Nya antiepileptika: genomgång av effekt och evidens.

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Sahlgrenska Universitets sjukhuset,
Göteborgs Universitet, Göteborg,
## Disclosures

<table>
<thead>
<tr>
<th>Name of Commercial Interest</th>
<th>Type of Financial Relationship</th>
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<tbody>
<tr>
<td>UCB</td>
<td>Research Grant, Consult</td>
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<td>Chief Editor</td>
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# Available Medical Treatment for Epilepsy in Sweden

<table>
<thead>
<tr>
<th>Conventional AEDs</th>
<th>Newer AEDs</th>
<th>3rd Generation AEDs</th>
</tr>
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<tbody>
<tr>
<td>Carbamazepine</td>
<td>Felbamate</td>
<td>Lacosamide</td>
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<tr>
<td>Clonazepam</td>
<td>Gabapentin</td>
<td>Rufinamide</td>
</tr>
<tr>
<td>Clobazam (licens)</td>
<td>Lamotrigine</td>
<td>Eslicarbazepine</td>
</tr>
<tr>
<td>Ethosuximide</td>
<td>Levetiracetam</td>
<td>Retigabine</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Oxcarbazepine</td>
<td>Perampanel</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Pregabalin</td>
<td>(Stiripentol)</td>
</tr>
<tr>
<td>Primidone</td>
<td>Topiramate</td>
<td>Coming up:</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Vigabatrin</td>
<td>Brivaracetam,</td>
</tr>
</tbody>
</table>

Conventional AEDs: Felbamate, Gabapentin, Lamotrigine, Levetiracetam, Oxcarbazepine, Pregabalin, Topiramate, Vigabatrin, Zonisamide

Newer AEDs: Lacosamide, Rufinamide, Eslicarbazepine, Retigabine, Perampanel (Stiripentol)

3rd Generation AEDs: Coming up: Brivaracetam,
Responder rate to newly administered AED depends on previous AED treatment history

≥50% reduction in seizure frequency

![Graph showing responder rate (%) against number of previous failed AEDs.](image)

- **Patients who failed previous AEDs due to inefficacy**
- **Patients who failed previous AEDs due to inefficacy or adverse events**
- **Newly diagnosed patients**

Prospective study n=429

Adapted from Schiller & Najjar. *Neurology* 2008;70:54-65
Seizure freedom with newly administered AED depends on previous AED treatment history

Seizure freedom

Prospective study n=429

Adapted from Schiller & Najjar. *Neurology* 2008;70:54-65
Progression with established structures

(Piracetam) → Levetiracetam → Brivaracetam

Talampanel → Perampanel

Gabapentin → Pregabalin

Carbamazepine → Oxcarbazepine → Eslicarbazepine acetate

(Tricyclic)
Mechanisms of Action of Antiepileptic Drugs

Excitatory synapse

- Presynaptic terminal
- Propagated action potential
- Voltage-gated Na⁺ channel
- Levetiracetam
- KCNQ K⁺ channel
- Retigabine
- Perampanel
- Postsynaptic neuron
  - NMDA receptor
  - AMPA receptor
  - Ca²⁺, Na⁺
  - Na⁺ (Ca²⁺)
  - (Extrasynaptic)
  - (Synaptic spine)

Phenytoin, carbamazepine, lamotrigine, lacosamide, zonisamide, oxcarbazepine

- Gabapentin, pregabalin
- α2δ subunit of P/Q-type Ca²⁺ channel
- Glutamate
AEDs with several known MOAs

- **Levetiracetam**: SV2a, Calcium, GABA
- **Topiramate**: VGSC, Calcium channel, Kainate receptor
- **Valproate**: GABA, T-type Calcium channels, weak VGSC
- **Zonisamide**: Calcium channel, GABA, even some VGSC action
- **Lacosamide**: slow acting VGSC and maybe more MOAs
Drugs with only one mechanism of action

- **Vigabatrin** = GABA transaminase

- **Tigabine** = GABA uptake (never available in Sweden)

- **Retigabine** = Potassium Channel agonist

- **Perampanel** = Non-competitive AMPA receptor inhibition
Lacosamide-Vimpat

Synthetic analogue of the amino acid D-serine
[Conley and Kohn, 1987]

Selective attenuation of slow inactivation of voltage-gated sodium channels: A sodium channel modulator
Lacosamide in the Treatment of Complex Partial Seizures

Percentage of patients with at least 50 or 75% reduction in seizure frequency from baseline period to maintenance period
Intent to treat: SP667, SP754, SP755   *p<0.05; ** p<0.001

Lacosamide: Incidence of Common AEs Reported by ≥5% of Patients

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Placebo (%) (n=364) forced titration phase</th>
<th>Placebo (%) (n=364) maintenance phase</th>
<th>VIMPAT® 200 mg/day (%) (n=270) forced titration phase</th>
<th>VIMPAT® 200 mg/day (%) (n=270) maintenance phase</th>
<th>VIMPAT® 400 mg/day (%) (n=471) forced titration phase</th>
<th>VIMPAT® 400 mg/day (%) (n=471) maintenance phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>6.6</td>
<td>1.5</td>
<td>10.4</td>
<td>7.3</td>
<td>24.6</td>
<td>8.4</td>
</tr>
<tr>
<td>Nausea</td>
<td>3.6</td>
<td>1.2</td>
<td>5.6</td>
<td>2.0</td>
<td>8.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Diplopia</td>
<td>1.1</td>
<td>0.9</td>
<td>4.4</td>
<td>3.7</td>
<td>8.3</td>
<td>3.6</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.9</td>
<td>0.9</td>
<td>4.8</td>
<td>4.1</td>
<td>6.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5.2</td>
<td>0.3</td>
<td>6.7</td>
<td>1.2</td>
<td>6.8</td>
<td>1.0</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>1.6</td>
<td>0.6</td>
<td>1.9</td>
<td>1.2</td>
<td>6.2</td>
<td>3.1</td>
</tr>
<tr>
<td>Abnormal coordination</td>
<td>1.4</td>
<td>0.3</td>
<td>2.2</td>
<td>2.4</td>
<td>5.9</td>
<td>1.8</td>
</tr>
<tr>
<td>Tremor</td>
<td>3.3</td>
<td>0.9</td>
<td>1.5</td>
<td>2.4</td>
<td>4.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>3.0</td>
<td>0.9</td>
<td>1.5</td>
<td>0.8</td>
<td>4.0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Eslicarbazepine Acetate-Zebinix

- The differentiator vs. CBZ is no epoxide
- The differentiator vs. OXC is a higher ratio of S-licarbazepine

Almeida and Soares 2007
Eslicarbazepine: Phase III studies as add-on therapy in partial seizures

**Placebo-controlled data**

- **Efficacy:**
  - **Responder rate:** ≥50% reduction in seizure frequency over the 12-week maintenance period (ITT population)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Responder rate</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>21.5%</td>
<td>-</td>
</tr>
<tr>
<td>400 mg</td>
<td>22.9%</td>
<td>n.s.</td>
</tr>
<tr>
<td>800 mg</td>
<td>36.3%</td>
<td>0.0001</td>
</tr>
<tr>
<td>1200 mg</td>
<td>43.5%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Elger et al, Epilepsia. 2009; 50:454-63, Gil-Nagel et.al.,
Acta Neurol Scand. 2009:281-7, Data on file Bial, Portugal
ESL: Phase III studies as add-on therapy in partial seizures: *Placebo-controlled data*

Incidence of TEAEs affecting >2% of patients in any group

<table>
<thead>
<tr>
<th>Treatment-emergent AEs</th>
<th>Placebo</th>
<th>400 mg</th>
<th>800 mg</th>
<th>1200 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>7.3%</td>
<td>13.3%</td>
<td>21.1%</td>
<td>28.9%</td>
</tr>
<tr>
<td>Somnolence</td>
<td>9.3%</td>
<td>10.7%</td>
<td>13.0%</td>
<td>15.0%</td>
</tr>
<tr>
<td>Headache</td>
<td>8.7%</td>
<td>8.7%</td>
<td>10.2%</td>
<td>13.6%</td>
</tr>
<tr>
<td>Nausea</td>
<td>2.1%</td>
<td>5.1%</td>
<td>7.4%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Diplopia</td>
<td>1.7%</td>
<td>5.1%</td>
<td>8.1%</td>
<td>8.6%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.4%</td>
<td>2.0%</td>
<td>6.7%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Coordination abnormal</td>
<td>2.1%</td>
<td>3.1%</td>
<td>5.3%</td>
<td>6.1%</td>
</tr>
<tr>
<td>Vision blurred</td>
<td>1.0%</td>
<td>4.1%</td>
<td>3.9%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Influenza</td>
<td>2.1%</td>
<td>3.6%</td>
<td>2.1%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Vertigo</td>
<td>0.3%</td>
<td>2.0%</td>
<td>1.8%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1.0%</td>
<td>1.0%</td>
<td>4.2%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2.8%</td>
<td>2.0%</td>
<td>1.8%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Constipation</td>
<td>1.0%</td>
<td>3.1%</td>
<td>1.1%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Rash</td>
<td>0.3%</td>
<td>0.5%</td>
<td>1.1%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Depression</td>
<td>0.3%</td>
<td>3.1%</td>
<td>0.7%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Convulsion</td>
<td>2.1%</td>
<td>1.5%</td>
<td>1.1%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>
Perampanel

• Selective AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid)-type glutamate receptor antagonist
Perampanel pooled Phase III data – responder rates

Fifty percent responder rates for all partial seizures, CP + SG seizures, and SG seizures only (ITT analysis set)\(^4\)

*\(p > 0.05; ~**p < 0.01; ~***p < 0.001\) versus placebo.

CP + SG, complex partial plus secondary generalised; ITT, intent-to-treat; SG, secondarily generalised
Perampanel – long-term safety

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>TEAEs in ≥10% of patients (n=1216)</th>
<th>TEAE leading to study or perampanel withdrawal n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>1110 (91.3%)</td>
<td>195 (16.0%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>569 (46.8%)</td>
<td>48 (3.9%)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>258 (21.2%)</td>
<td>10 (&lt;1%)</td>
</tr>
<tr>
<td>Headache</td>
<td>222 (18.3%)</td>
<td>7 (&lt;1%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>159 (13.1%)</td>
<td>12 (&lt;1%)</td>
</tr>
<tr>
<td>Irritability</td>
<td>140 (11.5%)</td>
<td>16 (1.3%)</td>
</tr>
<tr>
<td>Weight increased</td>
<td>132 (10.9%)</td>
<td>8 (&lt;1%)</td>
</tr>
</tbody>
</table>

Adapted from Clement et al.\(^8\)

- 71.3% of the patients (n=867) were treated for at least 52 weeks
- Perampanel was generally well tolerated
- Most TEAEs were mild/moderate and dose responsive
- Relatively few patients discontinued treatment (16.0%), opting instead to reduce the dose (39.7%)\(^8\)
PGTC Seizures: 50% Responder Rates

Rufinamide

- 1-(2,6-Difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide
- Approved for Lennox-Gastaut Syndrome and refractory partial seizures
- Triazole derivative; exact mechanism of action unknown
  - Thought to regulate voltage dependent sodium channels
Rufinamide: Responder rate and seizure freedom: tonic-atactic seizures (secondary endpoints)

### AEs with Incidence ≥5% vs. Placebo in Subjects with Lennox-Gastaut Syndrome

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rufinamide, %</th>
<th>Placebo, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=74</td>
<td>N=64</td>
<td></td>
</tr>
<tr>
<td>Somnolence</td>
<td>24.3</td>
<td>12.5</td>
</tr>
<tr>
<td>Vomiting</td>
<td>21.6</td>
<td>6.3</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>13.5</td>
<td>17.2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9.5</td>
<td>7.8</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>9.5</td>
<td>4.7</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>9.5</td>
<td>3.1</td>
</tr>
<tr>
<td>Headache</td>
<td>6.8</td>
<td>4.7</td>
</tr>
<tr>
<td>Rash</td>
<td>6.8</td>
<td>1.6</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>5.4</td>
<td>4.7</td>
</tr>
<tr>
<td>Ataxia</td>
<td>5.4</td>
<td>0</td>
</tr>
</tbody>
</table>

*Double-blind adjunctive therapy study in LGS; includes only AEs occurring at higher incidences with Rufinamide than placebo*
Retigibine- Ezogabine

**N-(2-amino-4-(4-fluorobenzylamino)-phenyl) carbamic acid ethyl ester**

KCNQ K+ agonist
Opens voltage-gated K+ channels and therefore enhances M-type K+ currents

\[ C_{16}H_{18}FN_3O_2 \]
Small molecule: molecular weight 303.3 g/mol
Retigabine Dose-ranging Trial for Partial-onset Seizures: Primary Efficacy Results

Intent-to-treat population

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Change in Total Monthly Partial-Seizure Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-13.1%</td>
</tr>
<tr>
<td>600 mg/day</td>
<td>-23.4% *</td>
</tr>
<tr>
<td>900 mg/day</td>
<td>-29.3% *</td>
</tr>
<tr>
<td>1200 mg/day</td>
<td>-35.2% *</td>
</tr>
</tbody>
</table>

*P<0.001 for overall difference across all treatment arms
†P<0.047 for overall difference across retigabine 300, 600, and 1,200 mg/day arms

Retinal pigment clumping and blue skin discoloration with Ezogabine (Potiga)
Medical Marijuana and Epilepsy in USA

• Began with a few anecdotal reports – even a few negative

• Overall efficacy, safety, dosing not defined

• “Charlotte’s Web” – cannabidiol (CBD) – (CNN)

• Legal in 15 states in USA

• AES and AAN: supported well designed clinical research
"Medical Marijuana"-Cannabidiol

- FDA: Granted orphan status for Epidiolex (GW) – Dravet, LGS, Phase 1, CBD, 158 patients

- About 50% better in 12 week follow up

Devinsky O. Lancet Neurology2015 S1474-4422(15)00379-8
Which Drug for Which Seizure Type as Adjunctive Therapy?

- Is it best to choose drug with different mechanism of action than the first drug?
Rationale Polypharmacy

• Little support in clinical trials but intellectually enticing

• Rational Polypharmacy has been proposed for the last 15 years but only 2 instances of success

• This means that if an AED does not control seizures then adding an AED with another mechanism of action might be more effective than adding one with the same.
Types of Rational Polytherapy

• Combination of AEDs with several mechanisms of action have an additive effect

• Two drugs can potentiate each other to have a super additive effect = synergism

• Treating epilepsy and a comorbidity with one or two drugs

• Using two drugs to counteract side effects
Efficacy: 50% Responder Rates (ITTm)*

P values (panel B) are based on a pairwise treatment logistic regression model with terms for treatment and trial * P<.05, ** P<.01

* The ITTm population included all randomized patients receiving ≥1 dose of trial medication with ≥1 post-baseline efficacy assessment, excluding those who discontinued during the Titration Phase

§ Lacosamide is approved up to a dose of 400 mg/d
Safety: Incidence of Common TEAEs By Dose

**Pooled Phase II/III Population**

TEAEs are those occurring at a rate of ≥5% for lacosamide (all doses combined) and greater than placebo in the pooled Phase II/III population; LCM = lacosamide

Lacosamide is approved up to a dose of 400 mg/d

Davies et al. Poster Scientific Exhibition AES 2009; UCB data on file
Efficacy: 50% Responder Rates with Adjunctive Lacosamide in Patients Only using Concomitant AEDs that act on Non-Sodium Channel Targets (ITTm)*

* The ITTm population included all randomized patients receiving ≥1 dose of trial medication with ≥1 post-baseline efficacy assessment, excluding those who discontinued during the Titration Phase

P values based on a pairwise treatment logistic regression model with terms for treatment and trial; ** P<.01

§ Lacosamide is approved up to a dose of 400 mg/d

Davies et al. Poster Scientific Exhibition AES 2009
TEAEs that occurred at an incidence of ≥5% and greater than placebo for patients randomized to lacosamide (all doses combined) in the overall pooled Phase II/III population were identified: the incidence of these specific TEAEs are presented here for those patients only using concomitant AEDs that act on non-sodium channel targets.
Which Drug for Which Seizure Type as Adjunctive Therapy?

• Probably best to choose drug with different mechanism of action than first drug

• There are exceptions!
Possible Rational Combinations

**VGSC Blockers:**
- Phenytoin
- Carbamazepine,
- Oxcarbazepine
- Lamotrigine
- Lacosamide
- Eslicarbazepine

**Can be combined with**
- Clobazam
- Brivaracetam
- Gabapentin,
- Levetiracetam
- Perampanel
- Pregabalin
- Topiramate
- Valproate
- Vigabatrin,
- Zonisamide
Major Considerations for Antiepileptic Drug Selection:

- Seizure Control
- Gender
- Age
- Interactions
- Side Effects
- Formulations
- Expense
Enzyme Induction
Potential for Drug-Drug Interactions With AEDs

**Inducers** (1A2, 2C, 3A4, UGT)
- Phenytoin
- Carbamazepine
- Phenobarbital
- Primidone

**Inhibitors** (2C9, UGT, EH)
- Valproate
- Felbamate

**Mild inducers (3A4) or inhibitors (2C19)**
- Oxcarbazepine
- Topiramate
- Eslicarbazepine

**Cytochrome P450**

**Negligible or no effect**
- Brivaracetam
- Gabapentin
- Lacosamide (Lamotrigine)
- Levetiracetam
- Perampanel
- Pregabalin
- Rufinamide
- Vigabatrin
- Zonisamide

When should non-inducing AEDs be used

• 1. To avoid systemic side effects
• 2. To avoid drug-drug interactions when treating concomitant illnesses
• 3. When using the contraceptive pill to avoid loss of protection
• 4. In the elderly who are already taking multiple medications
• 5. In men and women with reproductive issues and disorders
• 6. In people with risk of osteoporosis
Rash Rate: Lacosamide, Rufinamide, Eslicarbazepine Acetate and Perampanel

- Rash Rate for ESL acetate in monotherapy = 2-3%
- No significant increase in rash rate compared to placebo (2.9% vs 3%) for LCM at 400 mg
- No significant increase in rash rate compared to placebo (0.3% vs 1.1%) for PER at 8 mg
FDA Alert- Oxcarbazepine but not Eslicarbazepine Acetate

• 12/4/2015 On Dec 4, 2015, the FDA approved updated Prescribing Information (PI) for oxcarbazepine. Serious, potentially life-threatening, dermatologic reactions such as toxic epidermal necrolysis (TEN) and Stevens Johnson syndrome (SJS) have occurred in adults and children treated with oxcarbazepine.

• Median time of onset was 19 days. Patients with Human Leukocyte Antigen (HLA) allele B*1502 may be at increased risk. The HLA-B*1502 allele is present in 2-15% of patients from various countries with Han Chinese ancestry.

• Prior to initiating oxcarbazepine treatment, testing for HLA-B*1502 should be considered in patients of Asian ancestry. Oxcarbazepine should be avoided in patients positive for HLA-B*1502, unless the benefits clearly outweigh the risks.

• - See more at: https://www.aesnet.org/clinical_resources/treatments/drug_alerts_fda_news#sthash.nBv6vNtt.dpuf
Uncontrolled epilepsy is not synonymous with drug-resistant epilepsy

• Reasons in patients with chronic epilepsy:
  – Inadequate use of AEDs in terms of dosage or duration of treatment (44%)
  – Lack of information on treatment response
  – Failure of only 1 adequately used AED (14%)
  – Risk behavior like alcohol consumption
  – Combination of epilepsy and psychogenic seizures
Basic Principles of Treatment

• Important to **correctly diagnose** the seizure type and syndrome in order to select the most appropriate AED

• Important to select the most **appropriate initial treatment** and individualize therapy, also considering factors such as: tolerability profile, titration regimen, simplicity of use (once daily) and impact on overall patient outcomes.

• Selection of an appropriate monotherapy should consider the **current level of evidence** available in conjunction with patient factors and AED characteristics.
### AEDs approved for Monotherapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td></td>
</tr>
<tr>
<td>Clonazepam</td>
<td></td>
</tr>
<tr>
<td>Gabapentin (Europe)</td>
<td></td>
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<td>Lacosamide (USA)</td>
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<tr>
<td>Levetiracetam</td>
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<td>Oxcarbazepine (Europe)</td>
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<td>Eslicarbazepine (USA)</td>
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<td>Primidone</td>
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<td>Phenobarbital</td>
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<td>Phenytoin</td>
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<td>Topiramate</td>
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<td>Valproic Acid</td>
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<tr>
<td>Zonisamide</td>
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Yellow = New indication 2015
Most Recent head-to-head monotherapy studies

Percentage of patients achieving seizure freedom for ≥6 months

**LEV non-inferior to CBZ-CR**

- **LEV**: 73.0% (n=237)
- **CBZ-CR**: 72.8% (n=235)

**ZNS non-inferior to CBZ-CR**

- **ZNS**: 79.4% (n=223)
- **CBZ-CR**: 83.7% (n=233)

**PGB inferior to LTG**

- **PGB**: 52% (n=314)
- **LTG**: 68% (n=308)

CBZ-CR, controlled-release carbamazepine; LEV, levetiracetam; LTG, lamotrigine; PGB, pregabalin; ZNS, zonisamide

AED treatment options by seizure type according to EBM and Guidelines

Secondarily generalized

Focal Onset
- Tonic-clonic

Generalized onset
- Tonic
- Myoclonic
- Atonic
- Absence

- CBZ, OXC, PHT.
- LCM, ESL, RET

VPA, LTG*, TPM**, ZNS**, LEV, CLB, CLB, PER

** (broad-spectrum agents)

*?Myoclonic  **?Absence?
Strategies for Optimizing AED Use

• Match choice of AED to seizure type(s) and to a patient’s specific characteristics
• Use monotherapy if possible
• Use polytherapy if necessary
• When adding an AED start low and go slow, but push to maximum tolerated dose if necessary
• Consider changing timing of dosing to reduce toxicity
• Use pharmacokinetec principles to fine-tune dose
• Adjust dose for drug-drug interactions
• **Do not give up**

Everyone has to be treated Individually according to their special needs.