was favorable for the use of phentermine-topiramate ER. Similar to other medications, there were concerns about the differences in patients' values and preferences and an increase in the burden on monitoring with pharmacotherapy (eg, blood pressure and heart rate monitoring, pregnancy tests). Taken together, the panel made a conditional recommendation for the use of phentermine-topiramate ER.

Special Clinical Considerations

Phentermine-topiramate ER is available in capsules with doses of 3.75 mg/23 mg, 7.5 mg/46 mg, 11.25 mg/69 mg, and 15 mg/92 mg. It is recommended to initiate treatment with the starter dose of 3.75 mg/23 mg taken once daily for 14 days, followed by a maintenance dose of 7.5 mg/46 mg daily. After 12 weeks, if the patient has not lost at least 3% of their body weight, consider discontinuation or further dose escalation, depending on tolerance, adverse effects, and patient preference. For escalating the dose, titrate up to 11.25 mg/69 mg daily for 14 days, followed by the maintenance maximum dose of 15 mg/92 mg daily. Although 7.5 mg/46 mg is considered the standard dose, our analysis demonstrated superior efficacy for the 15 mg/92 mg option, and we recommend this as the target dose, as long as the balance of benefit and risk is favorable for a given individual patient. If the patient has not lost 5% or more of their weight after 12 weeks on the maximum dose, treatment should be discontinued with dose titration by taking 1 capsule every other day for at least 1 week, then stopping, to minimize the risk of precipitating a seizure. Because of the potential benefits for patients with migraine headaches, phentermine-topiramate ER should be considered in patients with obesity and migraines.

One of the most important concerns among prescribers surrounds the cardiovascular safety of phentermine. Perceptions regarding cardiotoxicity with sympathomimetic AOMs can be categorized into 2 different pathophysiologic domains. The first, regarding serotonergic stimulation of myocardial tissues (pulmonary hypertension, valvulopathies), is addressed in Recommendation 7 for phentermine monotherapy. The second domain reflects adrenergic hemodynamic effects (eg, heart rate and blood pressure) and the potential for adverse cardiovascular outcomes. In pivotal clinical trials for phentermine-topiramate ER, blood pressure generally declined, and there was a very modest increase in heart rate, usually at higher doses.[54,55,58] Observational data from phentermine monotherapy do not seem to demonstrate significant increases in blood pressure or heart rate in treated individuals.[74–76] Currently, there are no large cardiovascular outcome trial data for long-term use of phentermine-topiramate ER. Hence, caution is advised and phentermine-topiramate ER should be avoided in patients with a history of cardiovascular disease or uncontrolled hypertension. Pivotal phase 3 trials enrolled subjects up to the age of 70 years, but there are no high-quality data to guide the use of phentermine-topiramate ER in the geriatric population. It should also be avoided in patients treated with, or within 14 days, of monoamine oxidase inhibitors. Due to concerns for arrhythmias and seizures, medications with phentermine should not be used in patients with untreated hyperthyroidism.

Fetal exposure to topiramate during the first trimester is associated with an increased risk of oral clefts.[77] Female patients with child-bearing potential should be counseled on the risks of teratogenicity and consistent use of reliable contraception while using phentermine-topiramate ER. Monitoring with monthly pregnancy tests can be considered. Topiramate has carbonic anhydrase inhibitor properties and can induce metabolic acidosis and elevated urine pH with hypercalciuria and hypocitraturia.[78] With higher doses and prolonged exposure, there may be in an increased risk of kidney stones. Caution is advised in patients with a history of significant nephrolithiasis. Consideration should be given to periodic monitoring of serum bicarbonate levels in patients treated with phentermine-topiramate ER long term.

Due to the potential for insomnia, it is recommended that phentermine-topiramate ER be taken early in the day. Other commonly reported adverse effects include cognitive impairment, constipation, dry mouth, palpitations, paresthesias, dysgeusia, and irritability.[54,55,58] Phentermine-topiramate ER is classified as a schedule IV-controlled substance based on concerns for abuse and dependence.

Recommendation 5. In adults with obesity or overweight with weight-related complications, the AGA suggests using naltrexone-bupropion ER with lifestyle interventions, compared with lifestyle interventions alone. *(Conditional recommendation, moderate certainty)*

Implementation Considerations

- Naltrexone-bupropion ER may be considered for the treatment of overweight or obesity in patients who are attempting smoking cessation, and in patients with depression.
- Naltrexone-bupropion ER should be avoided in patients with seizure disorders and used with caution in patients at risk of seizures.
- Naltrexone-bupropion ER should not be used concomitantly with opiate medications.
- Blood pressure and heart rate should be monitored periodically while taking naltrexone-bupropion ER, especially in the first 12 weeks of treatment.

Summary of the Evidence

We identified 5 RCTs comparing naltrexone-bupropion ER vs placebo for long-term treatment for obesity (all studies were with a follow-up time of 56 weeks).[79–83] Demographic and baseline characteristics of the population were similar across the studies. Mean age ranged between 43 and 61 years and the population was predominantly female; baseline weight was approximately 100 kg, BMI was