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DUR DIGEST

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The use of Benzodiazepines and Opioids with Sleep Apnea

Obstructive sleep apnea (OSA) is a chronic disorder that affects at least 2% to 4% of the adult population.[1] OSA is defined by the occurrence of daytime sleepiness, loud snoring, witnessed breathing interruptions, or awakenings due to gasping or choking in the presence of at least five obstructive respiratory events per hour of sleep.[1] The signs and symptoms of OSA are a result of the derangements that occur due to repetitive collapse of the upper airway.[1] Benzodiazepines are contraindicated in sleep apnea or significant respiratory disease since they can cause respiratory depression. In addition, the risk of sleep apnea increases with the use of opioids. Prescribers should weigh the benefit versus risk of using the combination of benzodiazepines and opioids in a patient with sleep apnea, given the synergistic risk of respiratory depression.

Given the increased risk of using a benzodiazepine in OSA the DUR Commission looked at the data more closely to see if members are at an increased risk of an adverse event.

Analysis: A review of medical claims was conducted to identify Iowa Medicaid members with a diagnosis of sleep apnea. Once identified, three months of non-reversed, paid pharmacy claims data from November 2012 through January 2013 were reviewed to identify members taking a benzodiazepine with a diagnosis of sleep apnea. The following observations were made:

	Number of Members
Unique Members with Sleep Apnea Diagnosis	12,935
Unique members using a Benzodiazepine	2,886
Unique members combining a benzodiazepine and opioid	518

This discussion prompted the DUR Commission to make the recommendation to look at members with a diagnosis of anxiety combining an SSRI or SNRI with a benzodiazepine. If members with an anxiety diagnosis are combining an SSRI or SNRI with a benzodiazepine, letters could be sent to prescribers asking if the benzodiazepine is needed and if the dose of the SSRI or SNRI could be optimized thus eliminating the need for the benzodiazepine. This topic will be discussed at a future DUR meeting.

References

1. Epstein LJ; Kristo D; Strollo PJ; Friedman N; Malhotra A; Patil SP; Ramar K; Rogers R; Schwab RJ; Weaver EM; Weinstein MD. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med 2009*;5(3):263-276.

Duplicate Antidepressants

In the United States, 9% of adults meet the criteria for current depression and 3.4% meet the criteria for major depression based on a survey conducted by the CDC from 2006 through 2008.[1] The major classes of drugs to treat depression are selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), Tricyclic antidepressants (TCAs), monamne oxidase inhibitors (MAOIs) and a few drugs with unique modes of action (bupropion, mirtazapine, nefazodone, trazodone).

The goal of treatment of depression should be remission of symptoms. Response to an antidepressant is defined as a 50% reduction in symptoms. In eight-week clinical trials, response rates are typically 50% to 55%, while remission rates are only 35% to 40%[2]. Therefore, more than half the patients treated with an antidepressant continue to have symptoms. Approaches to achieve response or remission include increasing the dose of the antidepressant, combining antidepressants, or augmentation with a nonantidepressant. Generally, one antidepressant is prescribed initially. If after four weeks there is no response or after six weeks there is a partial response to an antidepressant despite adherence, treatment should be re-evaluated.[3,4] For those patients showing a partial response, dose optimization should be attempted.[5] Patients that have shown no response four to eight weeks after dose optimization should be switched to a different antidepressant.[6]

The effectiveness of antidepressant medications is comparable.[6] Choice of medication should be based on the following: 1) patient preference; 2) nature of prior response to medication; 3) safety, tolerability and anticipated side effects; 4) co-occurring psychiatric or general medical conditions; 5) pharmacological properties of medication (e.g. half-life, drug interactions); and 6) cost.[6] Advantages of switching antidepressants versus adding a second medication are that switching costs less, and minimizes risk of adverse effects, drug interactions, and nonadherence.[1] Disadvantages of switching antidepressants include possible loss of any partial response from the first drug, occurrence of withdrawal symptoms, and delay in onset of the second drug.[3]

The DUR commonly observes multiple antidepressant use through profile reviews. Given the increased cost, risk of adverse effects, and drug interactions the DUR Commission looked at this more closely. This topic was initially reviewed at the February 2013 DUR meeting. The DUR recommended sending letters to prescribers of patients combining two or more SSRIs or two or more TCAs. In addition, the DUR requested trazodone be removed from the list of antidepressants as it was thought it was being used for sleep.

Antidepressants used in Data Analysis

SSRI	SNRI	TCA	MAOI	Other
Citalopram	Venlafaxine	Amitriptyline	Phenelzine	Bupropion
Escitalopram	Desvenlafaxine	Amoxapine	Selegiline	Mirtazapine
Fluoxetine	Duloxetine	Clomipramine	Tranylcypromine	Nefazodone
Fluvoxamine	Milnacipran	Desipramine		
Paroxetine		Doxepin		
Sertraline		Imipramine		
Vilazidone		Maprotiline		
		Nortriptyline		
		Protriptyline		
		Trimipramine		

Three months of non-reversed, paid pharmacy claims data from November 2012 through January 2013 were reviewed to identify: 1) the number of unique members combining antidepressants from the same class (MAO Inhibitors, SSRIs, TCAs, SNRIs) for ≥ 60 days, and 2) the number of unique members that were taking three or more antidepressants concurrently from the Antidepressant List (above) for ≥ 60 days. The following observations were made:

Drug Combination	Number of Members	Number of Prescribers
SSRIs (2 or more)	57	76
TCAs (2 or more)	13	15
MAOIs (2 or more)	0	2
MAOI plus SSRI/SNRI or TCA	2	3
SNRIs (2 or more)	17	25
SSRI plus SNRI	169	157
Three or more antidepressants (any mechanism of action)	135	184

References

1. MMWR Morb Mortal Wkly Rep 2010 Oct 1;59(38):1229.
2. Rush AJ, Trivedi MH, Wisniewski SR, et al. Bupropion-SR, sertraline, or venlafaxine-XR after failure of SSRIs for depression. *N Engl J Med* 2006;354:1231-42.
3. Mann JJ. The medical management of depression. *N Engl J Med* 2005;353:1819-34.
4. Marangell LB. Switching antidepressants for treatment-resistant major depression. *J Clin Psychiatry* 2001;62 Suppl 18:12-7.
5. Papakostat GI, Petersen TJ, Green C, et al. A description of next-step switching versus augmentation practices for outpatients with treatment-resistant major depressive disorder enrolled in an academic specialty clinic. *Ann Clin Psychiatry* 2005;17:161-5.
6. American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder (3rd Edition). October 2010. http://www.psych.org/guidelines/mdd2010. Accessed December 28, 2012.

Updated Drug PA Criteria

ADHD/ADD/Narcolepsy

Changes are italicized:
Prior authorization (PA) is required for ADD/ADHD/Narcolepsy agents for patients 21 years of age or older *under the following conditions:*

1. *Attention Deficit Disorder (ADD) or Attention Deficit Hyperactivity Disorder (ADHD) meeting the DSM-IV criteria and confirmed by a standardized rating scale (such as Conners, Vanderbilt, Brown, SNAP-IV). Symptoms must have been present before twelve (12) years of age and there must be clear evidence of clinically significant impairment in two or more environments (social, academic, or occupational).*
2. *Narcolepsy with diagnosis confirmed with a recent sleep study (ESS, MSLT, PSG).*
3. *Excessive sleepiness from obstructive sleep apnea/hypopnea syndrome (OSAHS) with documentation of non-pharmacological therapies tried (weight loss, position therapy, CPAP at maximum titration, BiPAP at maximum titration or surgery) and results from a recent sleep study (ESS, MSLT, PSG) with the diagnosis confirmed by a sleep specialist.*

Payment for a non-preferred agent will be authorized only for cases in which there is documentation of previous trial and therapy failure with a preferred agent. *If a non-preferred long-acting medication is requested, a trial of the preferred immediate release and extended release product of the same chemical entity is required.

The required trials may be overridden when documented evidence is provided that the use of these agents would be medically contraindicated.

DUR Activities

Medicaid Statistics for Prescription Claims

from October 1, 2012 to December 31, 2012*

Number of claims paid: 1,177,662

Total dollars paid: $68,314,527.40

Percent controlled substances: 18.23%

Average amount paid per claim: $58.01

Average amount paid per claim, brand: $247.33

Average Amount paid per claim, generic: $13.74

Top Drugs by Number of Prescriptions	Top Drugs by Dollars Spent	Top Therapeutic Class by Dollars Spent
ProAir HFA $52.46/RX	*Abilify* 5mg $1,468,317 $473.50/RX	Antipsychotics – Atypicals $9.0 million
APAP 325mg $6.97/RX	Methylphenidate ER 36mg $1,292,231 $200.25/RX	Stimulants – Amphetamines – Long Acting $4.8 million
Loratadine 10mg $9.42/RX	*Novoseven RT Inj* 2mg $952,780 $105,864/RX	Antihemophilic Agents $3.9 million
Methylphenidate ER 36mg $200.25/RX	*Abilify* 10mg $1,007,618 $484.43/RX	Stimulants – Methylphenidate-Long Acting $3.5 million
Ventolin HFA $46.37/RX	Methylphenidate ER 54mg $878,804 $182.51/RX	Anticonvulsants $3.1 million

*All dollars reported are Pre-Rebate