Mountain-Pacific Quality Health

DUR PROGRAM NEWS

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The Drug Utilization Review (DUR) Program, administered by Mountain-Pacific through a contract with the Allied Health Services Bureau of the Montana Department of Public Health and Human Services, is the quality assurance body seeking to assure the quality of pharmaceutical care and to help provide rational, cost-effective medication therapy for Montana's Medicaid recipients.

Reducing Benzodiazepine and Opioid Combinations

The concomitant prescribing of opioids and benzodiazepines in the U.S. has increased **41%** between 2002 and 2014. Because the currently available clinical evidence does not support chronic combination therapy and serious safety risks exist, concomitant therapy warrants reconsideration.

Why reconsider co-prescribing benzodiazepines and opioids?

- **The clinical evidence rarely supports combination therapy.** Limited published reports exist to support the benefits of combination therapy (i.e., pre-operative and treatment of agitation for ventilated patients).
- **The daily use of benzodiazepines for the treatment of anxiety-related disorders is rarely recommended in clinical guidelines.** First-line therapies for anxiety-related disorders should consist of anti-depressant or other non-benzodiazepine medications.
- **Combination use has been associated with an increased risk of overdose and death.** Concurrent benzodiazepine and opioid use has been associated with nearly a quadrupling of risk for overdose and death vs. opioid use alone. After an extensive review of the clinical evidence regarding safety concerns with combination use of benzodiazepines and opioids by the FDA in 2016, black box warnings are now required.

Implications for Treatment

- **Use evidence-based psychotherapies (i.e., cognitive behavioral therapy), anti-depressants, or other non-benzodiazepine medications for the treatment of anxiety.** If required, benzodiazepines are typically recommended last line and short-term.
- **Limit combination use of opioids and benzodiazepines only to patients for whom all other alternative treatment options are inadequate; educate patients.**
  - ✓ If the decision is made to prescribe a benzodiazepine with an opioid, limit dosage and duration to the minimum possible.
  - ✓ Counsel patients regarding serious safety risks.
- **If tapering is required to reduce risk in patients receiving both opioids and benzodiazepines, consider tapering opioids first. Taper benzodiazepines slowly if discontinued.** Cognitive behavioral therapy increases success, and coordination with the patient's mental health care professional is recommended.

Between 2004 and 2011, benzodiazepine involvement in opioid analgesic deaths increased from 18% to 31%.

Please see page 3 for references and resources.

For drug-specific prior authorization information, please contact the Medicaid Drug Prior Authorization Unit @ Mountain-Pacific 1-800-395-7961

EVIDENCE-BASED PRESCRIBING: MEDICATIONS TO AVOID

Use of Codeine-Containing Products in Patients <18 Years of Age

Mechanism of Action

Codeine (3-methylmorphine) is a pro-drug, opioid analgesic with low affinity for opioid receptors within the central nervous system and has been used extensively as an analgesic and antitussive. Although codeine was historically considered safe with a wide therapeutic index, current understanding of pharmacogenetic variations in metabolism warrant closer scrutiny for its use. Codeine must first be metabolized to its active form, morphine, by the CYP 2D6 enzyme within the liver in order to exert its analgesic effect.

Rationale for avoiding use < 18 y.o. ➔ CYP 2D6 Genetic Variability➔ Unpredictable Therapeutic Response

URGENT

Codeine was a factor in 64 cases of severe respiratory depression and 24 deaths in children between 1965 and 2015, according to a FDA review of Adverse Event Reporting Sytem data.

Toxicity potential in pediatrics

- Substantial genetic variations in codeine conversion to active metabolite (morphine)
- **Ultra-rapid metabolizers can produce toxic levels of morphine, resulting in respiratory depression, apnea, or death after a therapeutic dose**
- EVIDENCE-BASED ALTERNATIVES: Mild to moderate pain-acetaminophen or ibuprofen. Severe pain-morphine. Cough-vaporizer, humidifier, fluids

Limited efficacy potential in pediatrics

- Substantial genetic variations in codeine conversion to active metabolite (morphine)
- **Slow metabolizers may produce low morphine levels and have little or no analgesic effect**

Summary: The use of codeine in pediatrics should be avoided due to the potential for toxicity, overdose and limited effectiveness. A 2015 FDA Advisory Committee has recommended the FDA change labeling to contra-indicate use under 18, and the American Academy of Pediatrics (2016) is warning against its use. ***The use of an alternative agent with a superior safety and efficacy profile is strongly recommended in all pediatric patients <18 years old.***

Sources:

Professional Resource, Analgesics in Kids: FAQs. Pharmacist's Letter/Prescribers Letter. November 2016.

Tobias JD, Green TP, Cote CJ, AAP SECTION ON ANESTHESIOLOGY AND PAIN MEDICINE, APP COMMITTEE ON DRUGS. Codeine: Time to Say "No". Pediatrics. 2016; 138 (4); e20162396.

Naloxone is a covered product under Montana Medicaid.

The Drug Prior Authorization unit has received numerous questions regarding Medicaid coverage of naloxone. The Montana Medicaid Preferred Drug List (PDL) preferred formulations are naloxone syringe/vial and Narcan Nasal Spray. These preferred products are currently available without a prior authorization (with a prescription), and do not have any limitations. For questions, please call the Drug PA Unit, administered by Mountain-Pacific, at 800-395-7961.

Montana Medicaid Preferred Drug List Snapshot-Opioid Reversal Agents

Preferred Agents (available without a prior authorization)	Non-Preferred Agents	Limitations
naloxone syringe naloxone vial Narcan® Nasal Spray	Evzio®	None

REFERENCES AND RESOURCES-CONT. PAGE 1

American Psychiatric Association Practice Guideline for the Treatment of Patients with Panic Disorder. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/panicdisorder.pdf. Accessed 2/2/2017.

American Pyschiatric Association Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/panicdisorder.pdf. Accessed 2/2/2017.

Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016; 65(No. RR-1):1–49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1. Accessed 2/2/2017.

Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive compulsive disorder: A revision of the 2005 guidelines from the British Association for Psychopharmacology. https://www.bap.org.uk/pdfs/BAP_Guidelines-Anxiety.pdf. Accessed 2/2/2017.

FDA Drug Safety Communication: FDA warns about serious risks of death with combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/drugs/drugsafety/ucm518473.htm. Accessed 2/2/2017.

National Collaborating Centre for Mental Health. Social anxiety disorder: recognition, assessment and treatment. London (UK):

National Institute for Health and Care Excellence (NICE); 2013 May. 44 p. (Clinical guideline; no. 159). https://www.guideline.gov/summaries/summary/46234/social-anxiety-disorder-recognition-assessment-and-treatment?q=anxiety. Accessed 2/2/2017.

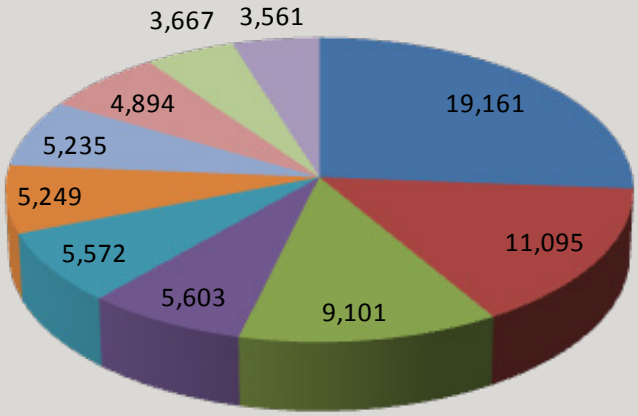
National Institute for Health and Care Excellence; Clinical Guideline for Generalized Anxiety Disorder and Panic Disorder in Adults: management. https://www.nice.org.uk/guidance/cg113. Accessed 2/2/2017.

Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. (December 18, 2014). The DAWN Report: Benzodiazepines in Combination with Opioid Pain Relievers or Alcohol: Greater Risk of More Serious ED Visit Outcomes. Rockville, MD.

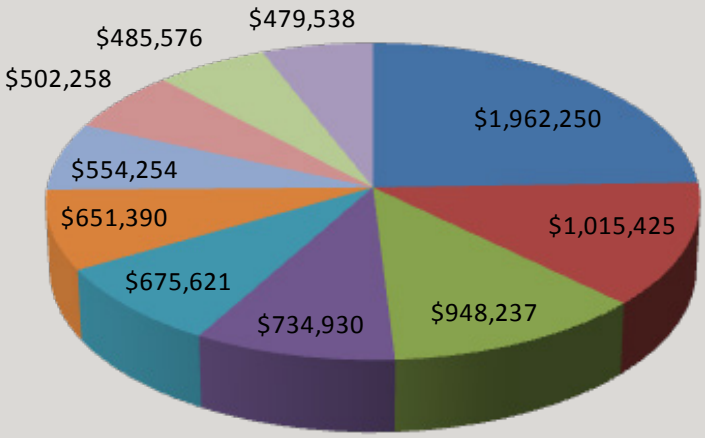
US Department of Veterans Affairs Clinical Practice Guideline for Management of Post-Traumatic Stress. http://www.healthquality.va.gov/guidelines/MH/ptsd/cpgPTSDFULL201011612c.pdf. Accessed 2/2/2017.

Montana Medicaid
Top 10 Therapeutic Drug Classes YTD 2017

By number of claims



By claim cost



• Antidepressants • Opiate agonists • Anticonvulsants • Antipsychotic Agents • Penicillins • Beta-adrenergic agonists • Non-sterodial anti-inflamatory agents • Proton-pump inhibitors • Anxiolytics sedatives and hypnotics • Contraceptives

• Antipsychotic agents • Disease-modifying antirheumatic agents • Insulins • Anticonvulsants • Corticosteroids (respiratory tract) • HCV antivirals • Amphetamines • Immunomodulatory agents • Respiratory and CNS stimulants • Hemostatics

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