# SCORE SOUTH CAROLINA OFFERING PRESCRIBING EXCELLENCE Newsletter FAQs - Fall 2008

## Frequently Asked Questions

### *What is the role of bupropion for smoking cessation in patients with depression?*

Bupropion (marketed as Wellbutrin® for depression, Zyban® and others for smoking cessation) is a good choice for initial monotherapy treatment in patients who desire to stop smoking. It can also be added to another antidepressant (e.g. selective serotonin reuptake inhibitor [SSRI]) to aid smoking cessation in addition to boosting the antidepressant effect of the first medication. When adding bupropion to a current antidepressant, it should be initiated at a low dose then gradually titrated to a goal of 300 mg daily (either XR 300 mg once daily or SR 150 mg twice daily) for smoking cessation so that both antidepressants are at full therapeutic dose.

Switching to bupropion is another alternative, especially in case of intolerance, lack of improvement with initial antidepressant, or if the use of multiple medications is not advised. When switching treatment, antidepressants should be cross tapered if the mechanism of action is different, such as going from an SSRI to bupropion. The following tapering schedule can be followed for discontinuing SSRIs: taper over 3 to 7 days, or taper by 25% per week if patient has been on an SSRI for more than 5 weeks. Of the SSRIs, paroxetine (Paxil®, others) should be tapered more slowly, with some recommending as slow as 25% every 4-6 weeks. Bupropion should be initiated slowly and titrated up as stated above.

### *What is the risk of suicidality from antidepressant use in pediatric patients?*

An FDA published meta-analysis of 24 pediatric randomized, controlled trials evaluating various antidepressants observed an overall suicidality risk ratio (RR) of 1.66 (95% CI 1.02-2.68) for selective serotonin reuptake inhibitors (SSRIs) in depression trials and 1.95 (95% CI 1.28-2.98) for all antidepressants across all indications. There were no completed suicides. Based on these data, the FDA issued a black box warning on suicidality associated with the use of all antidepressants in pediatric patients.

A more recent meta-analysis of pediatric trials (Bridge et al, 2007) found a non-significant 1% difference in suicidal thoughts/behaviors when comparing antidepressants to placebo in the treatment of major depression. Antidepressants were more efficacious than placebo for the treatment of non-OCD anxiety disorders, OCD, and depression. The authors concluded that “benefits of antidepressants appear to be much greater than risks from suicidal ideation/suicide attempt across indications, although comparison of benefit to risk varies as a function of indication, age, chronicity, and study conditions.”

The FDA black box warning has placed physicians in a difficult position. Although the use of antidepressants has helped thousands of pediatric patients with a variety of challenges, the possible increase in suicidal thoughts and behaviors cannot be discounted. Therefore, good communication between the parent, child, and physician is critical.

## *What differentiates an augmentation strategy from a combination strategy in the treatment of major depressive disorder?*

The SCORxE Algorithm for the Treatment of Major Depressive Disorder uses the term *augmentation* when a medication is added to an ongoing antidepressant treatment. Augmentation is a consideration for use in patients who partially respond or fail to respond to first-line antidepressant treatment despite adequate dose, duration and patient adherence. Traditionally, other sources have defined augmentation as the use of a non-antidepressant medication with an antidepressant to boost the antidepressant response.

The SCORxE Algorithm for the Treatment of Major Depressive Disorder uses the term *combination therapy* when two medications are initiated at the same time. Combination therapy is a consideration for use in patients with treatment-resistant depression defined as depression that is resistant to 2 courses of monotherapy with pharmacologically different antidepressants given in an adequate dose and duration. Traditionally, other sources have defined combination therapy as the concomitant use of two antidepressants.

## *What is the evidence supporting the use of liothyronine (T3) to augment antidepressants?*

Early studies with tricyclic antidepressants (TCAs) support the efficacy of T3 (Cytomel®) as augmentation strategy in cases of non-response to antidepressants, as well as accelerating response when given concurrently with TCAs. Recent data support the efficacy of T3 augmentation of newer antidepressants such as selective serotonin reuptake inhibitors (SSRIs), although further controlled studies are needed to definitely assess the efficacy of that augmentation strategy.

There are relatively few studies of T3 as an accelerating, enhancing, or augmenting agent in patients with major depressive disorder (MDD) treated with specific SSRIs. However, results from the recent Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study provide the most helpful information. Augmentation treatment with T3 or lithium (Eskalith®, Lithobid®, others) was compared after a mean of 9.6 weeks and remission rates were not statistically different (~25% with T3 vs. ~ 15% with lithium). The authors conclude that “in cases where an augmentation trial is deemed appropriate for the patient, T3 has slight advantages over lithium in efficacy and tolerability. Compared to lithium, T3 offers the advantages of ease of use and lack of need for blood level monitoring.”

## *Can you provide more comparative clinical information about paliperidone and risperidone?*

Paliperidone, the 9-hydroxy metabolite of risperidone, contributes significantly to the therapeutic effects of risperidone (Risperdal®, Risperdal Consta®). Paliperidone (Invega®) is now available in an oral extended-release (ER) formulation, and an intramuscular depot formulation is under development. Advantages of paliperidone over risperidone are unclear right now since there are no studies adequately powered to compare paliperidone directly with other second-generation antipsychotics, including risperidone. The ER formulation allows for a therapeutically effective and well tolerated starting dose to be given. Disadvantages include its propensity to increase plasma prolactin levels, perhaps to a greater extent than its parent drug risperidone. Cost may become an issue with using paliperidone since risperidone is now available in generic form.