Texas Medicaid

Combined Use of Opioids and CNS Depressants Drug Use Evaluation

Educational RetroDUR Mailing	☑Initial Study ☐Follow – up /Restudy

Executive Summary

Purpose:	This intervention is designed to improve the management of patients on potentially harmful combinations of opioids and various CNS depressants (i.e., benzodiazepines, antipsychotics, muscle relaxants, sedative hypnotics, and gabapentinoids).		
Why Issue was Selected:	The prescribing of opioids should be based on careful consideration of benefits and risks associated with their use. Serious risks of opioid pain medications include opioid use disorder, overdose, and death. Medical professionals are advised to help mitigate these risks by evaluating the use of all central nervous system (CNS) agents while paying special attention to medications likely to cause sedation or respiratory depression.[1] CNS depressants include medications such as benzodiazepines, antipsychotics, muscle relaxants, sedative hypnotics, and gabapentinoids (i.e., pregabalin and gabapentin). Drug classes like benzodiazepines, when combined with opioids, have resulted in such serious adverse effects, including death, that the U.S. Food and Drug Administration (FDA) issued its strongest warning against their combined use.[2] The FDA also required an updated Boxed Warning for all benzodiazepines regarding the risks of abuse, addiction, physical dependence, and withdrawal reactions.[3] Similarly, The Centers for Medicare & Medicaid Services (CMS) provided guidance on risks associated with opioids in H.R.6 section 1004, more commonly known as the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act.[4] The recommendations are geared toward increasing patient safety by requiring states to have an automated review process in place that monitors patients concurrently prescribed opioids, benzodiazepines and other CNS depressants, and/or antipsychotics.[4]		
Program Specific Information:	**Performance Indicators**	**Exceptions**	
		(<18 Years) FFS	**(<18 Years) MCO**
	• Use of opioid analgesics in combination with benzodiazepines	(0) 8	(6) 1,739

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	• Use of opioid analgesics in combination with antipsychotics	(0) 1	(1) 1,200
	• Use of opioid analgesics in combination with benzodiazepines and antipsychotics	(0) 0	(3) 571
	• Use of opioid analgesics in combination with muscle relaxants	(0) 4	(4) 2,489
	• Use of opioid analgesics in combination with benzodiazepines and muscle relaxants	(0) 2	(5) 570
	• Use of opioid analgesics in combination with sedative hypnotics	(0) 0	(0) 780
	• Use of opioid analgesics in combination with benzodiazepines, sedative hypnotics or gabapentinoids without naloxone	(2) 29	(30) 11,689
Setting & Population:	All patients with drug therapy for targeted medications within the past 30 days.		
Types of Intervention:	Cover letter and modified patient profiles.		
Main Outcome Measures:	The performance indicators will be re-measured when six months of outcome data are available.		
Anticipated Results:	Reduction in concomitant use of opioid therapy with other CNS depressants, decreased adverse drug events associated with opioid therapy, and increased use of naloxone to prevent opioid overdose.		

Performance Indicator #1: Use of opioid analgesics in combination with benzodiazepines

Why has this indicator been selected?	Combining an opioid analgesic with benzodiazepines greatly increases the risk of serious side effects including extreme sleepiness, respiratory depression, overdose, and even death.[1-6]
Candidates (denominator):	Patients with opioid (Appendix A) analgesic therapy in the past 30 days. Excluded: medication-assisted treatment (MAT) drugs (Appendix B).
Exception criteria (numerator):	Candidates with 14 days or more of overlapping benzodiazepine (Appendix C) therapy in the past 35 days. Excluded: patients with cancer, sickle cell disease or a hospice designation in the past 730 days.

Performance Indicator #2: Use of opioid analgesics in combination with antipsychotics

Why has this indicator been selected?	Combining an opioid analgesic with an antipsychotic increases the risk of serious side effects including extreme sleepiness, respiratory depression, and even death. Patients with mental health conditions also have a higher probability of experiencing opioid-related harms. This can be due to concomitant medication use (i.e., antipsychotics, benzodiazepines, and other CNS

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	depressants), comorbidities such as alcohol or substance abuse, and the increased risk of opioid misuse in this population leading to overdose or addiction.[1,4,5]
Candidates (denominator):	Patients with opioid (Appendix A) analgesic therapy in the past 30 days. Excluded: medication-assisted treatment (MAT) drugs (Appendix B).
Exception criteria (numerator):	Candidates with 14 days or more of overlapping antipsychotic (Appendix D) therapy in the past 35 days. Excluded: patients with cancer, sickle cell disease or a hospice designation in the past 730 days.

Performance Indicator #3: Use of opioid analgesics in combination with benzodiazepines and antipsychotics

Why has this indicator been selected?	Combining an opioid analgesic with benzodiazepines and antipsychotics greatly increases the risk of serious side effects including extreme sleepiness, respiratory depression, overdose, and even death. Coordination of care should be used to improve the treatment of co-morbid mental health disorders while being cognizant of the high rate of opioid use disorder in this population.[1-6]
Candidates (denominator):	Patients with opioid (Appendix A) analgesic therapy in the past 30 days. Excluded: medication-assisted treatment (MAT) drugs (Appendix B).
Exception criteria (numerator):	Candidates with 14 days or more of overlapping benzodiazepine (Appendix C) and antipsychotic (Appendix D) therapy in the past 35 days. Excluded: patients with cancer, sickle cell disease or a hospice designation in the past 730 days.

Performance Indicator #4: Use of opioid analgesics in combination with muscle relaxants

Why has this indicator been selected?	Combining opioid analgesics with muscle relaxants has been shown to increase the risk of overdose due to additive respiratory and central nervous system depression.[1,4-6]
Candidates (denominator):	Patients with opioid (Appendix A) analgesic therapy in the past 30 days. Excluded: medication-assisted treatment (MAT) drugs (Appendix B).
Exception criteria (numerator):	Candidates with 14 days or more of overlapping muscle relaxant (Appendix E) therapy in the last 35 days. Excluded: patients with cancer, sickle cell disease or a hospice designation in the past 730 days.

Performance Indicator #5: Use of opioid analgesics in combination with benzodiazepines and muscle relaxants

Why has this indicator been selected?	Combining opioid analgesics with muscle relaxants and benzodiazepines has been shown to increase the risk of overdose due to additive respiratory and central nervous system depression.[1-6]
Candidates (denominator):	Patients with opioid (Appendix A) analgesic therapy in the past 30 days. Excluded: medication-assisted treatment (MAT) drugs (Appendix B).

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Exception criteria (numerator):	Candidates with 14 days or more of overlapping muscle relaxant (Appendix E) and benzodiazepine (Appendix C) therapy in the last 35 days. Excluded: patients with cancer, sickle cell disease or a hospice designation in the past 730 days.

Performance Indicator #6: Use of opioid analgesics in combination with sedative hypnotics

Why has this indicator been selected?	Combining opioid analgesics with sedative hypnotics has been shown to increase the risk of overdose due to additive respiratory and central nervous system depression.[1-6]
Candidates (denominator):	Patients with opioid (Appendix A) analgesic therapy in the past 30 days. Excluded: medication-assisted treatment (MAT) drugs (Appendix B).
Exception criteria (numerator):	Candidates with 14 days or more of overlapping sedative hypnotic (Appendix F, select agents) therapy in the last 35 days. Excluded: patients with cancer, sickle cell disease or a hospice designation in the past 730 days.

Performance Indicator #7: Use of opioid analgesics in combination with benzodiazepines, sedative hypnotics or gabapentinoids without naloxone

Why has this indicator been selected?	The risk of opioid overdose increases in patients who use opioids concurrently with benzodiazepines, sedative hypnotics or gabapentinoids. Concomitant use of opioids with other CNS depressants increases the risk of respiratory depression, coma, and even death. The CDC and FDA recommend offering naloxone to those at risk of overdose.[1-7]
Candidates (denominator):	Patients with opioid (Appendix A) analgesic therapy in the past 30 days. Excluded: medication-assisted treatment (MAT) drugs (Appendix B).
Exception criteria (numerator):	Candidates with greater than 14 days of overlapping benzodiazepine (Appendix C), sedative hypnotic (Appendix F) or gabapentinoid (Appendix G) therapy in the past 35 days and no history of naloxone therapy in the past 730 days.

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Appendices:

Appendix A – Opioid Analgesics	
Specific Therapeutic Category (STC)	**STC Description**
H30	OPIOID ANALGESIC, SALICYLATE, AND XANTHINE COMB
H3A	OPIOID ANALGESICS
H3M	OPIOID, NON-SALICYL.ANALGESIC, BARBITURATE, XANTHINE
H3N	OPIOID ANALGESIC AND NSAID COMBINATION
H3R	OPIOID AND SALICYLATE ANALGESICS, BARBIT, XANTHINE
H3U	OPIOID ANALGESIC AND NON-SALICYLATE ANALGESICS
H3X	OPIOID ANALGESIC AND SALICYLATE ANALGESIC COMB
H3Z	OPIOID ANALGESIC, NON-SALICYLATE, XANTHINE COMB
S7G	SKELETAL MUSCLE RELAXANT, SALICYLAT, OPIOID ANALGESC

Appendix B – Medication-Assisted Treatments (MAT)	
Generic Code Number (GCN)	**GCN Description**
44187	BUPRENORPHINE 100 MG/0.5 SOLER SYR SUBCUT
44186	BUPRENORPHINE 300 MG/1.5 SOLER SYR SUBCUT
64672	BUPRENORPHINE HCL 2 MG TAB SUBLINGUAL
41432	BUPRENORPHINE HCL 74.2 MG IMPLANT
64673	BUPRENORPHINE HCL 8 MG TAB SUBLINGUAL
42843	BUPRENORPHINE HCL/NALOXONE HCL 0.7-0.18MG TAB SUBLINGUAL
34904	BUPRENORPHINE HCL/NALOXONE HCL 1.4-0.36MG TAB SUBLINGUAL
37824	BUPRENORPHINE HCL/NALOXONE HCL 11.4-2.9MG TAB SUBLINGUAL
33744	BUPRENORPHINE HCL/NALOXONE HCL 12 MG-3 MG FILM SUBLINGUAL
28958	BUPRENORPHINE HCL/NALOXONE HCL 2 MG-0.5MG FILM SUBLINGUAL
18973	BUPRENORPHINE HCL/NALOXONE HCL 2 MG-0.5MG TAB SUBLINGUAL
36677	BUPRENORPHINE HCL/NALOXONE HCL 2.1-0.3 MG FILM BUCCAL
39394	BUPRENORPHINE HCL/NALOXONE HCL 2.9-0.71MG TAB SUBLINGUAL

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Appendix B – Medication-Assisted Treatments (MAT)	
36678	BUPRENORPHINE HCL/NALOXONE HCL 4.2-0.7 MG FILM BUCCAL
33741	BUPRENORPHINE HCL/NALOXONE HCL 4MG-1MG FILM SUBLINGUAL
34905	BUPRENORPHINE HCL/NALOXONE HCL 5.7-1.4 MG TAB SUBLINGUAL
36679	BUPRENORPHINE HCL/NALOXONE HCL 6.3MG-1MG FILM BUCCAL
28959	BUPRENORPHINE HCL/NALOXONE HCL 8 MG-2 MG FILM SUBLINGUAL
18974	BUPRENORPHINE HCL/NALOXONE HCL 8 MG-2 MG TAB SUBLINGUAL
37823	BUPRENORPHINE HCL/NALOXONE HCL 8.6-2.1 MG TAB SUBLINGUAL
52540	LOFEXIDINE HCL 0.18 MG TABLET ORAL
27095	NALTREXONE MICROSPHERES 380 MG SUS ER REC INTRAMUSC

Appendix C - Benzodiazepines	
STC	**STC Description**
H20	ANTI-ANXIETY - BENZODIAZEPINES
H21	SEDATIVE-HYPNOTICS – BENZODIAZEPINES
H2X	TRICYCLIC ANTIDEPRESSANT-BENZODIAZEPINE COMBINATIONS
H4A	ANTICONVULSANT - BENZODIAZEPINE TYPE

Appendix D - Antipsychotics	
STC	**STC Description**
H2G	ANTIPSYCHOTICS, PHENOTHIAZINES
H7O	ANTIPSYCHOTICS, DOPAMINE ANTAGONISTS, BUTYROPHENONES
H7P	ANTIPSYCHOTICS, DOPAMINE ANTAGONISTS, THIOXANTHENES
H7S	ANTIPSYCHOTICS, DOPAMINE ANTAGONST, DIHYDROINDOLONES
H7T	ANTIPSYCHOTIC, ATYPICAL, DOPAMINE, SEROTONIN ANTAGNST
H7U	ANTIPSYCHOTICS, DOPAMINE AND SEROTONIN ANTAGONISTS
H7X	ANTIPSYCHOTICS, ATYP, D2 PARTIAL AGONIST/5HT MIXED
H7Z	SSRI-ANTIPSYCH, ATYPICAL, DOPAMINE, SEROTONIN ANTAG
H8W	ANTIPSYCHOTIC-ATYPICAL, D3/D2 PARTIAL AG-5HT MIXED

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Appendix E – Muscle Relaxants	
Hierarchical Ingredient Code (HIC)	**HIC Description**
001949	BACLOFEN
001944	CARISOPRODOL
001942	CARISOPRODOL/ASPIRIN
001720	CARISOPRODOL/ASPIRIN/CODEINE
001941	CHLORZOXAZONE
047065	CYCLOBENZAP/LIDO/PRILOC/GLYCER
001950	CYCLOBENZAPRINE HCL
035728	CYCLOBENZAPRINE/IRR CNTR-IRR 2
046613	CYCLOBENZAPRINE/LIDOCAIN/MENTH
044514	CYCLOBENZAPRINE/TENS ELECTRODE
044513	CYCLOBENZAPRINE/TENS UNIT/ELEC
001947	DANTROLENE SODIUM
001945	METAXALONE
001938	METHOCARBAMOL
001906	ORPHENADRINE CITRATE
001791	ORPHENADRINE/ASPIRIN/CAFFEINE
011582	TIZANIDINE HCL
036990	TIZANIDINE/IRRITANT CNTR-IRRT2

Appendix F – Sedative Hypnotics	
STC	**STC Description**
H2E	SEDATIVE-HYPNOTICS, NON-BARBITURATE
H7W	ANTI-NARCOLEPSY, ANTI-CATAPLEXY, SEDATIVE-TYPE AGENT

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Appendix G – Gabapentinoids	
HIC	**HIC Description**
008831	GABAPENTIN
037574	GABAPENTIN ENACARBIL
046213	GABAPENTIN/LIDOCAINE
046682	GABAPEN/LIDOCAINE/GAUZE/SILCON
043174	GABAPENTIN/LIDOCAINE/MENTHOL
046643	GABAPENTIN/LIDOCAINE/SILICONE
026470	PREGABALIN

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2. FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. August 31, 2016. Available at: 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. Accessed 8/2021.
3. FDA Drug Safety Communication: FDA requiring Boxed Warning updated to improve safe use of benzodiazepine drug class. September 23, 2020. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requiring-boxed-warning-updated-improve-safe-use-benzodiazepine-drug-class. Accessed 8/2021.
4. Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act of 2018, H. R. 6, 115th Cong. (2018). Available at: https://www.congress.gov/115/bills/hr6/BILLS-115hr6enr.pdf. Accessed 8/2021.
5. Department of Health and Human Services, Centers for Medicare & Medicaid Services, CMCS Informational Bulletin. Best Practices for Addressing Prescription Opioid Overdoses, Misuse and Addiction, January 28, 2016. Available at: https://www.medicaid.gov/federal-policy-guidance/downloads/cib-02-02-16.pdf. Accessed 8/2021.
6. FDA Drug Safety Communication: FDA recommends health care professionals discuss naloxone with all patients when prescribing opioid pain relievers or medicines to treat opioid use disorder. July 23, 2020. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommends-health-care-professionals-discuss-naloxone-all-patients-when-prescribing-opioid-pain. Accessed 8/2021.
7. FDA Drug Safety Communication. FDA warns about serious breathing problems with seizure and nerve pain medicines gabapentin (Neurontin, Gralise, Horizant) and pregabalin (Lyrica, Lyrica CR). December 19, 2019. 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 8/2021.

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TEXAS
Health and Human Services

Cecile Erwin Young
Executive Commissioner

<<Date>>

«dea»
«name»
«add1»
«add2»
«add3»

RE: Safe and Effective Management of Patients Receiving Opioids and CNS Depressants

Dear Dr. <<Name>>:

Thank you for providing quality care for Texas Fee-For-Service (FFS) Medicaid patients. The content of this letter has been approved by the Texas Drug Utilization Review (DUR) Board, whose function is to promote safe and cost-effective drug therapy and provide opportunities for continuous improvement of care.

This retrospective claims review was designed to assist you in identifying patients who may be at risk of opioid-related adverse drug events due to combined use with other central nervous system (CNS) depressants. In 2016, the Centers for Disease Control and Prevention (CDC) issued recommendations for safer and more effective use of opioid therapy. The guidelines focused on prudent use of long- and short-acting opioids, risk assessment and mitigation strategies, coordination of care among prescribers and the dangers of combining opioids and other CNS depressants.[1] In 2018, the United States Congress passed "The Substance Use–Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act'' or the ''SUPPORT for Patients and Communities Act'' to promote opioid use disorder prevention, recovery, and treatment.[2] Some provisions in the SUPPORT Act include safety edits for opioids, maximum daily morphine equivalents as well as prescription drug monitoring programs. The SUPPORT Act also requires states to have an automated review process in place to monitor patients concurrently prescribed opioids, benzodiazepines and/or antipsychotics, and other CNS depressants to increase patient safety.[2]

Several other agencies have offered guidance on strategies to address prescription opioid overdoses and risk mitigation. The Centers for Medicare & Medicaid Services (CMS) issued an informational bulletin to highlight strategies for preventing opioid-related harms in the Medicaid population.[3] In a continued effort to improve patient safety surrounding opioid therapies, the U.S. Food and Drug Administration (FDA) issued several safety communications regarding risks of overdose and additive respiratory and CNS depression when using opioids with CNS depressants such as benzodiazepines, antipsychotics, muscle relaxants, sedative hypnotics, and gabapentinoids.[4-6] Finally, in 2020, the FDA also required label changes for opioids and opioid use disorder (OUD) medications regarding co-prescribing of naloxone for opioid overdose reversal.[7]

The intense focus on safe use of opioids by so many well-respected organizations, as well as the desire of the Board and Medicaid leadership to provide quality care to Texas patients, was the foundation for this review. Information and guidance on opioid prescribing are available at:

- The CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016 is available at: https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6501e1er.pdf.

- FDA Drug Safety Communications are available at: https://www.fda.gov/drugs/drug-safety-and-availability/drug-safety-communications and may be searched by date, drug class or by specific medications.

- The Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act of 2018 is available at: https://www.congress.gov/115/bills/hr6/BILLS-115hr6enr.pdf.

- The Texas Prescription Monitoring Program is available at: https://www.pharmacy.texas.gov/PMP/.

The total Texas Medicaid Fee-For-Service performance indicators for all patients (including those <18 years) with opportunities for improving the safe and effective management of opioids when combined with other CNS depressants are shown in the table below.

Total Texas Medicaid FFS Specific Data

Combined Use of Opioids and CNS Depressants Drug Use Evaluation	Number of Opportunities*	
	<18 Years	**>/=18 Years**
• Use of opioid analgesics in combination with benzodiazepines	0	8
• Use of opioid analgesics in combination with antipsychotics	0	1
• Use of opioid analgesics in combination with benzodiazepines and antipsychotics	0	0
• Use of opioid analgesics in combination with muscle relaxants	0	4
• Use of opioid analgesics in combination with benzodiazepines and muscle relaxants	0	2
• Use of opioid analgesics in combination with sedative hypnotics	0	0
• Use of opioid analgesics in combination with benzodiazepines, sedative hypnotics or gabapentinoids without naloxone	2	27

*Based on data through 9/3/2021

The enclosed patient profiles reflect one or more of the above issues and are provided as a medical record reminder for when your patients return for their next appointments.

We acknowledge that there may be clinical variables influencing an individual patient's management that are not apparent in claims data. However, we believe the issues identified may assist you in caring for your patient(s). It is possible that your license number may have been inadvertently assigned to the claim as an error at the pharmacy during the billing process. **Also, some prescribed medications as well as some recommended laboratory monitoring or physical examinations may not appear on the patient's profile because they may have been privately purchased or were not billable to Medicaid Services.** We thank you for reviewing this information and caring for Texas Medicaid patients, and we welcome the opportunity to discuss any comments or concerns you may have about our quality management program. Please feel free to call our office at 1-866-923-7208 with questions or concerns. If your mailing address is incorrect, it must be updated through the Texas Medical Board online at **http://www.tmb.state.tx.us/page/change-address.**

Sincerely,

Medicaid Drug Use Review Board
Vendor Drug Program H-630

Intervention Indicator Summary
Avoid the use of opioids concurrently with benzodiazepines[1-5,7] • Concurrent use of these drug classes can result in excessive drowsiness, respiratory depression, overdose, and death. This drug combination should be reserved for patients with inadequate alternative treatment options. If the combination is required, the dose and duration should be the lowest/shortest to treat the condition and the patient should be monitored closely for respiratory depression and sedation. • Benzodiazepines are widely used to treat a variety of medical conditions, including insomnia, anxiety, and seizures. For both insomnia and anxiety, benzodiazepine use is recommended as short-term or adjunctive to other medications or behavioral interventions. Even at recommended doses, benzodiazepines can lead to misuse, abuse, and addiction. Physical dependence can occur when benzodiazepines and/or opioids are taken steadily for several days to weeks, even at prescribed doses. • Nonfatal and fatal drug overdoses in the United States increased overall from 2019 to 2020. During this same time frame, benzodiazepine overdose visits per 100,000 emergency department visits increased 23.7%, both with opioid co-involvement (34.4%) and without (21.0%). Benzodiazepine-related deaths also increased 42.9% from second quarter 2019 to 2020; with increases in both prescription and illicit benzodiazepine-related deaths. During January–June 2020, 92.7% of benzodiazepine-involved deaths also involved opioids, highlighting the dangers of co-use.
Monitor and modify the treatment of patients using opioids and antipsychotics concurrently [1-3] • Concurrent use of these drug classes can result in excessive sleepiness, respiratory depression, overdose, and death. When this drug combination is used, the dose and duration should be the lowest/shortest to treat the condition and the patient should be monitored closely for respiratory depression and sedation. • Patients with mental health conditions have a higher probability of experiencing opioid-related harms. • Coordination of care is essential to improve the treatment of comorbid mental health disorders while being cognizant of the high rate of opioid use disorder in this population.
Monitor and modify treatment of patients using opioids and CNS depressants concurrently[1-9] • Many organizations (including the CDC, CMS, and FDA), and federal legislation in the SUPPORT Act, have provided guidance on concurrent use of opioids and CNS depressants to combat the opioid crisis. Using opioids with CNS depressants may result in excessive sleepiness, respiratory depression, overdose, and death. This retrospective claims review specifically targets concurrent use of opioids, benzodiazepines, antipsychotics, muscle relaxants, sedative hypnotics, and gabapentinoids. • When a patient is prescribed multiple CNS depressants, the risk of adverse drug events increases. To reduce that risk, guidance recommends: not using the drug combination when possible, monitoring for adverse events including respiratory depression and sedation, and providing patient education regarding the risks. If there are no alternative treatments, drug therapy should be used at the lowest dose for the shortest duration. • Opioids should not be abruptly discontinued in a patient who is physically dependent. No standard opioid tapering schedule exists that is suitable for all patients. Create a patient-specific plan to gradually taper the opioid dose and ensure ongoing monitoring and support, as needed, to avoid serious withdrawal symptoms, worsening of the patient's pain, or psychological distress. • Benzodiazepines should not be abruptly discontinued in a patient who is physically dependent. Abrupt cessation or reducing the dose too quickly can result in withdrawal reactions, including life-threatening seizures. No standard benzodiazepine tapering schedule exists that is suitable for all patients. Create a patient-specific plan to gradually taper the benzodiazepine dose and ensure ongoing monitoring and support, as needed, to avoid serious withdrawal reactions, worsening of the patient's underlying condition, or psychological distress. • Clinicians should regularly check their prescription monitoring program (PMP) for CNS depressants prescribed by other providers. Texas requires prescribers to check their patient's PMP history before prescribing opioids, benzodiazepines, barbiturates, or carisoprodol.

Intervention Indicator Summary
Promote the use of naloxone in patients using opioids with other CNS depressants[1,3,4,7,8] • The combination of opioids and other CNS depressants (i.e., benzodiazepines, antipsychotics, muscle relaxants, sedative hypnotics, and gabapentinoids) results in an increased risk of overdose and death due to severe drowsiness, decreased awareness, respiratory depression, and coma. • Patients with a prior history of substance abuse, an overdose, and those using medication-assisted treatment (MAT) for opioid use disorder are also at an increased risk of opioid overdose. MAT therapies include various buprenorphine products (e.g., oral sublingual tablets, Sublocade® injection), buprenorphine/naloxone products (e.g., Bunavail® buccal film, Suboxone® sublingual film, Zubsolv® sublingual tablet), lofexidine (Lucemyra®), and naltrexone extended-release injection (Vivitrol®). Methadone may also be used as part of an Opioid Treatment Program (OTP). • The FDA, CDC and CMS recommend prescribing a naloxone product indicated to reverse an opioid overdose in patients who are at an increased risk of overdose. Naloxone reverses the potential life-threating effects of opioids including respiratory depression, sedation, and hypotension by allowing the opioid overdose victim to resume normal breathing.

References:

1. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016; 65:1–49. DOI: Available at: https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6501e1er.pdf. Accessed 8/2021.
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External Messages

Flag	Internal Messages	External Messages
10083	Combination Opioid and Muscle Relaxant	According to submitted pharmacy claims, it appears your patient is receiving an opioid concurrently with a skeletal muscle relaxant. This combination is associated with additive central nervous system (CNS) and respiratory depression and increases the risk of overdose, coma, and death. Please review your patient's medication profile and consider if a change in therapy is warranted to improve the safety of this drug regimen.
10084	Combination Opioid, Benzodiazepine, and Muscle Relaxant	According to submitted pharmacy claims, it appears your patient is receiving an opioid, benzodiazepine, and a skeletal muscle relaxant concurrently. This combination of medications is not recommended due to increased risk of adverse events including excessive sedation, overdose, and death secondary to additive CNS and respiratory depression. Please review your patient's medication profile and consider if a change in therapy is warranted to improve the safety of this drug regimen.
113707	Combination Opioid, Benzodiazepine, and Antipsychotic	According to submitted pharmacy claims, it appears your patient is receiving concurrent therapy with an opioid, benzodiazepine, and an antipsychotic. This combination of medications is not recommended due to increased risk of adverse events secondary to additive CNS depression. Title I of H.R. 6 SUPPORT for Patients and Communities Act addresses Medicaid regulations to combat the opioid crisis. States must monitor when patients receive opioids concurrently with antipsychotics, benzodiazepines, and other CNS depressants as this combination can increase the risk of excessive sedation, respiratory depression, overdose, and death. Please review your patient's medication profile and consider if a change in therapy is warranted to improve the safety of this drug regimen.
113708	Combination Opioid and Benzodiazepine	According to submitted pharmacy claims, it appears your patient is receiving concurrent therapy with an opioid and a benzodiazepine. The U.S. Food and Drug Administration as well as the Centers for Disease Control and Prevention have issued warnings regarding the use of this combination of central nervous system depressants due to the risk of excessive sedation, respiratory depression, overdose, and death. Please review your patient's medication profile and consider if a change in therapy is warranted to improve the safety of this drug regimen.
113709	Combination Opioid and Antipsychotic	According to submitted pharmacy claims, it appears your patient is receiving concurrent therapy with an opioid and an antipsychotic. Title I of H.R. 6 SUPPORT for Patients and Communities Act addresses Medicaid regulations to combat the opioid crisis. States are required to monitor when patients receive opioids concurrently with antipsychotics due to the risk of adverse drug events secondary to additive central nervous system depression. Please review your patient's medication profile and consider if a change in therapy is warranted to improve the safety of this drug regimen.
116103	Opioids and other CNS Depressants Without Naloxone	According to submitted pharmacy claims, it appears your patient is receiving an opioid concurrently with a central nervous system (CNS) depressant such as a sedative hypnotic or gabapentinoid but does not have a pharmacy claim for naloxone. This combination is associated with additive CNS and respiratory depression and increases the risk of overdose, coma, and death. The Centers for Disease Control and Prevention,

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External Messages

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		U.S. Food and Drug Administration, and the Centers for Medicare & Medicaid Services recommend that providers consider co-prescribing naloxone for patients at risk for opioid overdose. Patient education along with naloxone therapy can reduce the risk of fatal overdose. Please evaluate the treatment plan for this patient to determine the best course of action.
116104	Opioids and Benzodiazepines Without Naloxone	According to submitted pharmacy claims, it appears your patient is receiving an opioid concurrently with a benzodiazepine but does not have a pharmacy claim for naloxone. Patients receiving opioids and benzodiazepines concurrently are at increased risk of serious adverse events including excessive sedation, respiratory depression, overdose, and death. The Centers for Disease Control and Prevention along with the U.S. Food and Drug Administration recommend that patients on this drug combination be co-prescribed a naloxone product indicated to reverse an opioid overdose. Patient education along with naloxone therapy can reduce the risk of fatal overdose. Please evaluate the treatment plan for this patient to determine the best course of action.
116128	Combination Opioid and Sedative Hypnotic	According to submitted pharmacy claims, it appears your patient is receiving concurrent therapy with an opioid and a sedative hypnotic. Title I of H.R. 6 Support for Patients and Communities Act addresses Medicaid regulations to combat the opioid crisis. States must monitor when patients receive opioids concurrently with other central nervous system depressants like sedative hypnotics as this combination can increase the risk of adverse events including excessive sedation, respiratory depression, overdose, and death. Please review your patient's medication profile and consider if a change in therapy is warranted to improve the safety of this drug regimen.

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