

Antiepileptic Drugs for Nonepilepsy Conditions

Update #2

Key Questions and Inclusion Criteria

Key Questions

1. For adult outpatients with bipolar disorders, fibromyalgia, migraine, or chronic pain, do antiepileptic drugs (AEDs) differ in effectiveness?
2. For adult outpatients with bipolar disorders, fibromyalgia, migraine, or chronic pain, do AEDs differ in safety or adverse events?
3. Among these patient populations, are there subgroups of patients based on demographics (age, racial groups, and gender), other medications, or comorbidities for which one AED is more effective or associated with fewer adverse events?

Inclusion Criteria

Populations

Adult outpatient populations with one of the following diseases or conditions:

- Bipolar Disorders (e.g. Bipolar II Disorder subtype, etc.) as diagnosed by DSM (*Diagnostic and Statistical Manual of Mental Disorders*) criteria.
- Fibromyalgia or fibromyalgia syndrome as diagnosed by the American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia: a history of spontaneous pain along the spine and all four quadrants of the body for more than 3 months and pain on digital palpation at 11 of 18 tender point sites.
- Chronic Pain
 - Chronic pain defined as continuous or recurring pain of at least 6 months' duration
 - Excludes neuropathic pain.
- Migraine
 - Definition of migraine must be explicit, to exclude other types of headache (e.g. tension headache). Any level of migraine (mild, moderate, severe) and with or without aura will be included.

Interventions

Generic Name	Trade Name(s)
Carbamazepine	Tegretol
Divalproex*	Depakote
Ethotoin	Peganone
Gabapentin	Neurontin
Lamotrigine	Lamictal
Levetiracetam	Keppra
Oxcarbazepine	Trileptal
Phenytoin	Dilantin
Pregabalin	Lyrica
Tiagabine	Gabitril
Topiramate	Topamax
Valproic acid*	Depakene, Depacon
Zonisamide	Zonegran

*sometimes known as Valproate

Effectiveness outcomes*Bipolar Mood Disorders*

- Response (rate, degree, speed of onset, duration, etc.)
- Remission (rate, speed of onset, duration, etc.)
- Response/remission maintenance, recurrence rate, relapse prevention, etc.
- Use of other medications for acute episodes
- Functional capacity (quality of life, work productivity)
- Danger to self (suicide attempts and completions)
- Hospitalization

Chronic Pain and Fibromyalgia

- Response (pain intensity and pain relief, change from baseline and proportion achieving relief)
- Use of Rescue Medications
- Functional capacity (quality of life, work productivity)
- Speed and duration of response
- Relapse

Migraine

- Attack frequency
- Days with migraine
- Response (intensity, duration, proportion of patients achieving, etc.)
- Use of acute treatments
- Functional outcome (e.g. Change in days of work lost)
- Quality of life

Safety outcomes

- Overall adverse effect reports
- Withdrawals due to adverse effects
- Major adverse events reported
- General adverse effects or withdrawals due to specific adverse events (e.g., dizziness, drowsiness/sedation, rash, hepatotoxicity, thrombocytopenia, hyperammonemia, Etc.)

Study designs

1. For effectiveness, controlled clinical trials and good-quality systematic reviews.
 - a. Trials directly comparing one anti-epileptic drug to another are preferred. If none exist, trials comparing an included anti-epileptic drug to placebo will be considered.
2. For safety, in addition to controlled clinical trials, observational studies will be included.