ACCEPT

Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics

How to Join:
https://iecho.org/public/program/PRGM1708646970665RHK0C7J5TR

For attendance purposes please text the following code: HEZVEY to 608-260-7097

Session Date: Friday, March 20, 2026

Didactic Topic and Presenter:
Kratom

Maxwell Butler, MD
Mark Wirtz, MD
Content experts: Sheila Weix and Joe Galey

- 12:15 PM: Attendance text-in – Introductions
- 12:25 PM: Case Presentation
  - Presenter: Mark Wirtz, MD
- 12:50 PM: Case Presentation
  - Presenter: Maxwell Butler, MD
- 1:15 PM End of Session

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2026 Universal Activity Number (UAN): JA0000358-0000-26-008-L01-P

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Interprofessional Continuing Education Partnership
UNIVERSITY OF WISCONSIN-MADISON
School of Medicine and Public Health
School of Nursing
School of Pharmacy

ECHO ACCEPT
Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics 2026
Kratom
3/20/2026
Didactic Presenter: Max Butler, MD
Case Presenter: Mark Wirtz, MD

Provided by the University of Wisconsin–Madison Interprofessional Continuing Education Partnership (ICEP)

Intended Audience:

Nurses, Nurse Practitioners, Pharmacists, Physicians, Physician Assistants, Pharmacy Technicians, Psychologists, Social Workers, Patient/Caregivers, Students

Objectives:

1) Summarize the history, epidemiology, and pharmacology of kratom and 7-hydroxymitragynine
2) Evaluate patients for use of kratom and other unregulated supplements
3) Describe ways to treat kratom withdrawal and kratom use disorder

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Name	Role	Financial Relationship Disclosures	Discussion of Unlabeled/Unapproved uses of drugs/devices in presentation?	COI completion date
David Leinweber	RSS Chair/Reviewer	No relevant financial relationships to disclose	Yes	12/9/2025
Nada Rashid	RSS Coordinator	No relevant financial relationships to disclose	No	12/10/2025
Kathleen Maher	RSS Coordinator	No relevant financial relationships to disclose	No	12/9/2025
Randall Brown	Planner	No relevant financial relationships to disclose	Yes	12/10/2025
Ritu Bhatnagar	Planner	No relevant financial relationships to disclose	Yes	12/6/2025
Paul Hutson	Planner	usona (Independent Contractor - Consultant), Midwest Pharmacokinetic Consulting, LLC (Independent Contractor - Consultant), Otsuka America Pharmaceutical, Inc. (Independent Contractor - Consultant), Tryptamine Therapeutics (Independent Contractor - Consultant)	Yes	12/9/2025
Susan Mindock	Planner	No relevant financial relationships to disclose	No	12/8/2025
Sheila Weix	Planner	No relevant financial relationships to disclose	No	12/11/2025
Kellene Eagen	Planner	No relevant financial relationships to disclose	No	12/8/2025

Joseph Galey	Planner	No relevant financial relationships to disclose	No	12/19/2025
Max Butler	Presenter	No relevant financial relationships to disclose	No	2/2/2026
Mark Wirtz	Presenter	No relevant financial relationships to disclose	No	2/2/2026

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Case Presentation: 7-OH kratom alkaloid

Mark Wirtz, MD
UW Health

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For this educational activity there are no reported conflicts of interest

Project ECHO University of Wisconsin

Case Introduction

- 40 year-old female presents to clinic after experiencing nausea, diaphoresis, hot/cold flashes, shaking when trying to stop using an online apothecary's 7-OH kratom alkaloid.
- Primary question for discussion: What is the appropriate management for a patient meeting criteria for a severe substance use disorder whose substance is is 7-OH mitragynine kratom alkaloid?

Medical & Behavioral Health Diagnosis:	Current Medications:
• Anxiety • Depression • PTSD • ADHD • Borderline PD • Prediabetes • Hypothyroidism	• Synthroid • Lisdexamfetamine • Zolpidem

Substance Use

- History: In December of 2025, patient had significant tooth pain. She was recommended to try “7-Oh” from a friend which she purchased from an online apothecary.
- Had excellent relief from pain and used for a few weeks until saw dentist.
- When trying to stop the medication felt very sick and wanted to take more of the medication. Tried weaning down and stopping for several days without success.
- Felt very scared of what was in the pill but also didn’t want to experience going off the medication. Consequences of Substance Use:
  - Social/occupational/educational: Purchased more without family’s knowledge, kept secret
  - Physical (including evidence of tolerance/withdrawal): Anxiety, yawning, rhinorrhea, shaking, flushes, restlessness, desire to use
- Past treatments: None

Social History:	Family History:
• Social Factors/History: • Housed • Married, two children, one with autism • Education/Literacy: Technical Degree • Income source:Home business	• Father – Alcohol Use Disorder • Mother – Depression

Patient strengths & protective factors:	Risk factors:
• Strong supports in mother and sister • Job • Fear of overdose	• Mood disorder

Labs

- Pain Management Profile:
- +Stimulant, +Amphetamine
- Negative for all other measured substances

Patient Goals & Motivations for Treatment

- Stop “7-Oh” completely.
- Afraid of addiction and overdose.
- Avoid withdrawal symptoms.

Proposed Diagnoses

- Severe Substance Use Disorder
  - Meets 8/11 Criteria
    - Consuming larger amounts/time
    - Desire to cut down/unsuccessful stop
    - Craving/pressure to use
    - Impair home obligations
    - Continue use despite causing disruption
    - Persistent substance use despite knowledge may cause problems
    - Tolerance
    - Withdrawal

Proposed Treatment Plan

- Called and discussed with Addiction Hotline Provider
- Start: Buprenorphine-Naloxone 2-0.5mg films – two films per day
- Day 1: Required total of 6 films to achieve symptom control.
- Day 3: Refilled at Buprenorphine-Naloxone 4-1 mg films – three films per day
- Day 6: Maintained at three films per day
- Day 14: Reduced to total of 2.5 films per day
- Day 21: Planned at Day 28 to reduce to 2 films per day
- Day 35: Currently doing well at 2 films per day, plan to reduce to 1.5 films per day

Discussion:

- Primary question:
- Is the use of Buprenorphine-Naloxone appropriate in the setting of a patient meeting severe substance use disorder whose only reported use is a 7-OH kratom alkaloid?

Discussion:

- Secondary question:
- Patient reported this online apothecary has continue to send “samples” of this 7-OH kratom alkaloid which is very distressing. Do we have any advocacy or regularly resources to level against this apothecary’s behavior?

DSM-5 Substance Use Disorder ("Addiction")

- Tolerance
- Withdrawal

} **Physical Dependence ≠ Use Disorder**

- Larger amts/longer periods than intended
- Persistent desire/failed attempts to quit/control use
- Much time obtaining/using/recovering
- Important activities sacrificed
- Continued use despite known adverse effects
- Failure to fulfill major obligations
- Recurrent hazardous use
- Craving
- Ongoing use despite interpersonal problems

2-3 = mild
4-5 = moderate
≥ 6 = severe

By initialing here _____ you have acknowledged that Project ECHO case consultations do not create or otherwise establish a provider-patient relationship between any ECHO clinician and any patient whose case is being presented in a teleECHO clinic.

Project ECHO University of Wisconsin

Kratom

Max Butler, MD

Addiction Medicine Fellow

University of Wisconsin School of Medicine & Public Health

March 20, 2026

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1. Summarize the history, epidemiology, and pharmacology of kratom and 7-hydroxymitragynine
2. Evaluate patients for use of kratom and other unregulated supplements
3. Treat kratom withdrawal and kratom use disorder

Agenda

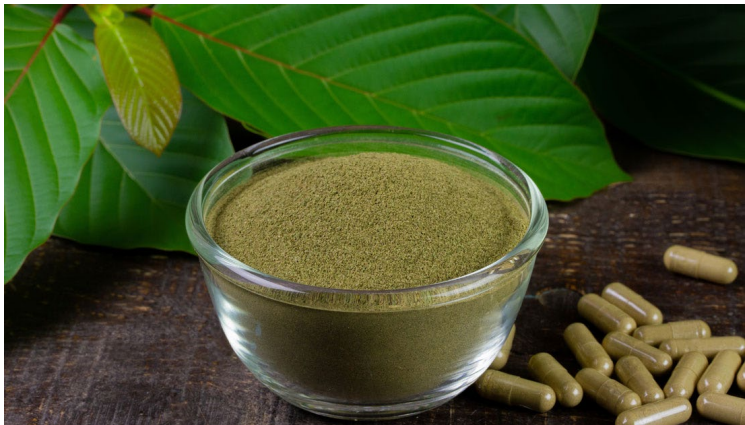
- Overview and history of kratom
- Pharmacology of kratom and its alkaloids
- Kratom intoxication
- Kratom withdrawal
- Kratom use disorder
- Regulatory aspects

Kratom: Overview

https://www.britannica.com/plant/kratom

- *Mitragyna speciosa*
- Evergreen tree native to Southeast Asia
- Related to coffee plant
- Contains >40 alkaloids
- Used for centuries for medicinal purposes (analgesic, antipyretic, antidiarrheal)
- Introduced in the US in 1990s and rose to popularity in the 2000s

https://vitalrecord.tamu.edu/you-asked-what-is-kratom/



History

- Traditional uses of kratom in Southeast Asia:
  - Chewing leaves – to stave off fatigue while working in the fields and fishing
  - Brewed into tea – for medicinal purposes
- 1921: Mitragynine isolated at University of Edinburgh
- 1990s: Introduced into the US and Europe
- 2000s-2010s: Grew in popularity, primarily used in powder form, either as loose powder, in capsules, or in tablets
  - Became available in gas stations, vape shops, and online retailers
- 2010s: Growing concern from DEA and FDA
- 2024 – present: Increased marketing and concentration of 7-OH in kratom products, more diversity of formulations

BEST SELLER

★★★★★ 1275 reviews

GREEN MAENG DA KRATOM POWDER

40% Off

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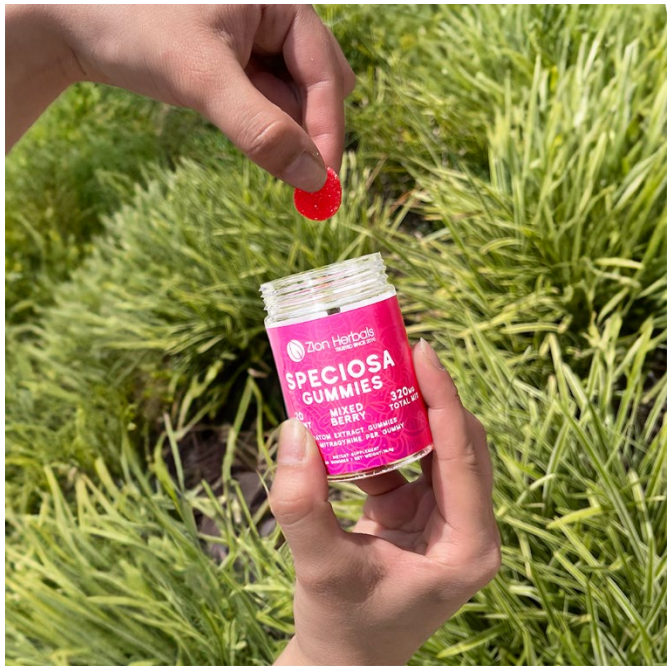
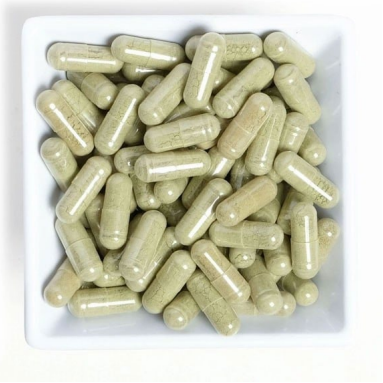
Elite White Vein Maeng Da Kratom Powder

★★★★½ 4.7 (1436)





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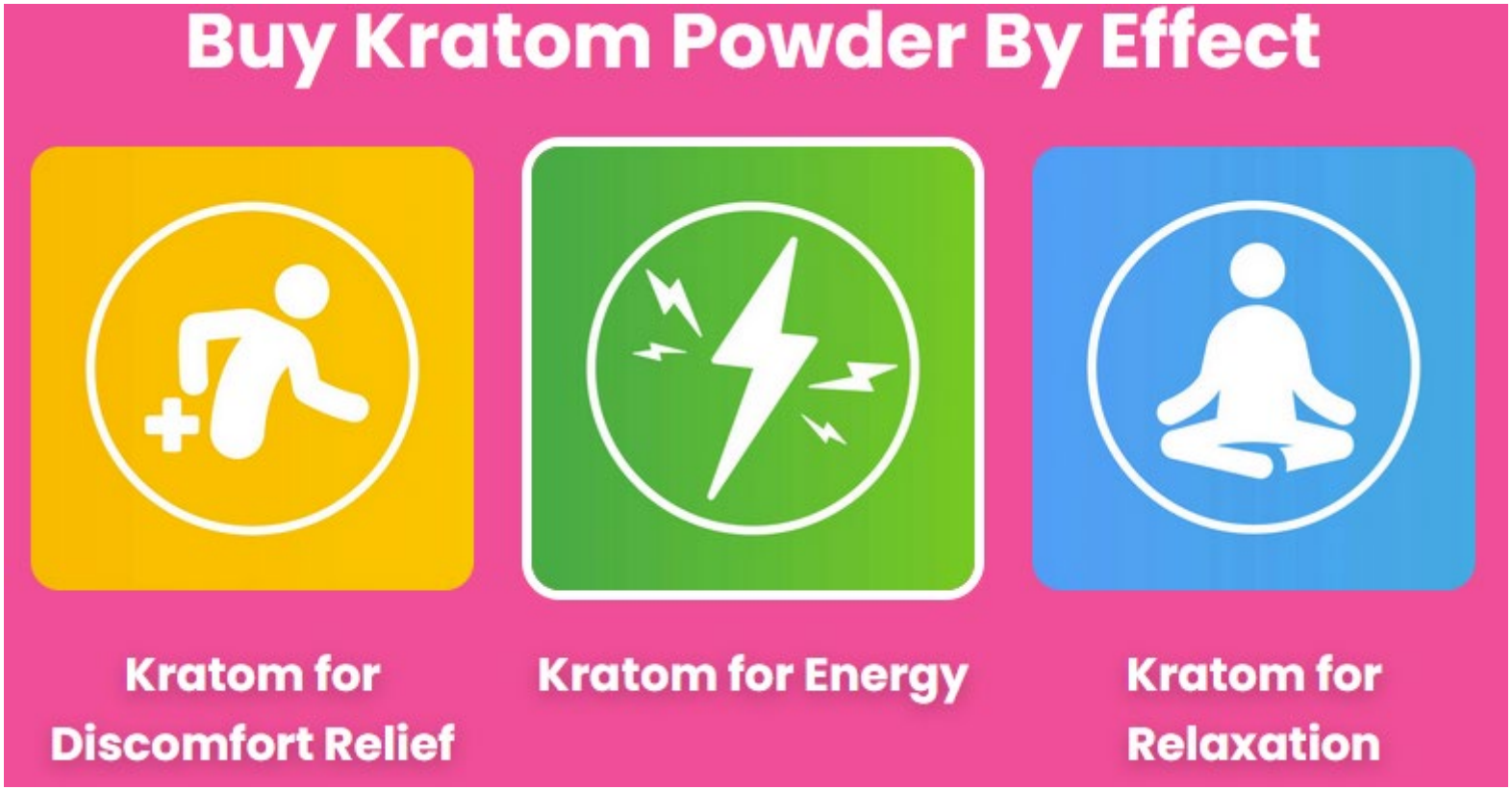
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Kratom Speeds

Fast (Energy)

Moderate (Balanced)

Slow (Relaxation)

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Kratom Colors

Green Vein

Red Vein

White Vein

Yellow Vein

View All

Kratom Strains

Maeng Da

Bali

Borneo

Thai

Sumatra

View All

Kratom Effects

Balanced

Calm Mentality

Clean Energy

Discomfort Relief

Enhanced Creativity

Happy Mind

Increased Focus

Joyful Spirit

Pro Social

Productivity

Relaxed Body

Restful Sleep

Super Energy

Workout Boost

Epidemiology

- NSDUH (2019-2021): 1.7-1.8 million people reported consumption of kratom in the past year
  - Some estimate that this number is closer to 10 million
- Frequency of use is variable, from occasional to daily
  - For those who use daily, typical use is 1-3 times per day
- Demographics: male, middle-aged, white, middle income, employed
- Most common reasons for use:
  - Chronic pain relief
  - Relaxation
  - Stress management
  - Anxiety
  - Energy enhancement
  - Depression
  - Self-management of opioid withdrawal

Kratom: Effects

- At low doses (<5g) → stimulant-like effects
  - These doses are used for energy, mood, and anxiety
- At higher doses (>5g) → sedative/opioid-like effects
  - These doses are used for pain and decreasing opioid use
- Has analgesic, anxiolytic, and antidepressant effects
- Heavy, daily use of kratom can produce physiological dependence and withdrawal upon abrupt cessation
  - Typically at doses >14 g/day
- Different preparations have different ratios of alkaloids, which changes the effects

Mitragynine

- Mitragynine (MG) is the predominant alkaloid in the fresh leaf and dried leaf products
- MG comprises 12-66% of total alkaloid content, 1-2% dry weight
- Effects:
  - Mu opioid receptor – partial agonist, low affinity, low potency. Biased towards G-protein pathway without significant recruitment of beta-arrestin pathway
  - Kappa opioid receptor – antagonist, greater affinity
  - Alpha-2 receptor – weak agonist
  - Serotonergic receptors – weak agonist effects
- In animal models, mitragynine is not very reinforcing
- Peak effect: 45 min – 1 hr
- Half-life: 3-4 hrs (or longer depending on formulation)
- Low risk of respiratory suppression

7-Hydroxymetragynine (7-OH)

- A potent mu opioid agonist. Similar in potency to oxycodone, 10-20x more potent than MG
- In fresh leaf, 7-OH undetectable
- In dried leaf, 7-OH <2% alkaloid content, <0.05% dry weight
- 7-OH is present in 3 main ways:
  - During drying process
  - In the body, MG → 7-OH via phase I oxidation via CYP3A4 and CYP2D6
  - Processing of products via oxidation reactions converts some of the MG to 7-OH, thus increasing concentration of 7-OH
- In animal studies, noted to be reinforcing
- Peak effect: 1.5 hrs
- Half-life: 2-5 hrs

7-Hydroxymetragynine (7-OH)

- In traditional uses (e.g. chewing fresh leaf, teas), 7-OH present in very low concentrations
- Products with enhanced concentration of 7-OH are becoming more common
  - Misleadingly marketed as kratom products
  - Marketed as more convenient than traditional kratom
- One study performed liquid chromatography on 5 different products marketed as kratom products with enhanced 7-OH concentrations
  - 7-OH concentrations ranged from 28.0 mg/g – 74.7 mg/g (compared to undetectable in kratom leaf material)
  - 7-OH doses do not always match the product label

Other alkaloids

- Speciogynine
- Paynantheine
- Speciociliatine
- These alkaloids have variable effects

Kratom Intoxication

- Sympathomimetic: HTN, tachycardic, hyperthermic, diaphoresis, agitation, vomiting
- Sedative: drowsiness, confusion
  - Typically not much respiratory suppression unless high 7-OH content
- Severe effects:
  - Hallucinations
  - Seizures
  - Cardiac arrest/VT
  - Respiratory suppression (more common with higher 7-OH content)

Kratom Intoxication (contd.)

- Idiosyncratic drug-induced liver injury, cholestatic pattern
  - Peaks 14-21 days after ingestion of kratom
- Effects from contaminants
  - *Salmonella* spp.
  - Heavy metals
  - Coingestion of other substances
  - Diphenhydramine, Dextromethorphan, Codeine
- Mortality: very low, and identified cases are almost always in the context of coingestion of other substances

Kratom Withdrawal

- Starts 6-12 hours after last dose
- Duration: typically <4 days, though can last up to 7 days
- Typically less severe than classic opioid withdrawal
- At risk for kratom withdrawal if multiple daily doses for prolonged period of time, typically total dose of >14 g/day
- Presentation is similar to opioid withdrawal
  - Symptoms: nausea, vomiting, myalgias, irritability, fatigue, anxiety, craving
  - Signs: mydriasis, diaphoresis, tremors, diarrhea, lacrimation, rhinorrhea, restlessness
  - Can produce hallucinations

Kratom Withdrawal: Treatment

- Similar to opioid withdrawal treatment
- Can use buprenorphine or full agonist opioids
- Can use alpha-2 agonists (e.g. clonidine)
- Adjunctive symptomatic treatment including:
  - NSAIDs
  - Trazodone
  - Gabapentin
  - Hydroxyzine
  - Dicyclomine
  - Cyclobenzaprine

Kratom Use Disorder

- Not in DSM5 or ICD10, though can apply DSM5 criteria for substance use disorder
- Majority of kratom users do not develop KUD
- Of those who have KUD, generally mild (61.1%), and the most common symptoms are tolerance and withdrawal
- Prevalence difficult to discern. One survey reported prevalence of KUD of 25.5% in regular kratom users

Kratom Use Disorder: Treatment

- No clear guidelines
- Multiple case reports of successful treatment with buprenorphine, typically stabilizing at “lower” doses (e.g. buprenorphine 2 to 8 mg/day), though up to 24 mg/day has been reported
- Behavioral management

Wait… so is kratom this legal?

Short answer:

Yes

Depends on the state

If you're 18, 21, or maybe any age?

Cannot be marketed as a supplement

Only natural kratom leaves, not synthetic products

NO

Regulatory Aspects

- Schedule 1 (aka banned) in seven US states and DC
  - AL, AK, IN, LA, RI, VT, **WI**
- Additional regulations in 17 other states
  - Age limits (18 in some states, 21 in other states)
  - Strength of alkaloid content
  - Labeling
  - Testing
  - Registration, Permitting
- DEA lists kratom as a drug of concern
- FDA considers kratom and its alkaloids as opioids and recommends that the DEA lists kratom as schedule 1
  - NOT considered a food or supplement

Regulatory Aspects

- 2016: DEA published notice of intent to place MG and 7-OH on Schedule 1 on an emergency basis
- Outcry from American Kratom Association, people who use kratom, and a letter signed by 51 members of US congress

As our nation continues to combat the public health crisis of opioid abuse, the federal government has invested significant resources to develop alternative pain management strategies. This includes a study funded by the National Institutes of Health in partnership with the University of Massachusetts and the University of Mississippi to investigate the use of kratom as a remedy for opioid withdrawal. This study led the researchers to apply for a patent identifying the kratom extract, mitragynine, as a useful treatment for other addictive drugs besides opiate derivatives. The DEA's decision to place kratom as a Schedule I substance will put a halt on federally funded research and innovation surrounding the treatment of individuals suffering from opioid and other addictions—a significant public health threat.

Other substances in legal gray zone

- Tianeptine ("gas station heroin," "Tianaa")
  - Tricyclic antidepressant developed in the 1960s in France
  - Also a full agonist at mu opioid receptor
  - Not federally illegal but state-level bans exist
- Phenibut
  - GABA analog first synthesized in USSR in 1960s
  - Primarily acts at GABA-B receptors (like baclofen and GHB)
  - In the US, phenibut is classified as a dietary supplement
- Racetams (e.g. piracetam)
  - Marketed as "nootropics" or "cognitive enhancers"
  - The only FDA approved agent is levetiracetam (Keppra)

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