

Wyoming Drug Utilization Review

Newer Agents to Facilitate Weight Loss or Weight Management in Overweight or Obese Patients

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Wyoming Medicaid does not cover weight loss agents. However, this topic may arise in discussion with patients and the information contained herein may be helpful when educating patients.

Garnering the label “epidemic”, obesity has become a recognized disease state and a major contributor to the quality of our population’s health. It is a risk factor of many other disorders including cardiovascular disease, diabetes

mellitus, and cancer.¹ Two terms used to classify weight above the “normal” range are overweight, defined as a body mass index (BMI) of 25 to 29.9 kg/m², and obese, defined as a body mass index of ≥ 30 kg/m².² Severe or morbid obesity is a term often used when body mass indices are ≥ 40 kg/m² or ≥ 35 kg/m² with comorbid conditions.²

Sedentary lifestyle, lack of adequate sleep, and diets high in fat and sugar all promote unhealthy weight gain.¹ An inactive lifestyle leads to lower energy expenditure and the pathogenesis of obesity. Perhaps one of the more insidious contributors is prolonged TV watching. After controlling for other variables, the Nurses’ Health Study found a 23 percent increase in the incidence of obesity in women for every two-hour per day increment of watching TV.³ Other sedentary activities, such as working a desk job, did not carry the same risk theoretically due to behaviors leading to changes in energy

intake while watching TV.³ The number of Americans sleeping less than seven hours per night has more than doubled over the past 40 years and may also be exerting a negative metabolic effect.¹ Researchers have found that sleep restriction is associated with decreased serum leptin and increased serum ghrelin leading to increased hunger and appetite. Prospective evaluation of over 120,000 men and women found direct association between weight gain and intake of meat products, potato products, and sugar-sweetened drinks. An inverse association was found between weight gain and consumption of fruits, vegetables, nuts, whole grains, and yogurt.¹ Interventions can be made to these lifestyle choices as nonpharmacologic treatment options and is considered a first line approach for most patients.²

A number of pharmacologic agents can be used to assist patients with losing weight, and there have been some recent additions to the list including Belviq® (lorcaserin HCl) approved by the FDA in 2012, Contrave® (naltrexone HCl and bupropion HCl, extended-release) approved in 2014, Qsymia® (phentermine and topiramate, extended-release) approved in 2012, and Saxenda® (liraglutide injection) approved in late 2014. These newer agents are used in combination with reduced calorie intake and increased physical activity to facilitate weight loss or weight management.² These medications are usually considered if lifestyle interventions alone do not achieve a weight loss of five percent of body weight within three to six months. Prescribers must carefully consider mechanism of action, adverse effects, safety, and efficacy when choosing a weight loss agent. Weight loss may increase the risk of hypoglycemic events in patients taking medications for type 2 diabetes and this population should be monitored more closely if a weight loss agent is initiated. If an agent does not achieve a decrease in body weight of five percent in six months, it should be discontinued and a different weight loss agent considered if necessary. Herbal products and dietary supplements available over-the-counter have limited data on efficacy and safety and are generally not considered to be beneficial.²

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continued on page 3

P & T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on May 14, 2015.

Highlights of this meeting include:

The RFP for PBM services will be released in the middle of June. The current contract ends June 30, 2016.

The Patient Centered Medical Home project has been implemented with four practices currently enrolled and participating.

The Hepatitis C prior authorization criteria will be updated to require a hepatitis B test no more than 30 days prior to the request. In addition, a patient form acknowledging the prescribed treatment and that Medicaid will only pay for one treatment per lifetime will be added to the prior authorization form.

The Committee did not find evidence of safety or efficacy advantages with Mircera versus the existing epoetin products. The Department of Health will conduct a cost analysis and determine its coverage relative to the existing products.

Movantik and Relistor will require the diagnosis of opioid-induced constipation and a three month trial of a secretory agent prior to approval.

Cholbam will be limited to its indication.

Cosentyx was determined to have evidence of safety and efficacy benefits over Enbrel for plaque psoriasis. The Department of Health will conduct a cost analysis and determine placement on the Preferred Drug List.

The utilization of duplicate antidepressants was reviewed and discussed. Prior authorization will be required for concurrent use. Exceptions to this rule will include trazodone, tricyclic antidepressants and SSRIs with bupropion or mirtazapine.

The proposed prior authorization criteria will be posted for public comment at www.uwyo.edu/DUR. Comments may be sent by email to alewis13@uwyo.edu or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to June 30, 2015 for prior authorization criteria.

The next P&T Committee meeting will be held August 13, 2015 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

New Drug Review: Possible P & T Committee Decisions

1. New drug, no other drugs for indication.
 - a. Take no action
 - b. Limit to approved indication
2. New drug, other drugs previously approved for indication. Class is not currently managed.
 - a. Take no action
 - b. Limit to approved indication
 - c. Efficacy or safety concerns? Require trial and failure of existing drugs or require a hard prior authorization.
 - d. Cost concerns? Make recommendation based on efficacy and safety and request that the Department of Health make final decision based on cost net rebate.
- e. Add entire class to the Preferred Drug List
- f. Do other drugs in the class need similar PA criteria? For instance, should they all be limited to indication?
3. New drug, current PDL class.
 - a. Recommendation regarding comparative safety and efficacy of new drug vs. existing drugs in class. If available evidence suggests no difference between new drug and existing drugs, Department of Health will make final decision regarding PDL placement after cost analysis. If there is clear superiority in safety or efficacy to all other agents in the class, cost will not be a factor.

Newer Agents, continued

It is believed that lorcaserin selectively activates serotonin receptors in the hypothalamus to decrease caloric intake and enhance satiety.⁴ Due to this serotonergic activity, the risk for serotonin syndrome exists and precaution should be used in patients with cardiovascular and psychiatric disorders. In clinical trials, the most common adverse events leading to treatment discontinuation included headache, depression, and dizziness. The percentage of patients losing at least five percent of total body weight in trials of this medication ranged from 37.5-47.1% versus 16.1-22.6% with placebo.⁴

Contrave is a combination of the aminoketone antidepressant bupropion and the opioid antagonist naltrexone.⁵ These two ingredients are thought to exert effects on the hypothalamus and limbic system to regulate appetite and feelings of reward, respectively. Nausea occurs in almost a third of patients, and it does have a black box warning for suicidality due to the bupropion component. It should not be used in patients taking chronic opioids or those who have recently used MAOIs, and caution should be used in patients with a history of seizures, heart or liver disease, and bipolar disorder. The percentage of patients losing at least five percent of total body weight in 56 week trials of the medication ranged from 36-57% versus 17-43% with placebo.⁵

Qsymia is a combination product containing the sympathomimetic amine, phentermine, which leads to increased catecholamine release in the hypothalamus, and topiramate which appears to suppress appetite and promote satiety.⁶ Common adverse reactions to this agent include paraesthesia, dizziness, distortion of taste, and insomnia, and occur in a dose-dependent manner. Warnings and precautions for this medication exist due to elevated heart rate, sleep and mood disorders including suicidality, and metabolic acidosis due to inhibition of carbonic anhydrase by topiramate. Between 45% and 62% of patients lost at least five percent of body weight on lower doses of this combination agent versus placebo and 67-70% of patients experienced the same degree of weight loss on higher doses.⁶

Liraglutide is an injectable glucagon-like peptide-1 receptor agonist that helps regulate appetite and food intake.⁷ This medication is also used at lower doses under the brand name Victoza® to improve glycemic control in patients with type 2 diabetes. The most commonly occurring adverse reactions with this medication are related to GI

upset with nausea occurring in 39.3% of patients. Animal studies have detected malignant thyroid C-cell carcinomas with clinically relevant exposures of liraglutide, but human relevance of this data is yet unknown. Patients should be educated on symptoms of thyroid tumors, and symptomatic patients may need further evaluation of serum calcitonin or thyroid ultrasound. All patients should also be monitored for pancreatic and gallbladder disease, increases in heart rate, hypersensitivity, and suicidality. This agent does decrease gastric emptying time which may affect some oral medications. Three 56 week trials have shown the percentage of patients losing at least five percent of body weight ranging from 44.2-62.3% with liraglutide versus 16.4-34.4% with placebo.⁷

Therapeutic lifestyle change is still considered first line therapy for patients struggling with issues of weight. However, medications can be useful in facilitating weight loss and weight management in patients who do not succeed in doing so with lifestyle changes alone. These agents primarily act on areas of the brain and GI tract to help regulate caloric intake by affecting aspects of appetite and satiety. When used in conjunction with diet and exercise, these agents have been shown to increase weight loss over placebo. Helping patients with comorbid conditions maintain a healthy weight may be particularly important from a secondary prevention standpoint, but weight loss may be considered a primary prevention measure in overweight and obese patients without complications.

References:

¹ Bray GA. Obesity in adults: etiology and natural history. In: Pi-Sunyer FX, Mulder JE (eds). UpToDate Online. Waltham (MA):UpToDate; 2015. Available from: <http://www.uptodate.com>. Accessed: March 4, 2015.

² Bray GA. Obesity in adults: drug therapy. In: Pi-Sunyer FX, Mulder JE (eds). UpToDate Online. Waltham (MA):UpToDate; 2015. Available from: <http://www.uptodate.com>. Accessed: March 4, 2015.

³ Hu FB, Li TY, Colditz GA, Willett WC, Manson JE. Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA* 2003;289:1785-1791.

⁴ BELVIQ- lorcaserin hydrochloride hemihydrate tablet [package insert]. Woodcliff Lake (NJ): Eisai, Inc. 2014 December.

⁵ CONTRAVE- naltrexone hydrochloride and bupropion hydrochloride tablet, film coated, extended release [package insert]. Deerfield (IL): Takeda Pharmaceuticals America, Inc. 2014 September.

⁶ QSYMIA- phentermine hydrochloride and topiramate capsule, extended release [package insert]. Mountain View (CA): Vivus, Inc. 2014 September.

⁷ SAXENDA- liraglutide injection, solution [package insert]. Plainsboro (NJ): Novo Nordisk. 2015 January.

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In This Issue

**Newer Agents to Facilitate Weight Loss or
Weight Management in Overweight or Obese Patients**

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P&T Committee Meeting Update

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New Drug Review: Possible P & T Committee Decisions

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