RX Primer

Primer for Prescription Medications: Antidepressants that Anticipate the Future

By Alan D. Schmetzer, MD, DAPA, and Harpriya A. Bhagar, MBBS

This 1-credit continuing education opportunity is co-sponsored by the American College of Forensic Examiners International (ACFEI) and the American Psychotherapy Association. ACFEI maintains responsibility for all continuing education accreditations. This article is approved by the following for 1 continuing education credit:

APA provides this continuing education credit for **Diplomates**.

ACFEI is approved by the **American Psychological Association** to offer continuing education for psychologists.

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education **(ACCME)** through the joint sponsorship of ACFEI and APA. ACFEI is accredited by the ACCME to provide continuing medical education for physicians. ACFEI designates this educational activity for a maximum of 1 hour(s) in category 1 credit towards the AMA Physicians Recognition Award. Each physician should claim only the number of hours he or she actually spent in the activity.

Since the past "Primer for Prescription Medications" columns surveying the antidepressants (see first, second, and third references below) were published, two new medicines for depression have been approved by the Food and Drug Administration (FDA).

The first to be introduced is escitalopram oxalate (Lexapro). Citalopram hydrobromide had been marketed in the United States earlier as Celexa (see first reference). Celexa is made up of what is called a "racemic mixture," an equal mix of the two possible forms of the citalopram molecule. Both forms have the same basic structure, but one rotates polarized light to the right and the other to the left. In other words, they are mirror images of each other. As it turns out, much of the activity of citalopram is due to the "S" rotated molecule. Given that all of the active ingredients of Lexapro are composed of "S" molecules, it is about twice as active, milligram for milligram, as Celexa. Thus, doses of Lexapro usually range from 10 to 20 milligrams per day, and dosages of Celexa, 20 to 40 milligrams per day. Of course, the types of side effects are essentially the same for both, but Lexapro has a somewhat decreased likelihood of most of these side effects for the same reason—side effects go up with a higher dose, and Lexapro, on average, can be given in smaller doses. Both are selective serotonin reuptake inhibitors (SSRIs). See references 1, 4, and 5 for a more thorough discussion of side effects. SSRIs, as you will recall, selectively block the re-uptake of serotonin at the presynaptic neuron and, at the usual therapeutic dose, generally do not have much effect on other neurotransmitters. Both Celexa and Lexapro offer the advantage of having a reduced drug-drug interaction profile compared to most SSRIs. All SSRIs now carry a warning in the United States for caution in children and adolescents because of a possible increase in suicidal thoughts and urges.

The second of the new medicines for depression to come out is duloxetine hydrochloride (Cymbalta). Duloxetine blocks the re-uptake of both serotonin and norepinephrine at the presynapse. The FDA has approved marketing of this medication for the treatment of depression. There is considerable interest, and ongoing studies, of its analgesic effects as well, and it has already been approved for the treatment of diabetic peripheral neuropathy. Side effects include increases in blood pressure, possible switching from depression to mania in susceptible people, and an increase in liver enzymes, especially in patients who also use alcohol heavily. Duloxetine is metabolized in the liver, so it does interact with other medicines metabolized there, such as other antidepressants, phenothiazines, and certain medicines for heart rhythm problems. The usual dose range for duloxetine is 40 to 60 milligrams per day, generally starting in two divided doses a day. Its use should be avoided in those who have severe kidney or liver disease.

The FDA classifies Lexapro and Cymbalta in "pregnancy category C," and therefore these medications should be used in pregnant women only if the benefits appear to outweigh the risks, and if at all possible, should be tapered prior to the third trimester. Both can also produce what has been called a "discontinuation syndrome"—withdrawal symptoms—if

stopped abruptly, although neither is considered addictive.

These medicines are particularly interesting because they may indicate some possible future directions for pharmacologic development. With escitalopram, this involves the isolation of a specific molecular form of a medicine. With duloxetine, this involves the development of another molecule along the lines of venlafaxine (Effexor) (see reference 2) and the older tricyclic antidepressants (see reference 3), which significantly impacts more than one potentially depression-related neurotransmitter.

References

1. *Physicians' desk reference, 59th edition*. (2005). Montvale, NJ: Thompson PDR.
2. Sadock, B. J, & Sadock, V. A. (2003). *Kaplan & Sadock's synopsis of psychiatry, 9th edition*. Philadelphia, PA: Lippincott Williams & Wilkins.
3. Schmetzer, A. (2002). Primer for prescription medications: The SSRIs. *Annals of the American Psychotherapy Association, (5)*1, 32.
4. Schmetzer, A. (2002). Primer for prescription medications: Atypical Antidepressants. *Annals of the American Psychotherapy Association, (5)*2, 33.
5. Schmetzer, A. (2002). Primer for prescription medications: The older antidepressants. *Annals of the American Psychotherapy Association, (5)*3, 31-32.

About the Authors

Alan D. Schmetzer, MD, DAPA, is a Diplomate of the American Psychotherapy Association and has been a member since 1998. He is a professor of psychiatry at the Indiana University School of Medicine.

Harpriya A. Bhagar, MBBS, is an assistant professor of clinical psychiatry at the Indiana University School of Medicine and is a new member of the American Psychotherapy Association.

Earn CE Credit
Take CE questions online at www.americanpsychotherapy.com (click "Online CE") or see the questions for this article on page 48.