Osteopathic Family Physician (2013) 5, 90–91

ELSEVIER

acofp Osteopathic Family Physician

An update on weight-loss medications

To the Editor:

This is an update to the article published in September/October 2012th issue of *Osteopathic Family Physician* entitled "Diabetes obesity: Link how to lower your risk of diabetes with weight management." As that article was originally submitted to osteopathic family physicians, there have been updates on the weight-loss medications. The Food and Drug Administration (FDA) recently approved 2 new drugs as adjuncts to a reduced calorie diet and increased physical activity for long-term weight management in adults who are obese (defined as having a body mass index >30) or overweight (body mass index >27) with at least 1 weight-related coexisting condition.

Belviq (lorcaserin, Arena pharmaceuticals) is the selective agonist of the serotonin (5-hydroxytryptamine) 2C (5-HT_{2C}) receptor.[1] Qsymia (phentermine plus extended-release topiramate, Vivus) is a fixed-dose combination of a sympathomimetic amine, phentermine, which is an anorectic agent, and the antiepileptic drug topiramate.[2] Both medications reduce appetite and in some people induce a negative energy balance.

Both drugs produced meaningful weight loss as defined by the FDA criteria[3] in the 1-year placebo-controlled clinical trials in which all participants received instruction in lifestyle modification. Compared with placebo, both drugs showed favorable changes in cardiometabolic factors, eg, blood pressure, waist circumference, and cholesterol levels. Both drugs also improved hemoglobin A1 C in overweight and obese patients with type II diabetes.

Belviq (lorcaserin)

It is a selective agonist of the 5-HT_{2C} serotonin receptor. At clinically effective doses Belviq does not activate the 5-HT_{2B} receptor, which appears to be the receptor primarily responsible for the cardiac valvular disease associated with fenfluramine. In 1997, fen-phen was withdrawn because fenfluramine caused heart valve damage. This effect is assumed to be related to activation of 5-HT_{2B} receptor on the heart tissue. When used at the approved dose of 10 mg twice a day, Belviq does not appear to activate the 5-HT_{2B} receptor.

In clinical trials of 1-year duration, echocardiographic criteria for valvular regurgitation doubled up for 2.4% of the patients receiving Belviq and 2% of the patients receiving placebo after 1 year (mild or greater aortic regurgitation or moderate or greater mitral regurgitation or both); none of these patients were symptomatic.

The safety and efficacy of the coadministration of these drugs with other products for weight loss have not been established. The effect of Belviq on cardiovascular morbidity and mortality has not been established as well.

Prescribers and patients should adhere to the recommendations on the labels regarding patient's initial weight-loss response to the treatment on the basis of FDA analysis of the clinical trial data. It was determined that if after 12 weeks of treatment with Belviq a patient has not lost at least 5% of the baseline body weight, use of the drug should be discontinued as it is unlikely that the patient will achieve meaningful weight loss with continued treatment.

The contraindications of this drug include pregnancy, concomitant use of medications that increase serotonin levels or activate serotonin receptors to avoid serotonin syndrome. Caution is advised while using this drug in patients with congestive heart failure (these patients may already have overexpression of 5-HT_{2B} receptors).

Additionally, Belviq may increase the risk of psychiatric disorder (euphoria and dissociation) and cognitive impairment if the dose is increased from the recommended dose of 10 mg twice a day.

This drug will be available in the market after FDA decides the Drug Enforcement Administration schedule.

Qsymia (phentermine plus extended-release topiramate)

Qsymia is a combination of phentermine and extended-release topiramate. Preliminary data suggest that the women who received topiramate during pregnancy were more likely to have infants born with an orofacial cleft.[4] If Qsymia is used during pregnancy or if the patient becomes pregnant while taking Qsymia, treatment should be discontinued immediately and the patient should be informed of the potential hazard to a fetus. Women in the reproductive age group should have a negative pregnancy test before starting Qsymia and monthly pregnancy tests should be performed thereafter during Qsymia therapy. They should use effective contraception during Qsymia therapy. It is for this reason, risk evaluation and mitigation strategy (REMS) is required before prescribing Qsymia by physicians. The REMS includes a medication guide, a patient brochure, and a formal training program for prescribers, all of which inform patients and prescribers of the teratogenic risk and stress the need for women in the reproductive age group to use

1877-573X/$ - see front matter

effective forms of contraception. The REMS also permits only specially certified pharmacist to dispense Qsymia.

The effect of Qsymia on weight loss in conjunction with reduced calorie intake and increased physical activity was studied in 2 randomized, double-blind, placebo-controlled studies in obese patients (study 1) and in obese and overweight patients with 2 or more significant comorbidities (study 2). The percentages of patients who lost weight greater than or equal to 5% body weight were 17% in the placebo group, 45% in Qsymia 3.75-mg/23-mg dose group, and 67% in Qsymia 15-mg/92-mg dose group in study 1. In study 2, these percentages were 21% in the placebo group, 62% in Qsymia 7.5-mg/46-mg group, and 70% in Qsymia 50-mg/92-mg group.

Qsymia is contraindicated in pregnancy, glaucoma, hyperthyroidism, and with known hypersensitivity or idiosyncrasy to sympathomimetic amines. It is also contraindicated during or within 14 days of taking monoamine oxidase inhibitors. The adverse reaction that needs to be monitored during the treatment phase is elevation in heart rate, suicidal behavior and ideation, acute angle-closure glaucoma, mood and sleep disorders, cognitive impairment, and metabolic acidosis. Although the Qsymia was associated with mean increases in heart rate of 0.6 bpm and 1.7 bpm at doses of 7.5 mg/46 mg and 15 mg/92 mg, respectively, the study participants had greater reduction in systolic blood pressure, diastolic blood pressure, and triglycerides compared with placebo. Taking into account the magnitude of the weight loss and the favorable changes in metabolic profile, the FDA concluded that the benefit-risk balance was positive and supported the approval of this drug.

Qsymia is taken once daily in the morning to avoid the possible side effect of insomnia. Recommended starting dose for Qsymia is 3.75 mg/23 mg (phentermine 3.75 mg/topiramate 23-mg extended release) daily for 14 days; then increase the dose to 7.5 mg/46 mg daily. If after 12 weeks of treatment with Qsymia at 7.5-mg/46-mg dose the patient has not lost at least 3% of the baseline weight, the drug should be discontinued or the dose increased. To escalate the dose, increase the dose of Qsymia to 11.25 mg/69 mg daily for 14 days followed by 15 mg/92 mg daily. If patient does not lose at least 5% of the baseline weight during an additional 12 weeks of treatment on the maximum daily dose of 15 mg/92 mg, the drug should be discontinued because the patient is unlikely to achieve meaningful weight loss with continued treatment. To discontinue the treatment, the 15 mg/92 mg dose should be taken every other day for at least 1 week prior to stopping it, because of the possibility of this precipitating a seizure (topiramate withdrawal).

Finally, as with any new drug, there may be yet unknown benefits and risk associated. Both the drugs should be used with caution while monitoring the patient for potential adverse reactions. Any antiobesity drugs should always be used in conjunction with a healthy eating lifestyle program.

Adarsh K. Gupta, DO, MS, FACOFP
Department of Family Medicine, Center for Medical Weight Loss & Metabolic Control, UMDNJ-SOM, Sicklerville, NJ

References

1. FDA Briefing Information: Meeting of the Endocrinologic and Metabolic Drugs Advisory Committee, May 10, 2012. Available at: 〈http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM303198.pdf〉.
2. FDA Briefing Information: Meeting of the Endocrinologic and Metabolic Drugs Advisory Committee, February 22, 2012. Available at: 〈http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM292315.pdf〉.
3. Guidance for Industry: Developing Products for Weight Management (Draft). Silver Spring, MD: Food and Drug Administration, 2007. Available at: 〈http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM071612.pdf〉.
4. Margulis AV, Mitchell AA, Gilboa SM, et al: Use of topiramate in pregnancy and risk of oral clefts. *Am J Obstet Gynecol.* 2012

Corresponding author: Adarsh K. Gupta, DO, MS, FACOFP, Department of Family Medicine, Center for Medical Weight Loss & Metabolic Control, UMDNJ-SOM, 61 Meetinghouse Cir, Sicklerville, NJ 08081-4896.

E-mail address: adarshgupta@gmail.com.