

Primer for Prescription Medications: Medication Symbiosis



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In this column we will discuss an antipsychotic and antidepressant combination, Symbyax, indicated for the treatment of depressive episodes in bipolar disorder. In general healthcare, two or more medications are often manufactured into a single preparation to increase convenience and medication adherence. Some popular examples are triamterene and hydrochlorothiazide [Maxzide] used for hypertension with a risk of hypokalemia; fluticasone propionate and salmeterol [Advair Diskus] for long-term maintenance therapy in asthma; ezetimibe and simvastatin [Vytorin] for elevated cholesterol; and several others (see reference 1). In contrast, there have been only a few such combinations in psychiatry prior to Symbyax, such as perphenazine and amitriptyline [Triavil, Etrafon] or chlordiazepoxide and amitriptyline [Limbital] (see reference 2). This may be explained partly by the large variation in individual clinical response to a typical dose of a psychotropic. One component of this variance is pharmacokinetic: the same dose will produce different plasma concentrations in different individuals. The other is pharmacodynamic: the same concentration will produce different responses

in different individuals (see reference 3). Furthermore, medicine combinations make matters more complex by virtue of their interactions. When two separate medications are co-administered, interactions can be minimized by adjusting the individual doses. This flexibility is compromised in a fixed dose amalgamation, and if there are side effects, it can be more difficult to decide which portion of the combined product is causing them. On the other hand, medicine combinations are designed to augment efficacy.

Bipolar affective disorder is a cyclical illness with possible manic, hypomanic, depressive, and mixed episodes. Olanzapine [Zyprexa] is indicated for the treatment of the acute mixed or manic phase and maintenance monotherapy in bipolar disorder. Olanzapine has a high affinity for serotonin 5HT_{2A/2C}, dopamine D₁₋₄, muscarinic M₁₋₅, histamine H₁, and adrenergic alpha 1 receptors. This receptor interaction explains some of its therapeutic and adverse effects. Fluoxetine hydrochloride [Prozac, Prozac weekly, Sarafem (see reference 4), and also available in generic form] is used for the treatment of depression. Fluoxetine is a selective serotonin receptor uptake inhibitor with weak inhibition of norepinephrine and dopamine transporters (see reference 5). Thus, Symbyax combines the two elements, olanzapine and fluoxetine, for therapeutic efficacy in bipolar depression. This has been established by two identically designed, 8-week, randomized, double-blind clinical studies. Although the exact mechanism of action is unknown, it is proposed that the activation of the three monoaminergic neural systems (serotonin, norepinephrine, and dopamine) is responsible for the enhanced antidepressant effect. These patients had no statistically significant increase in the incidence of mania, but due to the limited controlled-trial experience and the cyclical nature of bipolar illness, patients on Symbyax still should be monitored closely for emergence of mania or hypomania (see reference 4).

In order to retain some flexibility in administration, Symbyax capsules are avail-

able in four fixed olanzapine-fluoxetine doses: 6 mg/25 mg, 6 mg/50 mg, 12 mg/25 mg, and 12 mg/50 mg. It is usually administered once daily in the evening beginning with the 6 mg/25 mg capsule. Dose adjustments, if indicated, can be made according to efficacy and tolerability (see reference 4).

The significant side-effects of Symbyax are somnolence, weight gain, orthostatic blood pressure changes, and elevation of liver enzymes. As with most atypical antipsychotics such as olanzapine, caution should be maintained regarding development of hyperglycemia, diabetes mellitus, and, in the patient who is elderly and demented, cerebrovascular and cardiovascular adverse events (reference 4). The fluoxetine component inhibits the liver cytochrome system enzyme, CYP2D6. Therefore, caution should be maintained when co-administering other medications metabolized via this enzyme (see reference 6). Symbyax is contra-indicated in known hypersensitivity and with co-administration of monoamine oxidase inhibitors or thioridazine [Mellaril] (see reference 4). There have also been recent warnings about suicidality with SSRIs and vascular problems with elderly, demented patients prescribed atypical antipsychotics.

Recently, several atypical antipsychotics have been indicated for the acute manic or mixed phases in bipolar illness. However, there are only two preparations indicated for bipolar depression, Symbyax and lamotrigine [Lamictal]. It will be interesting to see how Symbyax is used and how successfully it is marketed, given that it is a psychotropic combination.

References:

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Chair's Corner

Establishing a Private Practice

Starting a private practice can be a daunting event. I suggest that practitioners try to make the transition in a gradual manner, rather than suddenly leaving their day jobs to establish new practices.

There are a number of ways to enter the water gradually. First, find a mentor you respect who will help you with the learning experience of independent practice and who will assist you in averting the spills and falls that newcomers often encounter. He or she should show a genuine concern, offer you office space at a fair price, and help you get to know the local gatekeepers.

There is much to learn about how to apply your skills, obtain the necessary insurances, advertise or market your skills, and make contacts with schools, agencies, industries, physicians, and others who will send you therapy patients.

Carefully consider what your start-up costs will be. Will you need a lawyer, an accountant, a secretary, and an assistant? Will your initial outlay exceed your income? Will you need a computer, billing system, fax machine, copier, business cards, and other marketing tools? How much will all of this cost?

It is important to understand why you want to enter into independent practice. Be honest with yourself! Is it for the money? Is it for the prestige? Is it because you want to be your own boss? Perhaps you feel you can do more for your clients in a private setting than you can in your present job. These are all legitimate questions, and you should try to answer them to the best of your ability.

My mentors and teachers taught me to learn everything I could, and to keep learning, prepare well, and do the best job I could. The rest, they said, would happen automatically. They were correct. In my practice I have concentrated on my patients and on being the best therapist I can be, and have mentored those in my practice whenever possible. A great deal of success has come my way, and I don't believe it was accidental. Yes, there was some luck involved, and there were some very difficult times. However, people in my community have in turn been very helpful and loyal to me. I think it is because they recognize genuine concern and caring.

I would advise that you put some money aside to invest in yourself. Open a small

practice with a mentor or an experienced psychotherapist. Start by learning to do your "job" well. Treat every patient/client professionally and with care. Know your limits. Never be afraid to ask for consultation or supervision. This is not about you; this is about the people who come to see you because they are in pain. Also, know your professional boundaries and don't be afraid to seek your own therapy from time to time—I do.

Continue to build your skills, whether statutes require you to or not. Knowledge in our field changes daily, and each client is different and brings fresh problems. Treat your clients with respect and do something that is becoming rare in our society: listen. This alone will ensure your success in private practice.

There are a lot of little concerns about starting a private practice. You can spend your time on the little things, or you can spend your time designing a solid philosophy of independent practice and treatment. If you do, I promise you will be a great success.



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