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*The Bulletin of  
Medicaid Drug  
Utilization Review  
in Iowa*

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## Safe Use of Benzodiazepine Drug Class

In September 2020, the U.S. Food and Drug Administration (FDA) released an [FDA Drug Safety Communication](#)<sup>1</sup> announcing the *Boxed Warning* for all benzodiazepines was being updated to address the serious risks of abuse, addiction, physical dependence, and withdrawal reactions. The current prescribing information for benzodiazepines does not provide adequate warnings about these serious risks and harms associated with these medications which may lead to them being prescribed and used inappropriately. These serious risks are increased when used with other medications and /or substances.

The FDA found benzodiazepines are widely prescribed in the U.S., often for long periods of time. In 2019, an estimated 92 million benzodiazepine prescriptions were dispensed from U.S. outpatient pharmacies, with alprazolam being the most common, followed by clonazepam and lorazepam. They are also widely abused and misused, frequently together with alcohol, prescription opioids, and illicit drugs, all of which increase the risks of serious adverse events. The FDA also found that some patients have had serious withdrawal reactions after benzodiazepines were stopped suddenly or the dose was reduced too quickly. Some patients experienced withdrawal symptoms over many months.

The FDA previously warned about the serious risks of combining benzodiazepines with opioid pain or cough medicines in [August 2016](#)<sup>2</sup>, and cautioned about withholding medication for opioid use disorder from patients taking benzodiazepines or CNS depressants in [September 2017](#)<sup>3</sup>.

Health care professionals should determine whether the benefits of prescribing a benzodiazepine outweigh the risks. Consideration should be given to the patient's condition

<sup>1</sup> <https://www.fda.gov/drugs/drug-safety-and-availability/fda-requiring-boxed-warning-updated-improve-safe-use-benzodiazepine-drug-class>

<sup>2</sup> <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-about-serious-risks-and-death-when-combining-opioid-pain-or>

<sup>3</sup> <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-urges-caution-about-withholding-opioid-addiction-medications>

and other medications being taken, and assess the risk of abuse, misuse, and addiction. Particular caution should be taken when benzodiazepines are prescribed with opioids and other medications that depress the central nervous system (CNS), which can result in serious side effects, including severe respiratory depression and death. When prescribing benzodiazepines, either alone or in combination with other medications, the dosage and duration of treatment should be limited to the minimum needed to achieve the desired clinical effect. Patients should be monitored for signs and symptoms of abuse, misuse, or addiction throughout therapy and if substance use disorder is suspected, patients should be referred for early substance abuse treatment.

When discontinuing benzodiazepines, a gradual taper to reduce the dosage should be used to reduce the risk of acute withdrawal reactions. Tapering schedules should be patient-specific to gradually reduce the dosage. There are no standard benzodiazepine tapering schedules suitable for all patients.

The federal Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities (SUPPORT) Act requires State Medicaid programs to review and monitor the use of opioids with benzodiazepines. The Iowa Medicaid Drug Utilization Review (DUR) Commission will accomplish this through ongoing retrospective claims review to identify concerning concomitant opioid and benzodiazepine treatment. A review of the most recent retrospective claims (4/1/2020 through 9/30/2020), for members with at least a one day overlap of an opioid and benzodiazepine, found the following:

Member Age	Fee-For-Service		AmeriGroup		Iowa Total Care		Overall	
	Unique Members	Unique Prescribers	Unique Members	Unique Prescribers	Unique Members	Unique Prescribers	Unique Members	Unique Prescribers
< 18 years of age	4	6	60	66	34	44	98	97
18 years of age and older	68	138	3,464	3,234	2,035	2,338	5,561	4,143

The Iowa Medication DUR Commission made the following recommendation(s):

- Narrow down the time period (90 days)
- Identify members with  $\geq 45$  days' overlap with an opioid and benzodiazepine
- Identify members with  $\geq 45$  days' overlap with an opioid and benzodiazepine that also received naloxone

The DUR Commission will review the additional data and determine if further steps need to be taken. This could include sending letters to providers regarding the concurrent use of an opioid and benzodiazepine, potential duration of therapy limits on benzodiazepines, or ProDUR edits.

**Medicaid Statistics for Prescription Claims  
September through November 2020**

	<b>FFS</b>	<b>Amerigroup</b>	<b>Iowa Total Care</b>
<b># Paid Claims</b>	21,985	1,102,276	761,226
<b>Total \$ Paid</b>	\$2,240,412	\$99,126,320	\$63,672,028
<b>Unique Users</b>	3,710	152,661	109,718
<b>Avg Cost/Rx</b>	\$101.91	\$89.93	\$83.64
<b>Top 5 Drugs by Prescription Count</b>	Trazadone	Omeprazole	Omeprazole
	Clonidine	Sertraline	Albuterol
	Omeprazole	Trazodone	Sertraline
	Sertraline	Atorvastatin	Atorvastatin
	Albuterol Aerosol	Gabapentin	Lisinopril
<b>Top 5 Drugs by Paid Amount (pre-rebate)</b>	Fintepla	Humira (CF) Pen	Humira Pen
	Evryydi	Vyvanse	Vyvanse
	Humira Pen	Latuda	Vraylar
	Vyvanse	Vraylar	Trikafta
	Biktarvy	Ozempic	Invega Sust
<b>Top 5 Therapeutic Class by Paid Amount (pre-rebate)</b> Therapeutic class taxonomy differs among each plan	Anticonvulsants	Antidiabetics	Insulin
	Atypical Antipsychotics	Antipsychotics/Antimanic Agents	Sympathomimetics
	Anti-Inflammatories, Non-NSAID	Antiasthmatic and Bronchodilator Agents	Antiretrovirals
	Muscular Dystrophy Agents	Analgesics - Anti-Inflammatory	Anti-TNF-alpha - Monoclonal Antibodies
	Antiretroviral Combinations	ADHD/Anti-Narcolepsy/Anti-Obesity/Aorexiant	Antipsychotics - Misc.
<b>Top 5 Therapeutic Class by Prescription Count</b> Therapeutic class taxonomy differs among each plan	Antidepressants – Selected SSRIs	Antidepressants	SSRIs
	Anticonvulsants	Antiasthmatic and Bronchodilator Agents	Anticonvulsants - Misc.
	Atypical Antipsychotics	Anticonvulsants	Sympathomimetics
	Antihypertensives - Central	Antihypertensives	PPIs
	PPIs	ADHD/Anti-Narcolepsy/Anti-Obesity/Aorexiant	HMG CoA Reductase Inhibitors