



What's All the "GABA" 'Bout? Pregabalin and Gabapentin Abuse

Abigail T. Brooks, PharmD, BCPS

Disclosures

- Consultant: Axial Healthcare
- The views and opinions expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of any agency of the United States government, including the Department of Veterans Affairs.

Learning Objectives

- Review the proposed mechanisms of action (MOA) for gabapentin and pregabalin.
- Explain the proposed rationale as to why gabapentin and pregabalin have become drugs of abuse.
- Identify signs and symptoms of withdrawal that an addicted or tolerant patient may experience upon abrupt discontinuation of gabapentin or pregabalin.
- Discuss updates on changes in pain management given the increase in gabapentin and pregabalin abuse.

PainWeek

Current Situation

Opioid overdose public health crisis

Rising use of nonopioid medications including gabapentin

Opioids and concomitant gabapentin increase risk for overdose

Reports of gabapentinoid abuse

Changes in PDMP and scheduling at state level

http://www.register-herald.com/news/manchin-asks-fda-dea-to-consider-rescheduling-gabapentin/article_442fa04b-7ed9-5bf8-8d19-b5440e9c278b.html

PainWeek

Gabapentin and Pregabalin: Pharmacology and Pharmacokinetics

PainWeek.

Fact or Alternate Fact?

- Gabapentin and pregabalin work on GABA.

PainWeek.

Mechanism of Action

Structurally related to GABA and has GABA-mimetic properties

Do not

- Alter uptake or breakdown
- Convert into GABA
- Bind to GABA_a or GABA_B

Binds to the $\alpha 2$ - δ subunit of the voltage-gated calcium channel

Reduces the Ca²⁺-dependent release of pro-nociceptive neurotransmitters

Decreases release of glutamate, NE, and substance P

Dworkin RH et al. Pain. 2007;1332:237-251.
 Schifano F. CNS Drugs. 2014;28:491-496.
 Micromedex 2.0 Online. <http://www.micromedexsolutions.com/micromedex2/librarian>.
 J Clin Psychiatry. 2007 Mar;68(3):483-4

PainWeek

FDA-approved Indications

▪ Pregabalin

- Neuropathic pain associated with diabetic peripheral neuropathy (DPN)
- Post-herpetic neuralgia (PHN)
- Adjunctive therapy for adult patients with partial onset seizures
- Fibromyalgia
- Neuropathic pain associated with spinal cord injury

▪ Gabapentin

- PHN
- Adjunctive therapy in treatment of partial onset seizures, with and without secondary generalization, in adults and pediatrics ≥ 3 years

PainWeek

Lyrica package insert. New York: Parke-Davis; Dec 2016.
 Neurontin package insert. New York: Parke-Davis; Sept 2015.

FDA-approved Indications

- Gabapentin encarbil
 - Moderate-to-severe restless legs syndrome
 - PHN
- Gabapentin ER
 - PHN
- Pregabalin CR
 - PHN
 - Neuropathic pain associated with DPN

Horizant package insert. Arbor Pharmaceuticals, Atlanta, GA: LLC: October 2016.
 Lyrica CR package insert. New York, NY; Pfizer: October 2017.
 Gralise package insert. Newark, CA; Depomed, Inc: Dec 2012.

PainWeek

Off-label Uses

Pregabalin

- Bipolar disorder
- Alcohol/narcotic withdrawal
- Anxiety
- ADHD
- Restless legs syndrome
- Trigeminal neuralgia
- Non-neuropathic pain

Gabapentin

- Insomnia
- Neuropathic pain
- Drug and alcohol addiction
- Anxiety
- Bipolar disorder
- Migraines

PainWeek

CNS Drugs. 2014;28:491-496.
 Addiction. 2016;111:1160-1174.

Role in Pain

- NICE
 - Gabapentin - 1st line treatment for neuropathic pain
- ADA Diabetic Peripheral Neuropathy
 - Consider pregabalin or duloxetine as initial approach
- AAN Diabetic Peripheral Neuropathy
 - Offer pregabalin
 - Consider gabapentin
- Neuropathic Pain Special Interest Group of International Association for the Study of Pain
 - Gabapentin, pregabalin first line

PainWeek

Addiction. 2016;111:1160-1174.
 Neurology. 2011;76(20):1758-1765.
 Diabetes Care. 2017;40(10):136-1564.
 May Clin Proc. 2010;85(3 Suppl):S3-S14.

Role in Pain

- Multimodal postoperative pain management
 - Pain scores
 - Opioid doses
 - Opioid side effects
 - Controversy around dosing and timing
- Acute or chronic sciatica
 - No benefit for pregabalin
- Nonspecific low back pain
 - Ineffective
 - Contribute to ADE

PainWeek

Pain. 2007. 132;237-251.
 PLoS Med. 2017;14(8):e1002369.
 Medicine. 2017;96(21):e6982.
 Spine. 2013;38(22):1947-1952.
 NEJM. 2017;376(12):1111-1120.
 Br J Anaesth. 2011;106(4):454-462.
 JAMA Surg. 2017;epub.

Gabapentinoid Use in U.S. 2002-2015

- 346,177 adults prescribed gabapentin or pregabalin between gabapentin or pregabalin from Medical Expenditure Panel Survey
- 82.6% of patients prescribed gabapentin
- Significant increase in gabapentinoid prescribing during study
 - 2002 1.2% prescribed gabapentin or pregabalin
 - 2015 3.9% prescribed gabapentin or pregabalin
- Changes in 2008
 - No increase in gabapentin until 2008
 - Pregabalin use plateaued and no increase following

JAMA Intern Med. 2018;epub2018/01/04.

PainWeek

Gabapentin Increases Overdose Odds

- Population-based nested case-control study
- Cases (1,256 cases) were opioid users who died of an opioid-related cause matched with up to 4 controls (4,619 controls)
- Primary exposure was gabapentin use 120 days preceding index date
- 12.3% of cases and 6.8% of control were prescribed gabapentin
- Odds increased 49% if prescribed gabapentin + opioid
- High dose gabapentin (1800 mg/day) about 60% increased odds compared to moderate dose
- Very high dose (2,200 mg/day) associated with 2-fold increased odds

PLoS Med. 2017;14(10):e1002396.

PainWeek

Dosing

Gabapentin

- Start at gabapentin 300 mg PO QHS
- Increase by 300 mg PO q3days
- Max dose of 3600 mg/day
- Adequate trial considered 6-8 weeks
- Requires renal dose adjustments beginning at CrCl <60ml/min
- Taper over 1 week if discontinuing

PainWeek

Dworkin RH et al. Pain. 2007. 132:237-251.
Drugdex® System. Micromedex®2.0. Greenwood Village, Colorado Accessed 8 Aug 2013

Dosing

Pregabalin

- Start at 50 mg PO TID
- Titrate to 100 mg PO TID
- Max dose 600 mg/day
- Adequate trial requires 6-12 weeks
- Requires renal dose adjustments beginning at CrCl <60 mL/min
- Gradually taper off if discontinuing

PainWeek

Dworkin RH et al. Pain. 2007. 132:237-251.
Drugdex® System. Micromedex®2.0. Greenwood Village, Colorado Accessed 8 Aug 2013

Dosing



Gabapentin encarbil (PHN)

Days 1-3: 600 mg AM
 Day 4: 600 mg BID
 No benefit beyond
 1200 mg/day



Gabapentin ER

Day 1: 300 mg daily
 Day 2: 600 mg daily
 Days 3-6: 900 mg daily
 Days 7-10: 1200 mg
 daily
 Days 11-14: 1500 mg
 daily
 Day 15: 1800 mg daily



Pregabalin CR

165 mg/day initial
 Increase to 330
 mg/day within 1 week
 Max 660 mg/day

PainWeek

Horizant package insert. Arbor Pharmaceuticals, Atlanta, GA: LLC: October 2016.
 Lyrica CR package insert. New York, NY; Pfizer: October 2017.
 Gralise package insert. Newark, CA; Depomed, Inc: Dec 2012.

Pharmacokinetics

Gabapentin

- Absorption
 - F=27-60%
 - Tmax=8h
- Distribution
 - Low protein binding
- Metabolism
 - None
- Elimination
 - Renal: 76-81%
 - t_{1/2}=5-7h

Pregabalin

- Absorption
 - F=90%
 - Tmax=1.5h
- Distribution
 - No protein binding
- Metabolism
 - None
- Elimination
 - Renal: 90%
 - t_{1/2}=6.3h

PainWeek

Drugdex® System. Micromedex®2.0. Greenwood Village, Colorado Accessed 8 Aug 2013
 CNS Drugs. 2016;30:647-654.

Comparing Pharmacokinetics

Gabapentin

- F=42-57%
- Nonlinear pharmacokinetics (PK)
- Slower onset
- Lower affinity for receptor

Pregabalin

- F=83.9-97.7%
- Linear PK
- Faster onset
- Higher affinity for receptor

PainWeek

Ifuku M et al. Pain Med. 2011;12:1112-1116.
 O'Connor AB ET AL. AM J Med. 2009;112(10A):S22-S32.
 Moulin DE et al. Pain Res manage. 2007;12(1):13-21.
 Neurontin® package insert. New York, NY; Pfizer;2013 June.
 Lyrica® package insert. New York, NY; Pfizer;2012 July

Focus on Suicidal Ideation

- Pooled analysis of 199 placebo-controlled trials of 11 different antiepileptic drugs (AED)
 - AED treated n=27,863 patients, Placebo n=16,029 patients
 - OVERALL: 0.43% AED treated patients vs. 0.24% of placebo patients
 - Relative risk 1.8, 95% CI: 1.2,2.7
 - Nonpsychiatric/epilepsy indications: 0.18% AED patients vs 0.1% placebo
 - Relative risk 1.9
- Presents as early as 1 week
- Persists for duration of treatment
- Did not vary by age
- Chronic pain associated with suicide
- Counsel patients

PainWeek

Lyrica package insert. New York: Parke-Davis; Dec 2016.
 Neurontin package insert. New York: Parke-Davis; Sept 2015.

Converting Case

- BT is a 57 yo male with diabetic peripheral neuropathy on gabapentin 600 mg PO TID. He continues to complain of symptoms and says he heard about pregabalin on TV. How would you convert this patient from gabapentin to pregabalin?

PainWeek

Converting

Pregabalin ~
6 x as
potent as
gabapentin

Cross-titration method

Stop-start
method

Reduce gabapentin
dose by 50% and
initiate 50% of
equivalent
pregabalin dose x 4
days

Discontinue
gabapentin and
increase pregabalin
to full equivalent
dose

Stop gabapentin
and start
equivalent dose of
pregabalin

PainWeek

Ifuku M et al. Pain Medicine. 2011;12:1112-1116.
Bockbader HN et al. American J Therapeutics. 2012; 0(0): 1-10.

Converting Case

- Cross-titration
 - Decrease gabapentin to 300 mg PO TID + initiate pregabalin at 75 mg PO BID x 4 days
 - Discontinue gabapentin + increase pregabalin to 150 mg PO BID
- Stop-Start
 - Discontinue gabapentin
 - Initiate pregabalin 150mg PO BID

PainWeek.

Tapering

- Avoid abrupt discontinuation to limit withdrawal symptoms
- Taper over at least 1 week

PainWeek.

Lyrica package insert. New York: Parke-Davis; Dec 2016.
Neurontin package insert. New York: Parke-Davis; Sept 2015.

Role in Addiction Treatment

▪ Pregabalin

- Alcohol withdrawal
- Alcohol relapse prevention (abstinence similar to naltrexone)
- Benzodiazepine/opioid withdrawal
- Some evidence to prevent cocaine relapse

▪ Gabapentin

- Evidence in opioid, THC, alcohol addictions
- Gabapentin *suggested* in APA AUD Guidelines
 - Goal of reducing or abstaining from alcohol
 - Prefer topiramate or gabapentin or intolerant or did not respond to naltrexone or acomprostate
 - No contraindications

CNS Drugs. 2014;28:491-496.
Practice Guideline for the Pharmacological Treatment of Patients with Alcohol Use Disorder. APA.
<https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9781615371969>

PainWeek.

Gabapentin and Pregabalin Abuse

PainWeek.

Patient Case

- Ms. Smith is a 67 yo woman with PMH significant for mood disorder, alcohol abuse, and polyneuritis
- Medications: naproxen 550mg PO daily, amitriptyline 100mg PO daily, and gabapentin titrated up to 4800mg PO daily
- Began to exhibit fraudulent behavior:
 - Requesting medication without a prescription
 - Exaggerated symptoms
 - Physician consulted and then changed when demands not met
- Ran out of medication and could not obtain refill



PainWeek

Pharmacopsychiatry. 2007 Jan;40(1):43-4.

Startling Statistics

- As of 2013 over a 5 year period in the UK
 - Pregabalin prescribing had increased by **350%** to 2.7 million
 - Gabapentin prescribing had increased by **150%** to 3.5 million prescriptions
- Approximately 1% prevalence rate in general population in UK

PainWeek

BMJ. 2013 Nov 8;347:f6747.
Br J Gen Pract. 2012 Aug;62(601):406-7.
Annals Pharmacother. 2016;50(3):229-233.

Startling Statistics

- The European Medicines Agency (EMA) trended the number of pregabalin ADRs reported from 3/2006-7/2015
 - Reports peaked in 2013 (2154 total), decreased in 2014 (1593 total), and totaled 1387 reports as of 7/15/2015
- The EMA received a total of 4301 ADR reports related to gabapentin abuse/dependence issues between 3/2004-7/2015
- Users of gabapentin are more likely to abuse oxycodone, buprenorphine, and benzodiazepines compared with nonusers

PainWeek

CNS Drugs. 2016 Jul;30(7):647-54.
Ann Pharmacother. 2016 Mar;50(3):229-33.
Am J Psychiatry. 2015 May;172(5):487-8.

Demographics

- Females > males or females = males
- Average age
 - Samples 21-43 years
 - Case reports 41 years
- Reports from
 - US (n=22)
 - UK (n=4)
 - Germany (n=1)
 - Poland (n=1)
 - India (n=1)
 - South Africa (n=1)
 - France (n=1)

Addiction Week 1160-1174.

Demographics – 2013

- A study of random UDS samples (N=124) in patients being treated for opioid dependence with agonist therapy (methadone or buprenorphine) significant for:
 - 12.1% of urine samples positive for pregabalin (n=15)
 - 11/15 patients admitted to buying pregabalin from heroin addicts or drug dealers
- Query of the German Federal Institute for Drugs and Medical Devices regarding pregabalin abuse/dependence significant for:
 - 55 total reports of pregabalin abuse and dependence
 - Mean daily dose: 1424mg
 - Mean age: 36 yo
 - 63.6% of reports were male patients

PainWeek

Eur J Clin Pharmacol. 2013 Dec;69(12):2021-5.
Eur J Clin Pharmacol. 2013 Jun;69(6):1335-42.

Demographics – 2015/2016

- From 3/2004-7/2015 4301 ADR reports related to gabapentin
 - 1.27:1 female to male ratio
- From 3/2006-7/2015 7639 ADR reports related to pregabalin
 - 1.13:1 female to male ratio
- Common to have history of substance use disorder

PainWeek

Annals Pharmacother. 2016;50(3):229-233.
CNS Drugs. 2016;30:647-654.

Demographics – Prison System

- Search of inmate lockers revealed only 19/96 inmates in possession of gabapentin were prescribed gabapentin
- Diverting gabapentin for high



Drugs. 2017;77:403-426.

Prevalence

- Lifetime prevalence in general population estimated at 1.1% of patients
- Prevalent in opioid abuse populations
 - 15-22% gabapentin misuse
 - 40-65% abuse of gabapentin with prescription
- > 50% of patients with history of substance use disorder
 - Opioid use disorder common



Addiction. 2016;111:1160-1174.

Retrospective Cohort Analysis from Insurance Claims Database

- Inclusion: Patients 16-64 years old and had ≥ 2 pharmacy claims for alprazolam, gabapentin, pregabalin, zolpidem, or any opioid medication (ex. patch formulations or fentanyl products)
- Potential abuse: ≥ 3 claims exceeding the daily dose threshold and ≥ 3 rolling quarters where the dispensed supply exceeded the threshold
- Results:
 - 3.2% and 4.9% of patients were potentially abusing gabapentin or pregabalin alone
 - 24% of gabapentin patients on opioids and 28% of pregabalin patients on opioids meeting criteria for potential abuse



Psychiatr Q. 2016;87(4):763-767.

Mechanism of Action: Abuse

- Reduces the release of neurotransmitters, including:
 - Glutamate
 - Noradrenaline
 - Serotonin
 - Dopamine
- GABA analogues which may induce addictive behaviors in the same manner as benzodiazepines
- Pregabalin:
 - Schedule V
 - Six-fold higher binding affinity for the $\alpha_2\text{-}\delta$ subunit
 - Quicker absorption rate and greater bioavailability



Eur J Clin Pharmacol. 2013 Jun;69(6):1335-42.

Pregabalin Package Insert

- In a small patient population (N=15) of recreational users of sedative/hypnotic drugs, pregabalin administered as a 450mg single dose produced the following results:
 - “Good drug effect”
 - “High”
 - “Liking”
- The above effects were similar to that reported with a 30mg single dose of diazepam
- In addition, controlled trials of >5500 patients found that 4% of patients treated with pregabalin reported *euphoria* as an ADR
 - Reported rates range from 1-12%



PainWeek

Lyrica package insert. New York, NY: Pfizer, Inc.; 2013.

Gabapentin Package Insert

- Small number of post-marketing reports of misuse and abuse
- Taking higher than recommended doses
- Unapproved uses or to treat withdrawal
- History of polysubstance abuse
- Assess history of drug abuse
- Monitor for s/sx of gabapentin misuse or abuse

PainWeek

Neurontin package insert. Pfizer; New York, NY: October 2017

Doses for Abuse

- Abused in a wide variety of doses
 - Therapeutic range – no prescription
 - Supratherapeutic range
- 3-20 times clinically used amounts
- Taken as one large dose
- Tolerance develops leading to dose increase



Addiction. 2016;111:1160-1174.
CNS Drugs. 2014;28:491-496.
Drugs. 2017;77:403-426.

Frequency of Abuse

- General population
 - More than once weekly 13.1%
 - Once weekly – once monthly 50%
 - Less frequently 36.8%
- Opioid abuse population
 - 25 of the last 30 days



Drugs. 2017;77:403-426.

Sources

- **Healthcare providers (52-63%)**
- Family or acquaintances (57.8%)
- Internet (47.3%)
- Drug dealer
- International (7.8%)



Addiction. 2016;111:1160-1174.
 Drugs. 2017;77:403-426.

Cost

- Street value and sold/traded for illicit drugs
- Gabapentin on the street (referred to as “gabbies” or “Budweiser’s” in the UK) costs approximately £1/300mg which is equivalent to \$1.65/300mg
- In Appalachian Kentucky, the street cost of gabapentin was reported to be <\$1/pill
- \$1-7 per pill depending on strength



Addiction. 2016;111:1160-1174.
 CNS Drugs. 2016 Jul;30(7):647-54.
 Ann Pharmacother. 2016 Mar;50(3):229-33.
 BMJ. 2013 Nov 8;347:f6747.
 Br J Gen Pract. 2012 Aug;62(601):406-7.
 Am J Psychiatry. 2015 May;172(5):487-8.

Coingestants

Gabapentin

- Alcohol
- Cannabis
- Selective serotonin reuptake inhibitors
- Lysergic acid diethylamide (LSD)
- Amphetamine
- Gamma-hydroxybutyrate
- Opioids
- Benzodiazepines

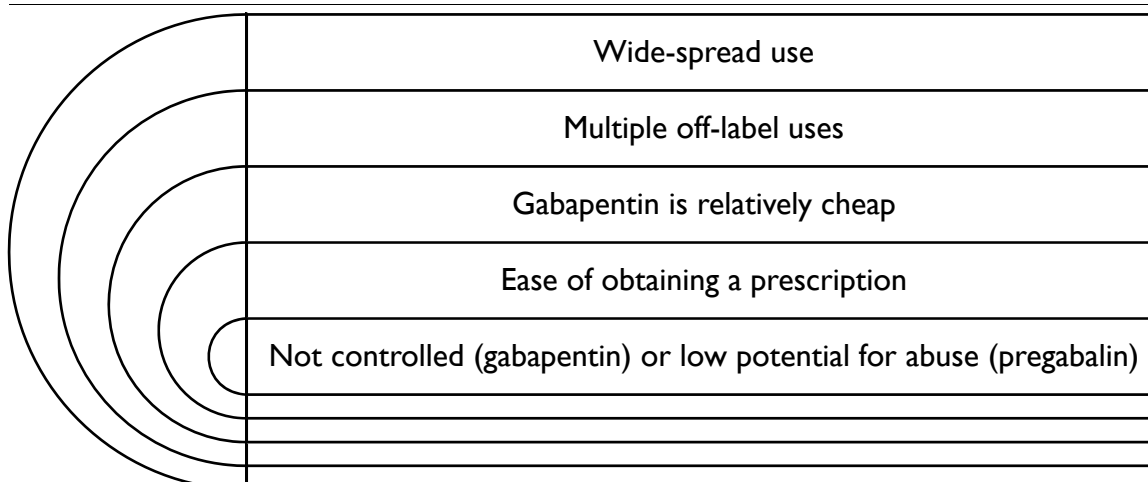
Pregabalin

- Alcohol/gabapentin/benzodiazepines
- Cannabinoids
- LSD
- Salvia
- Heroin/opiates
- Amphetamines/synthetic cathinones

Psychother Psychosom. 2011;80(2):118-22.
CNS Drugs. 2014;28:491-496.
Addiction. 2016;111:1160-1174.

PainWeek

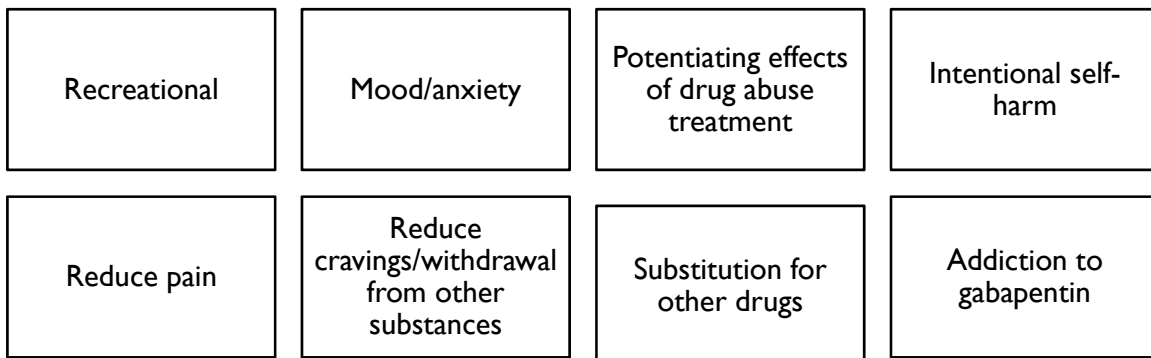
Factors Leading to Abuse



PainWeek

Addiction. 2016;111:1160-1174.
Drugs. 2017;77:403-426.

Reasons for Abuse



PainWeek.

Addiction. 2016;111:1160-1174.

Common & Novel Methods of Abuse

- Parachuting



PainWeek.

Common & Novel Methods of Abuse

Gabapentin

- Orally
- Intravenously (IV)
- Snorting
- Intramuscular (IM)
- “Cutting agent” in street heroin

Pregabalin

- Orally
- Intravenously (IV)
- Snorting
- Smoking
- Rectally (“plugging”)
- “Parachuting”

Br J Gen Pract. 2012 Aug;62(601):406-7.
 Psychother Psychosom. 2011;80(2):118-22.
 The LYRICA (pregabalin) Mega Thread. Available at: bluelight.org.
 Schifano F. CNS Drugs. 2014;28:491-496.

PainWeek

Effects of Abuse

Gabapentin

Euphoria
 Improve sociability
 Marijuana-like “high/relaxation”
 Zombie-like effects
 Sedative/opiate “buzz”
 Psychedelic/3,4-
 methylenedioxy-N-
 methylamphetamine-like
 effects

Pregabalin

Alcohol/GHB/benzodiazepine-
 like effects
 Euphoria
 Entactogenic feelings
 Dissociation
 Coping with opioid withdrawal

CNS Drugs. 2014;28:491-496.
 Eur J Clin Pharmacol. 2013 Jun;69(6):1335-42.
 Pharmacopsychiatry. 2007 Jan;40(1):43-4.

PainWeek

Effects of Gabapentin & Pregabalin Abuse

- "...the pregabalin erases my benzo, opiate withdrawal and cravings... In my opinion, anything over 900mg is a waste – too sedating"
- "The only downside to gabapentin so far as I can tell, is the onset. These little guys take upwards of an hour to really start to kick in, but luckily they last for 4-8 hours it seems..."
- "I feel as if I'm on a super amphetamine rush and can tackle anything, yet feel so content it's like I'm on a fully sedated opiate buzz."
- "...pregabalin outshines gabapentin. Far less dosage to achieve the same recreational high. Also not as strong of a half life allowing one to use the drug more frequently."

PainWeek

Psychother Psychosom. 2011;80(2):118-22.

Overdose

- Onset: soon after ingestion
- Duration: 10h
- Effects typically mild to moderate
- Fatalities or intubation – rare
- Common effects
 - Hypotension
 - Tachycardia
 - CNS effects
- Symptoms more likely after gabapentin 1200 mg
- Survivals reported with up to 11,500 mg of pregabalin and 91,000 mg of gabapentin

PainWeek

Drugs. 2017;77:403-426.

Overdose

- Severe events more of a concern in renal dysfunction
- Fatalities more common when ingested with other substances
- 90% of fatalities associated with opioids
- German toxicology reports from 2010-2012 with pregabalin
 - General population 2% of cases year 1, 4% of cases in year 2
 - Known substance use disorder 5.5% in year 1, 29.8% in year 2
- Finnish toxicology reports from 2010-2011
 - Pregabalin 2.3%
 - Gabapentin 0.31%

PainWeek

Drugs. 2017;77:403-426.

Withdrawal

- Onset ranges from 12 hours to 7 days after termination of use
 - Majority of cases report onset between 24-48 hours
- At least one reported case of a newborn baby experiencing withdrawal due to mother's gabapentin use while pregnant

PainWeek

Ann Pharmacother. 2016 Mar;50(3):229-33.

Withdrawal Signs/Symptoms

Psychomotor agitation	Confusion	Craving	Disorientation
Arterial HTN	Tachycardia	Tremor	Insomnia
Nausea	Headache	Diarrhea	Diaphoresis



J Addict Med. 2013 Mar-Apr;7(2):147-9.
 Eur J Clin Pharmacol. 2013 Jun;69(6):1335-42.
 J Clin Psychiatry. 2007 Mar;68(3):483-4.
 Ann Pharmacother. 2016 Mar;50(3):229-33.

PainWeek

Withdrawal Treatment

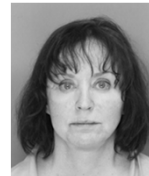
Benzodiazepines: ineffective?
Antipsychotics: ineffective?
Benzotropine: ineffective?
Anticonvulsants: effective (in terms of seizure control)
Pregabalin: effective
Gabapentin: effective

J Addict Med. 2013 Mar-Apr;7(2):147-9.
 Eur J Clin Pharmacol. 2013 Jun;69(6):1335-42.
 J Clin Psychiatry. 2007 Mar;68(3):483-4.
 Ann Pharmacother. 2016 Mar;50(3):229-33.
 Drugs. 2017;77:403-426.

PainWeek

Patient Case: Revisited

- Ms. Smith is a 67 yo woman with PMH significant for mood disorder, alcohol abuse, and polyneuritis
- She was actually taking *at least 7200mg of gabapentin daily!*
- Upon running out of gabapentin, she developed typical withdrawal symptoms and was hospitalized
 - Upon discharge, gabapentin discontinued
 - ~3 months later, gabapentin re-prescribed
 - ~5 months after discharge, she had resumed gabapentin abuse in combination with diazepam



PainWeek Pharmacopsychiatry. 2007 Jan;40(1):43-4.

Patient Case: Revisited

- Taper off gabapentin
- Behavioral Health referral
- Taper BZD

PainWeek

State Prescription Drug Monitoring Program (PDMP)

- Pregabalin is a Schedule V controlled substance
 - Already reported to the database in some states
 - Some states do not require the reporting of schedule V medications
- States that have ADDED gabapentin prescriptions to database reports include:
 - Minnesota
 - Ohio
 - Kentucky → now C-V status
 - Massachusetts
 - North Dakota
 - Virginia
 - West Virginia
 - Wyoming

<http://pmp.pharmacy.state.mn.us/>

<http://pharmacy.ohio.gov/Documents/Pubs/Special/OARRS/Reporting%20Gabapentin%20Products%20to%20OARRS%20%E2%80%93%20Effective%2012-1-2016.pdf>

http://ncpdp.org/NCPDP/media/pdf/State_PMP_Tracking_Document.xls

<http://www.chfs.ky.gov/os/oiq/KASPER.htm>



Indicators of medication abuse

- Requesting specific medications
- Requesting higher doses
- Doctor shopping
- Claims of lost/stolen medications
- Using multiple pharmacies
- Early refill requests
- Negative UDT – but not routinely part of testing



Addiction. 2017;77:403-426.

Summary

- Gabapentin and pregabalin abuse can occur
 - Common and novel routes of administration
 - Therapeutic and supratherapeutic doses
- More common in patients with history of substance use disorder
- Coingestants often involved
- Patients can experience withdrawal if gabapentin and pregabalin are stopped abruptly
- Certain state Prescription Drug Monitoring Programs (PDMPs) are adding gabapentin

PainWeek.

3 Things for Monday

1. Assess a patient's substance abuse history, psychiatric history, and concurrent medications before prescribing
2. Be aware of higher risk groups
3. Monitor for early refills and/or limiting the quantity supplied

PainWeek.

CNS Drugs. 2014;28:491-496.
Addiction. 2017; 77:403-426.

Assessment Q1

- The proposed MOA for gabapentin and pregabalin include
 - a) Binding to GABA receptors
 - b) Increasing glutamate, norepinephrine, and substance P
 - c) Binding to the $\alpha 2$ - δ subunit of the voltage-gated calcium channel
 - d) Inhibiting serotonin reuptake

PainWeek.

Assessment Q2

- Factors that have contributed to the abuse of gabapentin include all of the following EXCEPT:
 - a) High cost
 - b) Ease of obtaining a prescription
 - c) Non-controlled substance status
 - d) Multiple uses/indications

PainWeek.

Assessment Q3

- Signs of gabapentin and pregabalin withdrawal include all of the following EXCEPT:
 - a) Cravings
 - b) Hypotension
 - c) Insomnia
 - d) Headache

PainWeek.

PainWeek.

What's All the "GABA" 'Bout? Pregabalin and Gabapentin Abuse

Abigail T. Brooks, PharmD, BCPS