S AN D I E G O — When choosing a therapy for physical fatigue in patients being treated for depression, it is important to consider the presence or absence of residual sadness, Dr. Stephen C. Ellen said at a psychopharmacology congress sponsored by the Neuroscience Education Institute.

Two strategies exist for treating patients on antidepressants who complain that activities make them feel more physically tired, winded, or older than they felt before depression set in, despite getting help for the depression. Both bupropion and stimulants will boost dopamine and nor-epinephrine in the cortex, striatum, and spinal cord. Modafinil will boost histamine in the cortex, he said. Dr. Ellen is a speaker for GlaxoSmithKline, which makes Wellbutrin (bupropion). He also serves as a consultant and speaker for Cephalon Inc., which makes Provigil (modafinil).

If the patient’s antidepressant therapy has virtually eliminated the sadness and mood issues, choose modafinil or methylphenidate (for example, Ritalin) or another stimulant to treat the residual physical fatigue. If some sadness still remains, however, bupropion may boost antidepressant effects and reduce fatigue, said Dr. Ellen of the University of Massachusetts, Worcester.

Modafinil or stimulants work much better at “waking somebody up” from residual symptoms of depression than does bupropion, he said. Bupropion “is brightening, but I don’t think it is particularly wake promoting.”

Physical fatigue is common in patients with depression or obstructive sleep apnea, and the two problems overlap. One in six depressed people has obstructive sleep apnea, and one in five people with obstructive sleep apnea is depressed, he noted. A 2003 study of 60 patients found that the more severe the depression in a patient with sleep apnea, the greater the level of fatigue. In patients with both depression and obstructive sleep apnea, the fatigue usually derives from the depression. “So if you’re still getting words that sound like fatigue” after treatment, consider switching to a stronger antidepressant or increasing the dose, Dr. Ellen advised.

Bupropion is widely used to treat fatigue in patients with depression but it “takes a while to kick in,” typically 4-6 weeks, he said. Some reports suggest that bupropion may be less likely than other antidepressants to destabilize a patient with bipolar disorder, but other reports suggest that the risk is no different with bupropion.

A case series of 42 patients treated for depression with selective serotonin reuptake inhibitors found that energy levels stayed the same or improved in patients who received adjunctive bupropion but worsened in nearly half of patients who remained on monotherapy, Dr. Ellen said. Stimulants are not commonly used to treat fatigue in depressed patients, but they can quickly provide a boost in alertness with short-term use. Most studies of stimulants for fatigue focus on patients with HIV or AIDS. There are no controlled trials of stimulants for fatigue associated with depression, “but that shouldn’t throw you off, because there’s not a single controlled study of [bupropion for this indication] either, and we use that like crazy,” he said.

Stimulants, however, can cause cardiovascular or CNS side effects and have a high risk for abuse with long-term use. Patients may develop psychological or physical dependence on them, and tolerance to the drug develops rapidly, Dr. Ellen said. Adding modafinil to antidepressant therapy appears to significantly reduce patients’ fatigue scores if the drug is given in proper doses. The best effects are seen with 100-200 mg/day. Less benefit comes from a dosage of 300 mg/day, and a dosage of 400 mg/day can increase fatigue, he said.

Modafinil’s effects on fatigue in depression appear to be independent of mood, and the onset of action usually is immediate, he noted.

Sadness Alters Tx for Depression-Related Fatigue

Bupropion may boost the effect of an antidepressant and reduce fatigue if some sadness still remains.

DR. ELLEN