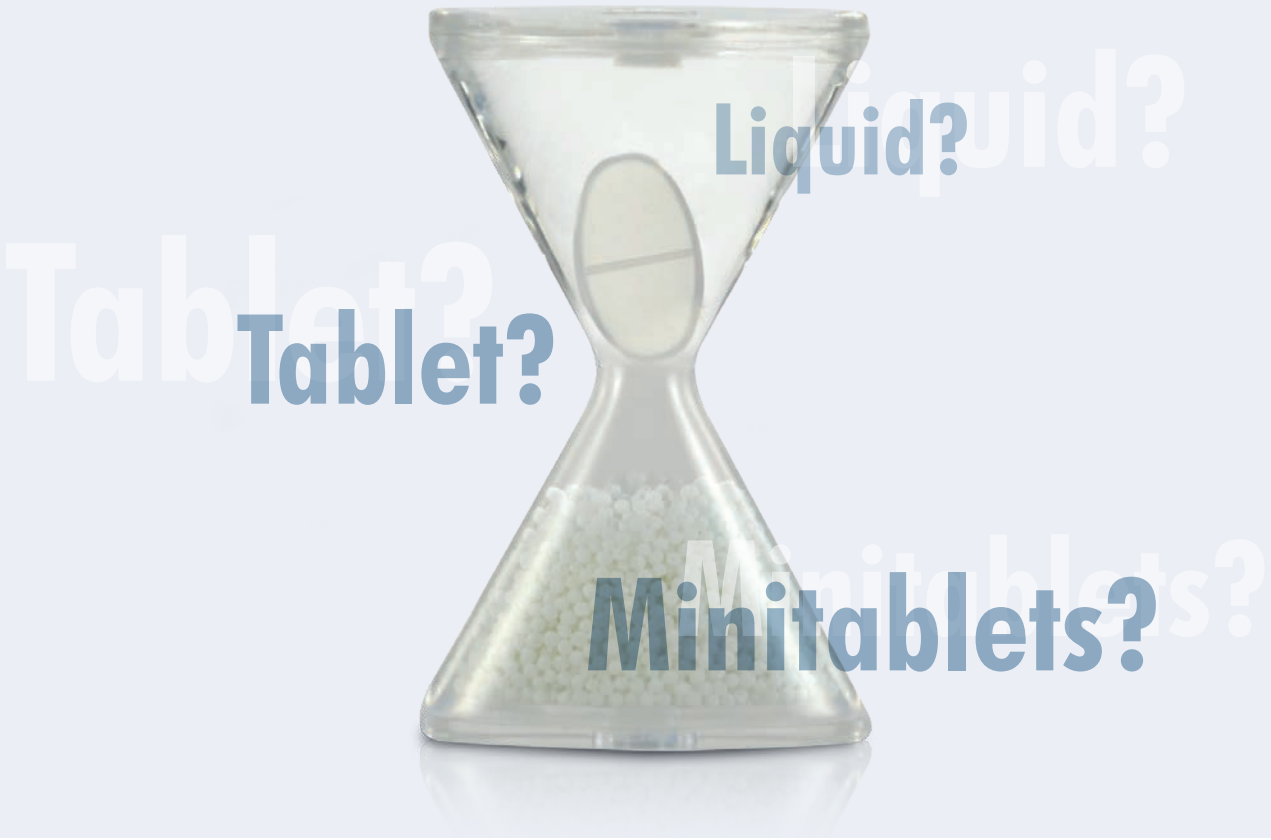
Choose the appropriate AED formulation for your patients



BECAUSE TABLET SIZE MATTERS

Desitrend®

Levetiracetam

Age- and ability-appropriate formulation designed to encourage adherence

FOR ADJUNCTIVE TREATMENT OF PARTIAL SEIZURES IN CHILDREN ≥6 YEARS

Prescribing Information can be found on the back cover.

Over 5000 new epilepsy diagnoses in children each year[1]

Choosing the right AED formulation for your patient is important. The size and shape of a tablet are fundamental to the ability of a child to swallow it. Children should be treated with medicines whose pharmaceutical design should be appropriate for use in the target age groups.[2]

Patient acceptability is likely to have a significant impact on patient adherence and consequently, on the safety and efficacy of the AED.[2]

For oral liquid preparations, the volume and palatability are among the characteristics of an AED that may have an impact on patient acceptability.[2] Small volumes are normally better accepted.[2]

Most importantly, it has been found that AED formulations have not been specified in 70% of clinic letters.[3]

ALARMING TREATMENT NON-ADHERENCE RATES IN CHILDREN

58% (Modi 2011)[5]

69% (Shetty 2016)[6]

Guidance on acceptable tablet sizes

AGE	MAXIMUM ACCEPTABLE SIZE	
	NUNN[7]	MISTRY[8]
2-5	3-5mm	<4mm
6-11	5-10mm	<7mm
12-17	10-15mm	(no data)

Guidance on acceptable liquid volumes[7]

AGE	VOLUME (MAX)
	NUNN[7]
0-3	5ml
4-12	10ml

RISKS FOR PATIENTS

- Children who are non-adherent to their AED's within the first six months of therapy are 3.24 times more likely to have seizures 4 years after diagnosis[4]

STRAIN ON NHS[9]

- 14,733 non-elective hospital admissions[9] in children ≤16 years old adding at least £23.6m to NHS costs in 2017/2018*[9,10]

**Number of finished episodes of care for admitted patients with a primary diagnosis of epilepsy/status epilepticus multiplied by the unit costs for a non-elective inpatient (£1,603).*

Ability-appropriate AED formulations

Choosing the right AED formulation for your patients with learning disabilities (LD) is particularly important. Almost 25% of people with epilepsy also have an LD.[11] LD patients are more likely to have dysphagia than others and may struggle to swallow tablets.[12] If not managed properly, it can lead to respiratory tract infections, a leading cause of death for people with a LD. According to the Royal College of Psychiatry, neurology reviews must include attention to swallowing difficulties even at the minimum level of service delivery.[13]

LEARNING DISABILITY PATIENTS WITH DYSPHAGIA AND SWALLOWING DIFFICULTIES

Liquids

Benefits include:

1. More dosage flexibility
2. NEWT Guidelines recommend levetiracetam liquid for swallowing difficulties (first choice)[14]

Challenges include:

1. Sugar content – patients with learning disabilities may be less active[15]
2. 'Sugar-free' labelled liquids may contain sugar alcohols with the associated calories
3. Not indicated for use in feeding tubes

Desitrend® minitablets

Benefits:

1. Ability-appropriate formulation
2. Desitrend® is the only formulation of levetiracetam licensed for feeding tube administration[16]
3. NEWT Guidelines recommend Desitrend® for swallowing difficulties (first choice) and feeding tube administration (second choice)[14]
4. Free from maltitol – maltitol has been suggested to decrease gut transit time and cause bloating in patients with feeding tubes[14,17]
5. Desitrend® is an ability-appropriate minitablet formulation which can be prescribed to support the needs of LD patients
6. Desitrend® prescription is accompanied by an Easy Read picture booklet which aims to engage patients with learning difficulties and promote understanding of their AED treatment, as well as involving them in the decision-making process, as recommended by NICE Clinical Guidelines[18,19]

Tablets

Benefits include:

1. Accurate dosing[2]
2. Free from maltitol and sorbitol[20]

Challenges include:

1. Dysphagia[12]
2. Requires safe management and for patients who struggle to swallow large tablets can lead to aspiration and upper respiratory tract infections (RTIs), a leading cause of early death for people with LD[12]

Patients should be informed of the formulation choices available to them, as well as the medication, during the consultation process, allowing a fully informed and accepting decision to be made.

Desitrend® vs leading brand*

*Keppra®

Significantly lower acquisition cost than Keppra®[21,22]

Per 60 doses	250mg	500mg	1000mg
Desitrend® minitablets	£22.41 (–33%)	£39.46 (–41%)	£76.27 (–43%)
Keppra® Oral Solution	£33.47 (+49%)	£66.95 (+70%)	£133.90 (+75%)

Per 60 doses	250mg	500mg	1000mg
Desitrend® minitablets	£22.41 (–20%)	£39.46 (–20%)	£76.27 (–20%)
Keppra® (tablets)	£28.01 (+25%)	£49.32 (+25%)	£95.34 (+25%)

Age-appropriate formulation algorithm for epilepsy[8]

	Are you treating neonates?	NO →	Are you treating infants?	NO →	Are you treating children aged 2-5 years?	NO →	Are you treating children aged 6-12 years?
	YES ↓		YES ↓		YES ↓		YES ↓
Liquid (including dispersible tablet or granules for reconstitution)	<0.5mL volume Neutral taste		<2.5mL volume Neutral taste		<2.5mL volume Neutral taste		<10mL volume Neutral taste
Conventional or mini monolithic tablet	**2mm minitablet acceptable**		**<3mm tablet – up to 3 tablets per dose**		**Up to 10 minitablets acceptable <4mm tablet – up to 3 tablets per dose**		**<7mm tablet – up to 3 tablets per dose**
Multi-particulate	✖		Neutral taste		Neutral taste		Neutral taste
Orodispersible tablet	✖		<6.5mm tablet Neutral taste		<9.5mm tablet Neutral taste		<9.5mm tablet Neutral taste
Chewable tablet	✖		✖		<9.5mm tablet Neutral taste		<14.7mm tablet Neutral taste

Adapted from Mistry et al, 2017.[8]
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Desitrend®
Levetiracetam

Age-appropriate AED formulations

6 to 16 years old (and ≥25kg)

Liquids

Benefits include:

1. Considered acceptable for children from full term birth and pre-term neonates who can swallow[2]
2. Dosing flexibility[2]

Challenges include:

1. Palatibilty[2] and portability[2]
2. Sugar content (incidence of obesity in children is increasing)[23]
3. Liquids are labelled "sugar-free" but may contain sugar alcohols with the associated calories
4. Risk of patient/carer dosing errors due to use of inaccurate devices and misreading dosing charts[24]
5. Excipients may include those not suitable for patients on a ketogenic diet[25]
6. Risk of aspiration with liquids
7. Some oral solution AED's require large volumes to deliver prescribed dose

Desitrend® minitablets

Benefits include:

1. Age-appropriate paediatric formulation: 2mm uniform minitablets designed to encourage adherence[16]
2. Free from maltitol, sorbitol and carbohydrate making it suitable for ketogenic diet[16]
3. Licensed for use via a feeding tube
4. Formulated to encourage adherence
5. Specifically formulated for young age group (≥6 years and ≥25kg)
6. Less expensive than Keppra® Oral Liquid and Keppra® Tablets[21,22]
7. Desitrend® minitablets contained within sachets – more convenient to carry than 300ml bottle of levetiracetam liquid

Challenges include:

1. 250mg starting dose[21]

16+ years old

Tablets

Benefits include:

1. Accurate dosing[2]
2. Free from maltitol and sorbitol[20]

Challenges include:

1. Large tablet size 13-19mm[26]
2. Demonstrated adherence issues[4,6]
3. Dysphagia[12]
4. Risk of aspiration with large tablets

Desitrend® – the 2mm uniform minitablet in a range of strengths

Desitrend®
Levetiracetam

Desitrend® (levetiracetam) Prescribing Information

Always consult the Summary of Product Characteristics before prescribing Desitrend®.

Levetiracetam available as Desitrend 250 / 500 / 1000 mg coated granules in sachet. **Indications:** Monotherapy: partial seizures with or without secondary generalisation in adults/adolescents from 16 years of age with newly diagnosed epilepsy. Adjunctive therapy: Partial seizures with or without secondary generalisation in adults, adolescents, children, and infants from 1 month of age, with epilepsy. Myoclonic seizures in adults/adolescents from 12 years of age with Juvenile Myoclonic Epilepsy. Primary generalised tonic-clonic seizures in adults/adolescents from 12 years of age with Idiopathic Generalised Epilepsy. **Dosage:** Use lowest effective dose. If discontinuation required, withdraw gradually. *Monotherapy:* Adults and adolescents ≥16 years: Starting dose 250 mg bid increasing to 500 mg bid after 2 weeks. Dose can be increased by 250 mg bid every 2 weeks to a maximum of 1500 mg bid. *Adjunctive therapy:* Adults and adolescents (12-17 years) weighing ≥50 kg: Initial dose 500 mg bid. Dose can be increased up to 1500 mg bid (changes made in 500 mg bid increases or decreases every 2-4 weeks). Elderly: Adjust dose in compromised renal function. Renal impairment: Individualise dose according to renal function (see SmPC). Hepatic impairment: In severe hepatic impairment, CLCr may underestimate renal function so reduce daily dose by 50% when CLCr <60 ml/min. Children: Prescribe the most appropriate presentation according to age, weight and dose. Granules not adapted for use in infants and children <6 years and not appropriate for initial treatment of children <25 kg, or doses <250 mg, or for doses not multiple of 250 mg when the dose is not achievable by taking multiple sachets: in all cases use levetiracetam oral solution. *Monotherapy:* No data in children or adolescents below 16 years. *Adjunctive therapy:* Infants, children and adolescents (aged 6 months to 17 years) weighing <50 kg: Starting dose for a child or adolescent weighing 25 kg: 250 mg bid. Max. dose 750 mg bid. Dose in children ≥50 kg, same as in adults. Infants from 1 month to <6 months: Use oral solution. **Administration:** Swallow granules with a sufficient quantity of liquid. Take with/without food. See SmPC for administration via a feeding tube. Each sachet is for single use only. **Contraindications**: Hypersensitivity to levetiracetam or other pyrrolidone derivatives or to any of the excipients. **Special warnings and precautions for use (see SmPC):** Patients with renal or severe hepatic dysfunction require dose adjustment. Rare reports of acute kidney injury. Rare reports of decreased blood cell counts, generally at the start of treatment: complete blood cell counts advised in patients with relevant clinical signs. Available data in children do not suggest impact on growth and puberty, but long-term effects remain unknown. Suicide, suicide attempt, suicidal ideation and behaviour have been reported: monitor patients for signs and consider treatment. Advise patients/carers to seek medical advice if signs emerge. **Interactions:** Decreases methotrexate clearance resulting in potentially toxic levels: carefully monitor methotrexate and levetiracetam levels. Isolated reports of decreased efficacy when administered with macrogol: macrogol should not be taken orally for 1 hour before/after taking levetiracetam. **Effects on ability to drive and use machines:** Minor or moderate influence. **Pregnancy/lactation:** A teratogenic risk cannot be completely excluded. Use during pregnancy and in women of childbearing potential without contraception is not recommended unless clinically necessary. Levetiracetam plasma levels decrease during pregnancy, particularly in the third trimester. Lactation: Excreted in breast milk therefore not recommended. If needed, consider benefit/risk. **Side effects (see SmPC for full list):** *Very common:* Nasopharyngitis; somnolence, headache. *Common:* anorexia (higher risk with concomitant topiramate); depression, hostility/aggression, anxiety, insomnia, nervousness/irritability; convulsion, balance disorder, dizziness, lethargy, tremor; vertigo; cough; abdominal pain, diarrhoea, dyspepsia, vomiting, nausea; rash; asthenia/fatigue. *Uncommon:* Thrombocytopenia, leukopenia; weight decrease/increase; suicide attempt, suicidal ideation, psychotic disorder, abnormal behaviour, hallucination, anger, confusional state, panic attack, affect lability/mood swings, agitation; amnesia, memory impairment, coordination abnormal/ataxia, paraesthesia, disturbance in attention; diplopia, vision blurred; liver function test abnormal; alopecia, eczema, pruritus; muscular weakness, myalgia; injury; *Rare:* Infection; pancytopenia (in some cases with bone marrow suppression), neutropenia, agranulocytosis; DRESS, hypersensitivity; hyponatraemia; completed suicide, personality disorder, thinking abnormal; choreoathetosis, dyskinesia, hyperkinesia; pancreatitis; hepatic failure, hepatitis; toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme; rhabdomyolysis, blood creatinine phosphokinase increased; acute kidney injury; encephalopathy. **Pack sizes and NHS price:** Packs of 60, 250 mg sachets £22.41 [PL14040/0029]; Packs of 60, 500 mg sachets £39.46 [PL14040/0030]; Packs of 60, 1000 mg sachets £76.27 [PL14040/0032]. **Legal category:** POM. **Marketing Authorisation Holder:** Desitin Arzneimittel GmbH, Weg beim Jaeger 214, 22335 Hamburg, Germany. **Prepared in:** Mar 2019. For further information on Desitrend® 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.

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Desitin Pharma is proud to have a long history of uninterrupted supply of their CNS manufactured medicines.

Desitrend®
Levetiracetam

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