continuing education for pharmacists

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Obesity: Treatment Guidelines and Update on Use of Belviq and Qsymia

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Dr. Mona T. Thompson has no relevant financial relationships to disclose.

Goal. The goal of this lesson is to provide a disease state overview of obesity and summary of newly released treatment recommendations. Two newly approved weight loss medications, Belviq® (lorcarserin) and Qsymia® (phentermine and topiramate), as well as orlistat (alli®, Xenical®) will be discussed in the role of chronic weight management with the inclusion of unique Ohio law requirements for prescribing these medications.

Objectives. At the completion of this activity, the participant will be able to:

1. recognize the epidemiology, etiology, risk factors, diagnostic criteria and associated long-term health consequences of obesity;
2. demonstrate an understanding of the role that anti-obesity medications play in weight loss and when they are appropriate;
3. demonstrate an understanding of the pharmacology, FDA-approved indications and key prescribing points for the weight loss medications, Belviq and Qsymia; and
4. identify the State Medical Board of Ohio Rules for prescribing controlled substances for weight reduction.

Background

Obesity, a state of excess storage of body fat, is a serious and costly public health crisis in the United States. Most recent data indicate that 69 percent of adults are either overweight or obese. Approximately half of these adults are obese, along with 17 percent of youths. This correlates with approximately 78 million adults over the age of 20 years and 12.5 million children and adolescents. While the prevalence remains high, analysis from the 2011-2012 National Health and Nutrition Examination Survey (NHANES) indicates that the increase has slowly stabilized or leveled off since 2003-2004 data. In June 2013, the American Medical Association officially recognized obesity as a disease.

Obesity affects some groups more than others. Non-Hispanic blacks have the highest age-adjusted rates of obesity (47.8 percent) followed by Hispanics at (42.5 percent), non-Hispanic whites (32.6 percent) and non-Hispanic Asians (10.8 percent). Additionally, obesity is higher among middle-aged adults, 40- to 59-years-old (39.5 percent), than among younger adults, age 20 to 39 (30.3 percent), or adults age 60 or above (35.4 percent).

Differences in prevalence are also observed among socioeconomic groups. Among non-Hispanic black and Mexican-American men, those with higher incomes are more likely to be obese than those with low income. Women with a higher income or those with college degrees are less likely to be obese when compared to women with lower income or less education. No significant relationship between obesity and education among men has been established. Obesity prevalence also varies across states and regions.

Higher rates of adult obesity were self-reported in 2012 for the Midwest (29.5 percent) and South (29.4 percent) regions of the United States, including Ohio at 30.1 percent.

In addition to ethnicity, race, and socioeconomic status, other risk factors may contribute to obesity. These include genetics, family lifestyle, physical inactivity, unhealthy diet and eating habits, quitting smoking, lack of sleep, certain medications, age, and pregnancy. Genetic and environmental factors appear to be intertwined. In addition to genetics, obesity that runs in families is also due to their similar eating, lifestyle, and activity habits. Reduced physical activity may currently be the most important factor in the recent rise in obesity. In the United States, less than half of all adults meet the Federal 2008 Physical Activity Guidelines, and fewer than three in 10 high school students get at least 60 minutes of physical activity every day. Medications that are associated with weight gain include some antidepressants, anti-epileptics, anti-glycemics, antipsychotics, steroids, and beta-blockers. Hence, the etiology of obesity is much more complex than a simple imbalance

Table 1
Obesity terminology

Definitions*

Grade 1 overweight (*overweight*): BMI of 25 to 29.9 kg/m^2

Grade 2 overweight (*obesity*): BMI of 30 to 39.9 kg/m^2

Grade 3 overweight (*severe* or *morbid obesity*): BMI >40 kg/m^2

Equations

BMI = weight(kg)/height(m^2)

Body fat percentage = 1.2(BMI) + 0.23(age in years) – 10.8(sex**) – 5.4

*According to the World Health Organization
**Sex = 1 for males and 0 for females

between energy intake and energy output.

Various indices are used to measure obesity, such as body fat percentage, skin thickness, waist or hip circumference, waist-hip ratio, and body mass index (BMI). The BMI typically correlates closely with body fat (except at lower BMIs). According to the 1998 Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults Evidence Report, *overweight* is defined as a BMI of 25 to 29.9 kg/m^2 and *obesity* as a BMI of ≥30 kg/m^2. *Severe* or *morbid obesity* is reserved for patients with a BMI >40 kg/m^2. Other experts define obesity based on the percentage of body fat present.

Healthy men have a body fat percentage of 15 to 20 percent, while healthy women have approximately 25 to 30 percent. For men, body fat greater than 25 percent defines *obesity*, with 21 to 25 percent considered borderline. For women, over 33 percent defines *obesity*, with 31 to 33 percent termed borderline. Table 1 contains the World Health Organization's accepted definitions of *obesity*, as well as the equations to determine BMI and body fat.

Overweight and obesity are major contributors to chronic disease in the U.S., and present a major public health challenge. Obesity raises the risk of morbidity from hypertension, dyslipidemia, type 2 diabetes mellitus, coronary heart disease, stroke, gallbladder disease, osteoarthritis, sleep apnea, respiratory problems, and some cancers. For a person with a BMI of 25 to 28.9 kg/m^2, the relative risk for coronary heart disease is 1.72, with a risk that progressively increases with increasing BMI. Individuals with BMIs greater than 33 kg/m^2 have a relative risk of 3.44. Overall, obesity is estimated to increase the cardiovascular mortality rate four-fold and the cancer-related mortality rate two-fold. Additionally, data indicate that pre-pregnancy maternal obesity appears to be a major risk factor for stillbirth.

The annual cost of managing obesity in the United States alone amounts to approximately $190 billion per year, or 20.6 percent of national health expenditures. A 2005 study conducted by Cawley and Meyerhoefer found that when compared with a non-obese person, an obese person incurs $2,741 more in annual medical costs. Additionally, a study conducted by Finkelstein *et al*. concluded that the cost of obesity among U.S. full-time employees is estimated to be $73 million including the cost of medical care, lost productivity, and absenteeism. Almost $121 billion is spent annually on weight-loss products and services.

Overview of Treatment Guidelines for Obesity

In 2013, updated guidelines for the treatment of obesity were released by the American Heart Association (AHA), American College of Cardiology (ACC) and The Obesity Society (TOS) urging physicians to consider obesity as a disease and actively treat patients for weight loss. The new guidelines were designed to address critical issues on overweight and obesity evaluation and treatment that are encountered in the primary care setting. While not discussed in this review, the issues are: 1) appropriateness of the current BMI and waist circumference cut points used to determine risk in overweight and obese adults across diverse populations; 2) impact of weight loss on risk factors for cardiovascular disease (CVD) and type 2 diabetes, as well as CVD morbidity and mortality; 3) optimal behavior, dietary intervention strategies, and other lifestyle treatment approaches for weight loss and weight loss maintenance; and 4) benefits and risks of various bariatric surgical procedures.

Critical questions that the Expert Panel did not examine include consideration of genetics in obesity, binge-eating disorders, pharmacotherapy, and cost effectiveness of interventions to manage obesity. While drug therapy was not a focus of the 2013 update, the Expert Panel did include the consideration of anti-obesity medication in the treatment algorithm.

The result of the Panel's work includes a treatment algorithm which strongly recommends counseling overweight and obese adults regarding CV risk and lifestyle changes that can produce meaningful health benefits; prescribing a weight loss diet; and participating in a comprehensive lifestyle program with trained interventionists. If the patient has been unable to lose weight or sustain weight loss with comprehensive lifestyle intervention and he/she has a BMI >30 kg/m^2 or >27 kg/m^2 with comorbidity, adjunctive therapies may be considered. Based on expert opinion, the panelists recommend that for individuals with BMI >30 or BMI >27 kg/m^2 with at least one obesity-associated comorbid condition who are motivated to lose weight, pharmacotherapy can be considered as an adjunct to comprehensive lifestyle intervention to help achieve targeted weight loss and health goals. Furthermore, the potential risks of medication should be considered against the potential benefits of successful weight loss.

The rationale for medication

use is to help patients adhere to a lower calorie diet more consistently in order to achieve sufficient weight loss and health benefits, when combined with increased physical activity. Medications work to reinforce lifestyle change and should be prescribed as an adjunct to lifestyle interventions. Bariatric surgery is also listed as an option for adjunctive therapy.

The guidelines also provide evidence statements (ES) serving as a basis for treatment recommendations to be used by clinicians evaluating and treating patients with obesity. All health care professionals can appreciate the level of evidence indicating that weight loss is associated with a positive impact on the risk of diabetes, hyperlipidemia, and hypertension — disease states which are predominantly treated with medications. Table 2 lists select evidence statements extracted from the guideline. These statements support the drive to treat obesity and improve the health of the U.S. population.

Both the Full Panel Report (http://www.nhlbi.nih.gov/guidelines/obesity/ser/) and Guideline (http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437739.71477.ee.full.pdf) are accessible online and are free of charge.

Anti-Obesity Medication Therapy

The goal of anti-obesity medication is to utilize a safe and effective agent in combination with diet and exercise to achieve a meaningful and substantial reduction in body weight. In order for medications to achieve FDA approval, the difference in mean weight loss between the drug and the placebo groups is at least 5 percent for at least one year and statistically significant. In addition, the proportion of subjects who lose at least 5 percent of baseline body weight in the active product group is at least 35 percent, and is approximately double the proportion in the placebo-treated group. Finally, the studied obese population must be heterogeneous with variations in degree and duration of overweight, age, and associated comorbidities so that it translates to a true representation and meaningful results. Agents must also possess an acceptable safety profile.

Several agents were previously approved and used for weight loss, but have since been removed from the market in the U.S. due to safety issues. A combination of the amphetamine analogs fenfluramine and phentermine, commonly referred to as Fen-Phen, was very effective and popular in the 1990s. Fenfluramine (Pondimin) and its relative compound, dexfenfluramine (Redux), were withdrawn from the U.S. market secondary to pulmonary hypertension and valvular heart disease. Phentermine (Adipex) remains available for short term use (defined as 12 weeks). When used alone, it rarely causes valvular disease.

Phenylpropanolamine was widely used for many years as a nasal decongestant in over-the-counter (OTC) and prescription drug products, as well as OTC for weight control. In 2000, FDA issued a public health advisory concerning phenylpropanolamine secondary to a study indicating that its use was associated with an increased risk of hemorrhagic stroke. Consumers were advised to avoid any products containing phenylpropanolamine. FDA requested that all drug companies discontinue the marketing of any product containing phenylpropanolamine.

Finally, sibutramine (Meridia) was shown to pose unnecessary cardiovascular risk in a post-marketing trial and was voluntarily withdrawn in 2010, 13 years after its initial approval in 1997.

Due to stringent criteria, only three agents are currently approved by FDA as adjunctive therapy for chronic weight management: orlistat (alli, Xenical), approved in 1999; lorcaserin (Belviq), approved in 2012; and phentermine/topiramate extended-release formulation (Qsymia), approved in 2012. These three agents will be discussed further in the next section of this lesson. Table 3 summarizes key prescribing points for these agents. Short-term sympathomimetic amines and medications used off-label for the treatment of obesity will not be discussed in this lesson.

Table 2
Select Evidence Statements (ES) from the 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults

1. In overweight and obese adults at risk for type 2 diabetes, average weight loss of 2.5 to 5.5 kg at >2 years, achieved with lifestyle interventions (with or without orlistat) reduces the risk of developing type 2 diabetes by 30 to 60 percent.

2. In overweight and obese adults with type 2 diabetes, those who achieve greater weight loss at 1 year with lifestyle intervention (with or without orlistat) have greater improvements in HbA1c. Weight loss of 5 to 10 percent is associated with HbA1c reductions of 0.6 to 1.0 percent and reduced need for diabetes medications.

3. In overweight and obese adults with type 2 diabetes, orlistat compared to placebo, both with lifestyle interventions, results in 2 to 3 kg greater weight loss at 1 and 2 years. The addition of orlistat is associated with greater reductions in fasting blood glucose averaging 11 and 4 mg/dL at 1 and 2 years, respectively, as well as an average greater reduction in HbA1c of 0.4 percent at 1 year.

4. In overweight and obese adults with or without elevated CVD risk, there is a dose-response relationship between the amount of weight loss achieved by lifestyle intervention and the improvement in lipid profile.

5. In overweight and obese adults with elevated CVD risk (including type 2 diabetes and hypertension), there is a dose-response relationship between the amount of weight loss achieved at up to 3 years by lifestyle intervention (alone or combined with orlistat) and the lowering of BP.

Table 3
Medications approved for chronic weight management

Medication	Dosage Form	Usual Daily Dose	Common ADRs	Key Points
Orlistat (Xenical)	120 mg capsule	120 mg TID	oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, fecal incontinence	•take with multivitamin at bedtime •non-controlled •total daily diet should include approximately 30 percent calories from fat
Orlistat (alli)	60 mg capsule	60 mg TID		
Lorcaserin (Belviq)	10 mg tablet	10 mg BID	*Non diabetic:* headache, dizziness, fatigue, nausea, dry mouth, and constipation *Diabetic:* hypoglycemia, headache, back pain, cough, and fatigue	•Discontinue use if 5 percent weight loss not achieved at 12 weeks •Cognitive impairment, psychiatric disorders, or valvular heart disease may occur •Caution with other serotonergic drugs
Phentermine/ Topiramate (Qsymia)	3.75 mg/23 mg 7.5 mg/46 mg 11.25 mg/69 mg 15 mg/92 mg extended-release capsules	7.5 mg/46 mg to 15 mg/ 92 mg once daily	paresthesia, dizziness, dysgeusia, insomnia, constipation, dry mouth	•Discontinue use if 5 percent weight loss not achieved at 12 weeks on max dose •Monitor heart rate •Monitor for sleep or mood disorder •Cognitive impairment may occur •REMS program to reduce fetal risk

Orlistat

Orlistat is not a stimulant or controlled substance, rather a gastrointestinal lipase inhibitor. It was approved by FDA in 1999 as Xenical, and then again in 2007 in an OTC reduced-dose formulation marketed as alli. Orlistat remains the only anti-obesity drug approved by the European Medicines Agency (EMA). This unique agent works by binding and inhibiting lipases that are produced by the pancreas and stomach which act in the small intestine to break down dietary triglycerides into free fatty acids. The fatty acids are then absorbed via fatty acid transporters. Hence, orlistat's inhibition of lipases reduces systemic fat absorption. Orlistat is indicated for chronic obesity management when used in conjunction with a reduced-calorie diet. Xenical is prescribed as 120 mg three times a day, with each main meal containing fat (during or up to one hour after the meal). Patients are advised to intake a nutritionally balanced, reduced-calorie diet that contains approximately 30 percent of calories from fat. Alternatively, alli is dosed at 60 mg three times a day with meals containing 15 grams of fat.

In order to ensure adequate absorption of fat soluble vitamins (A, D, E, K, and beta-carotene), individuals taking orlistat should be advised to take a multivitamin once a day at bedtime. The product labels suggest distributing the daily intake of fat, carbohydrate, and protein over three main meals. It is recommended that no more than three capsules be taken each day, as higher dosage studies indicate that it is unlikely to provide better results.

A Cochrane Collaboration review examining the long-term pharmacotherapy for obesity and overweight included 16 double-blind, randomized, placebo-controlled trials of one to four years in duration of orlistat use. The review concluded that orlistat was associated with modest efficacy (<5 kg weight loss) and reduced the number of high-risk patients who developed diabetes.

The most common adverse reactions of orlistat (>5 percent and at least double that of placebo) include oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, increased defecation and fecal incontinence. Gastrointestinal events may increase when Xenical is taken with a diet high in fat (>30 percent total daily calories from fat). In 2010, FDA approved a revised label for Xenical and alli to include safety information about cases of severe liver injury that had been rarely reported with the use of this medication. At the time of the drug safety communication in 2010, only 13 cases of severe liver injury had been reported among an estimated 40 million people who had used the medication worldwide. Therefore, a definite cause and effect relationship has not been established. However, it is important to be aware of post-marketing reports and to inform patients to report any symptoms of

hepatic dysfunction such as anorexia, pruritus, jaundice, dark urine, light colored stools, or right upper quadrant pain. Other risks of therapy include acute pancreatitis, acute renal failure, and precancerous colon lesions. Due to orlistat's non-scheduled status and safety profile, it is exempt from the Ohio Medical Board rules discussed later in this lesson.

Belviq

Lorcaserin hydrochloride (Belviq), a schedule IV controlled substance, was approved in 2012 as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial BMI of >30 kg/m^2, or >27 kg/m^2 in the presence of at least one weight-related comorbid condition (hypertension, dyslipidemia, type 2 diabetes). The dosage is 10 mg twice daily, with the caveat that use should be discontinued if 5 percent weight loss is not achieved by week 12. These patients are unlikely to achieve clinically meaningful weight loss with continued treatment.

Lorcaserin is a selective 5-HT_{2c} receptor agonist promoting anorexigenic effects and satiety through the serotonin receptor activation. Lorcaserin exhibits preferential affinity to 5-HT_{2c} in comparison to other 5-HT receptor subtypes. This selective activation limits the risk of hallucinations due to 5-HT_{2a} activation and the risk of cardiovascular side effects including valvulopathy and pulmonary hypertension through 5-HT_{2b} receptors.

The most common adverse events in non-diabetic patients include headache, dizziness, fatigue, nausea, dry mouth, and constipation. In diabetic patients, hypoglycemia, headache, back pain, cough, and fatigue are reported. Potential life-threatening serotonin syndrome or neuroleptic malignant syndrome-like reactions may occur when taken with other serotonergic or antidopaminergic agents. Other warnings or precautions in the product label include valvular heart disease; cognitive impairment; psychiatric disorders including euphoria and dissociation; hypoglycemia associated with weight loss; and priapism.

Approval of lorcaserin was based on three randomized double-blind trials, at least 52 weeks in length, in obese and overweight adults. The BLOSSOM and BLOOM trial reported at least 5 percent weight loss by 47.2 percent and 47.5 percent of the participants in the locaserin 10 mg twice daily group, compared to 25 percent and 20.3 percent in the placebo groups, respectively. The BLOOM-DM study differed in that it enrolled patients with a diagnosis of type 2 diabetes treated only with either metformin and/or a sulfonylurea. The proportion of patients achieving at least a 5 percent weight loss was 38 percent in the lorcaserin 10 mg twice daily group, compared to 16 percent in the placebo group. The average weight loss in clinical trials was 5.5 kg. The effect of locaserin on cardiovascular morbidity and mortality has not yet been determined.

Qsymia

Phentermine and topiramate extended-release (Qsymia) was approved in 2012, and is a schedule IV controlled substance approved for adjunct treatment of obesity under the same circumstances as Belviq. Phentermine is a sympathomimetic amine that has been available in the U.S. since 1959 for short-term management of obesity. Its mechanism of action is believed to be dependent on modulation of catecholamines in the satiety centers of the hypothalamus, thus reducing appetite. Topiramate, previously approved by FDA and primarily used to treat seizure disorders and migraines, was observed to produce weight loss. The exact mechanism by which topiramate regulates appetite and induces weight loss is unknown. However, significant clinical evidence exists to support its use as an anti-obesity drug.

The recommended initial dose is phentermine 3.75 mg/topiramate 23 mg XR once daily in the morning for 14 days, followed by 7.5 mg/46 mg daily. The dosage may be escalated if 3 percent weight loss is not achieved after 12 weeks on 7.5 mg/46 mg dose in 14-day increments to a maximum dose of 15 mg/92 mg. Qsymia should be discontinued if 5 percent weight loss is not achieved after 12 weeks on the maximum dose. Discontinuation should occur gradually, as abrupt withdrawal of topiramate can cause seizures, even in patients with no history of epilepsy. Patients with moderate or severe renal impairment or patients with moderate hepatic impairment should not exceed 7.5 mg/46 mg daily dose.

Qsymia is contraindicated in pregnancy, patients with glaucoma or hyperthyroidism, during or within 14 days of taking monoamine oxidase inhibitors, or known hypersensitivity or idiosyncrasy to sympathomimetic amines. The most common adverse reactions (greater than and at least 1.5 times placebo) are paraesthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth. Other warnings and precautions in the product label include: monitoring heart rates in all patients; acute myopia and secondary angle closure glaucoma, mood or sleep disorders, cognitive impairment, elevated creatinine, and weight loss may cause hypoglycemia with anti-diabetic medications. Because topiramate is a carbonic anhydrase inhibitor, metabolic acidosis and kidney stones can occur. Antiepileptic drugs, including topiramate, have been reported to increase the risk of suicide ideation and behavior. Qsymia is available through a limited program under a Risk Evaluation and Mitigation Strategy (REMS).

Qsymia was approved based on two 56-week trials in which patients were randomized to placebo or to one of two doses of phentermine/topiramate. Results for the EQUIP trial at one year are as follows: 44.9 percent of patients taking the 3.75 mg/23 mg dose achieved at least 5 percent weight

loss, compared to 66.7 percent taking 15 mg/92 mg and 17.3 percent in the placebo group. The same primary endpoint was utilized in the CONQUER trial which reported 62 percent in the 7.5 mg/46 mg group versus 70 percent in the 15 mg/92 mg group, and finally 21 percent in the placebo group. The data indicate that Qsymia may be more effective than lorcaserin, but may cause more troublesome adverse effects.

Ohio Rules for Prescribing and Dispensing Qsymia and Belviq

Qsymia and Belviq are FDA-approved schedule IV medications designed for chronic weight management in adults, and have potential for abuse or dependence. These agents have different restrictions regarding their prescribing for weight reduction in comparison to short-term weight reduction products like phentermine. The laws and rules regarding the use of controlled substances for weight reduction are found in the State Medical Board of Ohio section of the Ohio Administrative Code. Medical Board Rule 4631-11-04, Ohio Administrative Code (OAC), *Controlled substances: Utilization for weight reduction*, governs the use of schedules III and IV controlled substances to assist in weight loss. The rules can be found at http://codes.ohio.gov/oac/4731-11. These rules, as well as posted Q&A attachment to the rule, will be summarized in the next section of this lesson. Pharmacists are encouraged to access these documents for full prescribing guidance set forth by the Medical Board.

In general, before the decision to utilize weight loss medications, the physician must determine that the patient has made a good-faith effort to lose weight through a treatment program (caloric restriction, nutritional counseling, behavior modification, and exercise) that has been unsuccessful. In addition, the physician must decide if the patient meets the FDA requirements for prescribing controlled substances for weight loss through a physical examination and a thorough medical and social history. The physician must also evaluate and document that the patient has no signs of drug or alcohol abuse, or contraindications to the medication.

If the physician decides to begin treatment, the physician must meet with the patient face-to-face at least every 30 days to continually reassess and re-evaluate response to treatment. At every visit, the physician must document that the patient is demonstrating continual efforts to lose weight, dedicated to the treatment program and showing progress. The presence or absence of contraindications, adverse effects, and indicators of possible substance abuse must also be documented at these visits. A physician may only utilize a schedule III or IV controlled substance for purposes of weight reduction if it has an FDA-approved indication for this purpose.

The 12-week treatment limitation enforced for short-term weight loss agents (i.e., phentermine) does not apply to Qsymia and Belviq as they carry FDA-approval for chronic weight management. Patients may be switched to one of these two new drugs after completing 12 weeks on phentermine (or earlier), as long as there has been no interruption in treatment (defined as <7 days). Or, the patient may be switched to one of the two new drugs if treatment is interrupted for more than seven days due to one of the reasons outlined in OAC 4731-11-4(C)(3). If treatment was interrupted for over seven days for any other reason than listed, the patient may not begin treatment with one of these agents until six months after the last date the physician prescribed phentermine. Further, Rule 4731-11-04(C)(3) provides that except for specified situations, a physician may not initiate treatment for weight loss with a controlled substance if the patient has received controlled substances for weight loss within the last six months. The date the patient filled the last prescription is day 1 of the six-month period during which the physician may not initiate a course of treatment using a controlled substance for weight loss.

The Ohio Medical Board also provides guidance on how Qsymia prescriptions, in regard to dosing titrations, should be written. Essentially, each time a titration is to occur in 14 days, it is recommended that the patient return to the office for a new prescription for the increased dose. There is no explicit prohibition of refills on Qsymia or Belviq in the rule; however, it is strongly discouraged as this will deter patients from meeting face-to-face with their physician every 30 days. A refill on such a prescription would be appropriate as long as the day supply does not exceed 30 days. For instance, a prescription for Qsymia 7.5 mg/46 mg, #15, with one refill is acceptable. Physicians are discouraged from writing multiple prescriptions with the notation, "Do not fill before ___," as this will deter the visit and mandatory evaluation as well. There is no limit on the amount of time a patient can be on Qsymia or Belviq, as long as the physician is complying with required monitoring and documentation.

The physician shall discontinue utilizing these therapies if he/she ascertains or has reason to believe that the patient has a history or shows propensity for alcohol or drug abuse; has made any false or misleading statements regarding such use; the patient fails to lose weight while under treatment; or the patient fails to comply with treatment recommendations. Schedule III or IV controlled substances for weight reduction are prohibited during pregnancy.

Pharmacist Role in Dispensing Controlled Substances for Obesity

While the Medical Board has imposed stringent rules upon physicians prescribing such therapies, the pharmacist also has a corresponding responsibility to

ensure that these medications are prescribed for a legitimate medical purpose. Pharmacists who have concern, or question the legitimacy of these prescriptions, should contact the physician, discuss the patient's case with him/her, and document the conversation. If concern remains regarding legitimacy of medical purpose, the pharmacist may refuse to fill the prescription. Additionally, pharmacists cannot accept a prescription written by Advanced Practice Nurses (APNs) or Physician Assistants (PAs) as they are not authorized to prescribe any of the controlled substances for weight reduction.

Pharmacists may also request an Ohio Automated Rx Reporting System (OARRS) report on a patient to determine if the prescription is for a legitimate medical purpose. An OARRS report will identify any other controlled substances for weight reduction that a patient may have filled at any other pharmacy. Such information can be used to calculate duration of therapy for short-term agents, calculate a six-month break if required, and establish if a gap greater than seven days may have occurred and requires justification.

Pharmacists are not required to document that the patient is losing weight or to calculate the BMI. However, he/she should use professional judgment in dispensing the agent if it is apparent that the patient does not meet the BMI requirements.

Summary

In conclusion, obesity is a serious disease endangering the public health of the U.S. population and resulting in serious morbidity and mortality. Clinical trials suggest that even modest weight loss correlates with a reduction in the risk of developing diabetes, as well as improved glucose control, blood pressure control, and lipid profile. Anti-obesity therapy may be a suitable adjunct treatment to help patients who are unable to reach weight loss goals. Qsymia and Belviq are two agents, in addition to orlistat, that may be used for chronic weight management. When these medications are prescribed, physicians and pharmacists together have an obligation to not only ensure that patients are counseled on the potential adverse effects, but also that they are dispensed in accordance with Ohio rule.

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The author, the Ohio Pharmacists Foundation and the Ohio Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein. Bibliography for additional reading and inquiry is available upon request.

This lesson is a knowledge-based CE activity and is targeted to pharmacists in all practice settings.

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continuing education quiz

Obesity: Treatment Guidelines and Update on Use of Belviq and Qsymia

1. Which of the following groups has the highest age-adjusted rates of obesity?
   a. Hispanics
   b. Non-Hispanic whites
   c. Non-Hispanic blacks
   d. Non-Hispanic Asians

2. According to the 1998 Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults, *overweight* is defined as a:
   a. BMI 25 to 29.9 kg/m^2.
   b. BMI >30 kg/m^2.
   c. BMI >40 kg/m^2.

3. Due to safety issues, all of the following products have been withdrawn from the market EXCEPT:
   a. phentermine.
   b. fenfluramine.
   c. dexfenfluramine.
   d. sibutramine.

4. Orlistat is a/an:
   a. carbonic anhydrase inhibitor.
   b. sympathomimetic amine.
   c. selective 5-HT$_{2c}$ receptor agonist.
   d. gastrointestinal lipase inhibitor.

5. Individuals taking orlistat should be advised to:
   a. monitor heart rate.
   b. watch for cognitive impairment.
   c. take a multivitamin once daily at bedtime.
   d. take with caution with other serotonergic drugs.

6. FDA revised the labeling of orlistat products to include safety information relating to:
   a. renal impairment.
   b. liver injury.
   c. CNS impairment.
   d. cardiac function.

7. The dosage of lorcaserin is:
   a. 120 mg TID.
   b. 92 mg once daily.
   c. 60 mg TID.
   d. 10 mg BID.

Completely fill in the lettered box corresponding to your answer.

1. [a] [b] [c] [d]	6. [a] [b] [c] [d]	11. [a] [b] [c] [d]
2. [a] [b] [c]	7. [a] [b] [c] [d]	12. [a] [b]
3. [a] [b] [c] [d]	8. [a] [b] [c] [d]	13. [a] [b] [c] [d]
4. [a] [b] [c] [d]	9. [a] [b] [c] [d]	14. [a] [b] [c] [d]
5. [a] [b] [c] [d]	10. [a] [b] [c] [d]	15. [a] [b] [c] [d]

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8. Common adverse reactions with lorcaserin include:
   a. insomnia.
   b. fatigue.
   c. diarrhea.
   d. seizures.

9. The average weight loss in lorcaserin clinical trials was:
   a. 5.5 kg.
   b. 8.3 kg.
   c. 10.0 kg.
   d. 12.2 kg.

10. Abrupt withdrawal of topiramate may cause:
    a. tachycardia.
    b. hypotension.
    c. seizures.
    d. fecal incontinence.

11. Qsymia is contraindicated in all of the following conditions EXCEPT:
    a. pregnancy.
    b. glaucoma.
    c. hyperthyroidism.
    d. hypertension.

12. Which of the following active ingredients of Qsymia is associated with suicide ideation and behavior?
    a. Topiramate
    b. Phentermine

13. In order for a physician to prescribe controlled substances for chronic weight loss, he/she must see the patient face-to-face every:
    a. 15 days.
    b. 30 days.
    c. 60 days.
    d. 90 days.

14. If treatment with phentermine is interrupted for more than seven days, treatment with Belviq or Qsymia may not begin until how many months after the last date the physician prescribed phentermine?
    a. One month
    b. Three months
    c. Six months
    d. 12 months

15. All of the following statements are true for pharmacists dispensing controlled substances for obesity EXCEPT:
    a. the pharmacist should document conversations with the patient's physician.
    b. the pharmacist may refuse to fill the prescription if concerned about the legitimacy of medical purpose.
    c. an OARRS report will help the pharmacist determine if the prescription is for a legitimate medical purpose.
    d. the pharmacist must document patient's weight loss during therapy.

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