

Drug Utilization Review (DUR) Newsletter



COLORADO

Department of Health Care
Policy & Financing

Select HCPF Medication Use Policy Updates

FALL 2023

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Caution Warranted When Combining Gabapentin or Pregabalin with an Opioid and/or CNS Depressant

Robert L Page II, PharmD, MSPH

Growing evidence of misuse and overdoses involving gabapentin (GABA) and pregabalin—often in conjunction with opioids—is drawing attention to substantial off-label prescribing of these anticonvulsant medications.

The Centers for Disease Control and Prevention (CDC) recently published an analysis that found that showed between 2019 and 2020, coroners and medical examiners detected gabapentin in 5,687, or almost 10%, of the 58,362 overdose deaths that had available toxicology results in 23 states and the District of Columbia.¹ Officials determined that gabapentin was a cause of death in almost 3,000 of these cases. During the time period studied, the number of fatal overdoses that involved gabapentin detected or involved increased, apparently tracking with the overall increase in overdose deaths during the COVID-19 pandemic. More importantly, opioids were also involved in almost 90% of fatal overdoses in which gabapentin was detected, suggesting a potentially fatal combination. *(Continued on Page 2)*

SHARE YOUR EXPERTISE

Apply to become a voting member of the Health First Colorado DUR Board
HCPF is currently accepting applications from physicians and pharmacists

Meetings are held virtually four times a year

- FEBRUARY
- MAY
- AUGUST
- NOVEMBER



Meeting dates & times, agendas, minutes and recent newsletters are available at <https://hcpf.colorado.gov/drug-utilization-review-board>

Physicians and pharmacists are being recruited on a continuous basis to fill positions on the DUR Board. If you or a colleague have an interest in learning more about these professional opportunities, send an inquiry to Jeff Taylor, PharmD (jeffrey.taylor@state.co.us) and Julia Rawlings, PharmD (julia.rawlings@state.co.us)

Caution with Gabapentin Combinations, *continued from Page 1*

In 2019, The US Food and Drug Administration (FDA) issued a warning brief to health care providers that serious breathing problems had been reported with gabapentin exposure, especially when used with other central nervous system (CNS) depressants like opioids, anxiety medications, muscle relaxants, and antidepressants or when used by older adults and those with respiratory risk factors such as chronic obstructive pulmonary disease.² At that time, the agency had received 49 reports of respiratory depression among patients taking gabapentin or pregabalin, including 12 deaths. Additionally, the FDA is requiring the drug manufacturers to conduct clinical trials to further evaluate the abuse potential of gabapentinoids, particularly in combination with opioids, with special attention being given to assessing the respiratory depressant effects.

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These findings from federal agencies have also been reported in the literature. Using Medicare CMS chronic conditions data warehouse (CCW) data between 2013-2016, Olopoenia et al conducted a nested case-control study to examine the association between concurrent utilization of GABA, opiates and benzodiazepines (BZD) with respiratory depression, opioid, and substance related overdose among Medicare “disabled” beneficiaries.³ A total of 470,044 “disabled” beneficiaries received at least one prescription for GABA, an opioid, or a BZD during the entire study period. A subset of 131,817 beneficiaries met additional inclusion criteria for the overall nested cohort and were stratified based on diagnoses of acute pain (AP), chronic pain (CP), or mental health (MH) conditions in the 6 months prior to receipt of any of the medications of interest. **Overall, compared to opioid use only, the investigators found that GABA + opioid + BZD use was associated with increased odds of respiratory depression across all cohorts**

Association between concurrent medication utilization and adverse outcomes

Medication Category	Respiratory Depression	
	Unadjusted Odds Ratio 95% CI	Adjusted Odds Ratio* 95% CI
Acute Pain		
GABA + OP + BZD	1.62 (1.45-1.80)	1.35 (1.19-1.52)
GABA + OP	1.23 (1.12-1.34)	1.10 (1.03-1.18)
Chronic Pain		
GABA + OP + BZD	1.56 (1.41-1.72)	1.24 (1.11-1.38)
GABA + OP	1.22 (1.21-1.33)	1.06 (1.01-1.12)
Mental Health		
GABA + OP + BZD	1.37 (1.22-1.54)	1.16 (1.02-1.32)
GABA + OP	1.27 (1.13-1.42)	0.98 (0.86-1.12)

Table adapted from Olopoenia et al, Lancet Reg Health Am. 2022 Jun 23
Significant findings (p<0.05) highlighted in bold

**Demographic characteristics included age, race/ethnicity, and sex. Health insurance factors included Medicaid-Medicare dual eligibility. Clinical factors such as co-morbidities, service utilization and pharmacologic variables were assessed. Co-morbidities captured included chronic lung disease, diabetes, myocardial infarction, congestive heart failure, peripheral vascular disease, connective tissue disease, cerebrovascular disease, peptic ulcer disease, liver disease, hypertension, hypothyroidism, seizure disorder, substance-related disorders (alcohol, opioid and non-opioid) and dementia. To address confounding by indication related to these medications, the authors also required beneficiaries to have diagnoses of acute pain, chronic pain, or mental health conditions in the 6 months prior to receipt of any of our medications of interest.*

Caution with Gabapentin Combinations, *continued from Page 2*

An analysis conducted by the Colorado Evidence-Based Drug Utilization Review team of Health First Colorado members showed congruent findings. Using medical and pharmacy claims from October 1, 2021-September 30, 2022, we identified a total of 54,996 members who had at least one fill of a gabapentinoid during the study period, of which 659 members had an opioid overdose. After controlling for age, combined comorbidity score, concomitant use of gabapentin or pregabalin with CNS respiratory depressants or CNS respiratory depressants and opioid, we found statistically significant associations between opioid use and having an opioid overdose among members with at least one gabapentinoid fill, with the odds of having an overdose being significantly increased for members with at least 30 days of an opioid fill (OR=2.05, $p<0.05$) and for members with at least 30 days of concomitant opioid and gabapentinoid use (OR=2.153, $p<0.05$). While the magnitude of effect was highest in those prescribed higher gabapentinoid doses, the risk was statistically significant across all doses, and also increased incrementally as morphine dose equivalent increased.

Given the widespread incorporation of gabapentin into several pain management protocol, as well as its increasing off-labeled utilization particularly among those with psychiatric conditions, the benefits and risks of gabapentin or pregabalin co-prescribing with opioids and/or CNS depressants should be weighed by clinicians in these settings.

Patients should be educated at each health care visit encounter regarding the potential for respiratory depression when gabapentin or pregabalin is prescribed with these medication combinations.



**Health First
COLORADO™**
Colorado's Medicaid Program

In August 2023 there were
1,578,595 million members enrolled in
Health First Colorado (Colorado's Medicaid Program)



Johna Bezdek Thaut, Kelly Gaebel, Huy Ryan Tran, Tracy Van, Mandy Li
Not pictured: Michael Brace

DUR Intern Team

Doctor of Pharmacy candidates at the University of Colorado Skaggs School of Pharmacy who have an interest in public health policy, managed care, and population health management have a unique opportunity to gain one or two years of faculty mentoring and real-world experience as members of the intern team that skillfully supports Health First Colorado DUR activities.

A special thanks to our outgoing (and outstanding) DUR interns as they undertake their advanced clinical practice training year.

The Fentanyl Crisis: Cracking Down...

Gina Moore, PharmD, MBA

The Colorado Department of Healthcare Policy and Financing is joining the state's efforts to address fentanyl overdose deaths. The Fentanyl Accountability and Prevention Bill (HB22-1326) signed by Governor Polis in May of 2022 was one of the first steps taken after the COVID-19 pandemic to address the growing number of fentanyl deaths in our state. The bill charges individuals who knowingly possess fentanyl and fentanyl derivatives with a level 4 drug felony. Individuals involved with unlawful distribution and manufacturing of fentanyl and fentanyl derivatives will be charged with a level 1 drug felony and subject to mandatory sentencing. The bill has additional provisions to make naloxone more available, improve education efforts, and improve treatment services for incarcerated persons.



The Fentanyl Accountability and Prevention Bill ([HB22-1326](#)) signed by Governor Polis in May of 2022 was one of the first steps taken after the COVID-19 pandemic to address the growing number of fentanyl deaths in our state.

Of course, we all hope to prevent substance misuse before it even starts. Health First Colorado, in collaboration with the University of Colorado Skaggs School of Pharmacy, the state's DUR vendor, have implemented numerous strategies to address opioid use, provide safer pain medication alternatives, and improve naloxone uptake. Except for patients in hospice or palliative care, all short-acting fentanyl preparations require a prior authorization.

Members who are opioid naïve, exceed daily opioid quantity limits, or are on high doses of opioids are offered a telephone consultation with a pain management physician. This physician works closely with the prescriber to understand individual patient issues, encourage the use of non-opioid alternatives, and provide specific tapering strategies and recommendations.

Each quarter, the DUR team also sends educational letters to providers who are providing care to patients on chronic opioids who have not filled a naloxone prescription. These letters alert prescribers to the availability of naloxone with no prior authorization requirement and encourage co-prescribing of naloxone as an important safety measure.



DUR Spotlight

by Kelly Gaebel
PharmD Candidate
DUR Intern

Garth Wright, MPH

Garth Wright is a biostatistician for the Department of Clinical Pharmacy at the University of Colorado (CU). He splits his time among the DUR team, HCPF projects, and consulting for providers across the CU Anschutz medical campus. During his undergraduate years, Garth studied biology. Halfway through his studies he ruled out other career paths and set his sights on biostats. Garth earned his MPH with a concentration in biostatistics from CU. Immediately following graduation, he joined the Department of Clinical Pharmacy as its first biostatistician.

Garth enjoys the variety his job brings. He has a role in reports and research for the DUR team, analyzing medical and pharmacy claims for HCPF, and consulting on projects for a variety of disease states. He appreciates that his work helps make evidence-based decisions and drives policy that ultimately improves care for so many Coloradans. Garth has been a part of 25 to 30 peer-reviewed manuscripts in the last few years.

Garth's favorite part of his job is the ability to make a broad impact. He is passionate about improving healthcare. Garth shares that one rule he tries to live by is, "Just because something is not statistically significant doesn't mean it isn't clinically significant." He acknowledges that the opposite can also be true. After a statistical analysis has been completed, Garth works collaboratively with the project team to better understand the disease state, pharmacotherapy, and associated outcomes - good or bad.

Outside of work, Garth and his wife stay busy with their three kids. Between their kids' activities, Garth shares that they love to be outside and live at Water World during the summer months. He loves anything fitness related. He enjoys music, which is evident through his ability to play both piano and drums.

May 2023

PDL Drug Classes reviewed by the DUR Board

- Pulmonary Arterial Hypertension Therapies
- Anti-Psoriatic Agents
- Topical Immunomodulators
- Atopic Dermatitis & Antineoplastic Agents
- Bile Salts
- Antiemetics
- Chronic GI Motility Agents
- Hemorrhoidal, Anorectal, and related Topical Anesthetic Agents
- Anticoagulants
- Anti-Platelet Agents
- Colony Stimulating Factors
- Tetracyclines
- Alpha Blockers
- Beta Blockers
- Calcium Channel Blockers
- Angiotensin Converting Enzyme (ACE) Inhibitors & Combinations
- Angiotensin Receptor Blockers (ARBs) & Combinations
- Renin Inhibitors & Combinations
- Lipotropic Agents
- Statins & Combinations
- Topical Acne Agents
- Acne Agents - Oral Isotretinoin
- Rosacea Agents
- Topical Steroids
- *H. Pylori* Treatments
- Pancreatic Enzymes
- Proton Pump Inhibitors
- Non-Biologic Ulcerative Colitis Agents
- Erythropoiesis Stimulating Agents



DUR Spotlight Interview

by Johna Bezdek Thaut
PharmD Candidate
DUR Intern

Jeff Taylor, PharmD

What part of the country are you from?

Birmingham, Alabama. I received my Doctor of Pharmacy from Auburn University in Alabama and am in the sixth year occupying my current role as DUR Pharmacist for the Colorado Department of Health Care Policy and Financing. Prior to attending pharmacy school, I received my Bachelor of Science degree at the University of Alabama at Birmingham.

I see that you used to work in the community setting before becoming a DUR pharmacist. How do you feel working in that setting prepared you for your current role?

With a subset of DUR involving medication utilization management through prospective claims systems edits and development of medication coverage policies, retail pharmacy experience can provide a unique perspective into how these edits function in real time when processing prescription claims in the retail pharmacy setting. This perspective can prove valuable when evaluating the impact of proposed changes to claims limitations or medication coverage policies prior to implementation.

What inspired you to become a DUR pharmacist when you took this position?

Interestingly, I did not have extensive knowledge from my academic or professional experience regarding the specifics of DUR pharmacy programs prior to applying for the DUR pharmacist position. Following a conversation with the Chief Medical Officer for Health First Colorado (Colorado's Medicaid program) regarding an opening for the DUR pharmacist position, I did ample research on federal and state DUR program requirements and the unique responsibilities of pharmacists in this role. While my overall knowledge of DUR did increase significantly during that time, I think the true inspiration for the role came with the hands-on experience of working for the state of Colorado's DUR program and being given the opportunity to apply my knowledge and expertise as a pharmacist in serving the Health First Colorado member population.

In your opinion, what is the most valuable aspect of your job?

The most valuable aspect is having the opportunity to engage in work with individuals, leadership, and decision makers within the Department of Health Care Policy & Financing and other state agencies that impacts positive change for Health First Colorado members.

Are you involved with any professional pharmacy organizations?

I am the designated state DUR representative for the Colorado Department of Health Care Policy & Financing with the [American Drug Utilization Review Society \(ADURS\)](#). I also recently had the privilege to be a speaker at the annual ADURS symposium in Scottsdale, AZ.

What do you enjoy doing in your free time?

Like many Coloradans, I enjoy being outdoors; whether it be skiing, hiking, camping, or simply spending an afternoon at the Denver Botanic Gardens. I am a food enthusiast and like to explore new and unique culinary experiences whenever possible. I also enjoy college football and rooting for my alma mater, Auburn University. War Eagle!



Stop opioid overdoses! Get naloxone today.

Naloxone saves lives and it's free for Health First Colorado (Colorado Medicaid) members. If you or someone you know is at risk for opioid overdose, get naloxone today. Naloxone treats opioid overdoses. It is sprayed into the nose or injected.

You don't have to be a doctor or nurse to use it, but a person who is having an overdose cannot give naloxone to themselves. It is important to teach others where the naloxone is kept and how to use it during an emergency.

Call 9-1-1 as soon as possible if an overdose emergency is suspected.

Does Health First Colorado cover naloxone?

Yes. There is **no cost or co-pay**. No prior authorization is needed.

How can I get naloxone?

Ask your pharmacist for naloxone. Let the pharmacist know you are a Health First Colorado member.

What does an opioid overdose look like?

Small "pinpoint" pupils
No response when shaken
Breathing slows or stops

Blue or gray lips or fingernails
Gurgling or choking sounds
Pale or clammy skin

What if I'm not sure it's an opioid overdose?

Call 9-1-1, turn the person onto their side, and give naloxone right away. Naloxone is safe, even if the situation is not an overdose. It is safe for both children and adults.

For more information and videos about how to use naloxone, visit [cdc.gov/stopoverdose/naloxone/index.html](https://www.cdc.gov/stopoverdose/naloxone/index.html)

If a pharmacy has questions, they can contact **1-800-424-5725** (open 24 hours a day, seven days a week.)



References

Caution Warranted When Combining Gabapentin or Pregabalin with an Opioid and/or CNS Depressant

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2. Food and Drug Administration. FDA warns about serious breathing problems with seizure and nerve pain medicines gabapentin (Neurontin, Gralise, Horizant) and pregabalin (Lyrica, Lyrica CR). Available at: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-serious-breathing-problems-seizure-and-nerve-pain-medicines-gabapentin-neurontin>. Accessed June 19, 2023.
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Fentanyl Crisis. Cracking Down...

1. Colorado General Assembly. House Bill 22-1326, *Fentanyl Accountability and Prevention*. Retrieved May 11, 2023, from <https://leg.colorado.gov/bills/hb22-1326>

Images

1. Colorado flag. <https://pixabay.com/vectors/flag-colorado-state-symbols-usa-28562/>. Image by Clker-Free-Vector-Images. Accessed June 13, 2023.
2. Meeting room. https://www.freepik.com/free-vector/conference-room-interior-realistic-design-with-chart-screen-vector-illustration_2868604.htm#query=meeting%20room&position=12&from_view=keyword&track=ais (modified). Image by macrovector on Freepik. Accessed June 13, 2023.

Our mission is to improve health care equity, access and outcomes for the people we serve while saving Coloradans money on health care and driving value for Colorado.

<https://hcpf.colorado.gov>



The October 1, 2023

Colorado Preferred Drug List (PDL)

is available at

<https://www.colorado.gov/hcpf/pharmacy-resources>