

# Psychopharmacology BULLETIN

## Advancing the Treatment of Mood and Anxiety Disorders: The First 10 Years' Experience with Paroxetine

### Introduction

By *Charles B. Nemeroff, MD, PhD*

### Neuropharmacology of Paroxetine

By *Michael J. Owens, PhD, and  
Charles B. Nemeroff, MD, PhD*

### In Vivo Neuroimaging Correlates of the Efficacy of Paroxetine in the Treatment of Mood and Anxiety Disorders

By *Clinton Kilts, PhD*

### Pharmacokinetics, Drug Interactions, and Tolerability of Paroxetine and Paroxetine CR

By *C. Lindsay DeVane, PharmD*

### Paroxetine Treatment of Major Depressive Disorder

By *Martin B. Keller, MD*

### Treatment of Panic Disorder: Focus on Paroxetine

By *Mark H. Pollack, MD, and Alicia C. Doyle, BA*

### Paroxetine Treatment of Generalized Anxiety Disorder

By *David V. Sheehan, MD, MBA, and  
C. Gloria Mao, PharmD*

### Treatment of Posttraumatic Stress Disorder: The Impact of Paroxetine

By *Jonathan R. T. Davidson, MD*

### Obsessive-Compulsive Disorder: Implications of the Efficacy of an SSRI, Paroxetine

By *Philip T. Ninan, MD*

### Advances in Recognition and Treatment of Social Anxiety Disorder: A 10-Year Retrospective

By *Murray B. Stein, MD, FRCPC*

### Paroxetine Use in Medically Ill Patients

By *Steven Stout, MD, PhD,  
Wendy I. Somerset, MD,  
Andrew Miller, MD, and  
Dominique L. Musselman, MD, MS*

### Paroxetine Treatment of Depression in Late Life

By *Charles F. Reynolds III, MD*

### Paroxetine Treatment of Mood Disorders in Women: Premenstrual Dysphoric Disorder and Hot Flashes

By *Kimberly A. Yonkers, MD*

### Clinical Management of Perinatal Depression: Focus on Paroxetine

By *D. Jeffrey Newport, MD, MSCR, MDiv,  
and Zachary N. Stowe, MD*

### Paroxetine Treatment of Mood and Anxiety Disorders in Children and Adolescents

By *Karen Dineen Wagner, MD, PhD*

### Efficacy and Tolerability of Controlled- Release Paroxetine

By *Robert N. Golden, MD*

Key Words: paroxetine, women, premenstrual dysphoric disorder, menopause, breast cancer, hot flashes

# Paroxetine Treatment of Mood Disorders in Women: Premenstrual Dysphoric Disorder and Hot Flashes

By Kimberly A. Yonkers, MD

**ABSTRACT** ~ With the relatively recent introduction of the selective serotonin reuptake inhibitor (SSRI) class of antidepressants, increased attention has been focused on the use of antidepressants in the treatment of mood disorders across the female life cycle. Evidence for the efficacy of antidepressants in the treatment of premenstrual dysphoric disorder (PMDD) and hot flashes associated with menopause and breast cancer has emerged. The clinical trials experience with paroxetine and the controlled-release (CR) formulation of paroxetine is reviewed. *Psychopharmacology Bulletin*. 2003;37(Suppl 1): 135-147

## INTRODUCTION

Depression is one of the most significant and disabling illnesses in women. Findings from the World Health Organization's Global Burden of Disease study illustrate the relative ranking of depression as a source of death and disability worldwide and in the United States. Based on 1996 estimates, the leading cause of disability among both men and women in the United States was ischemic heart disease. Motor vehicle accidents were the second most common source of death and disability in men. In sharp contrast, the second largest contributor to disability in women was major depression, which in women was ranked higher than cerebrovascular disease, respiratory tract cancers, osteoarthritis, and breast cancer.<sup>1</sup>

For reasons that are not completely understood, women are at increased risk for mood disorders compared with men. Gender differences in the rates of major depression are not apparent in prepubertal children. However, beginning with puberty and continuing through the end of a woman's childbearing years in midlife, the ratio of major depression in females to males is 2:1.<sup>2,3</sup> There are particular times during a woman's reproductive life, such as pregnancy, the postpartum period, the

Dr. Yonkers is associate professor of psychiatry at the Yale University School of Medicine in New Haven, Conn.

To whom correspondence should be addressed: Kimberly A. Yonkers, MD, Yale University School of Medicine, 142 Temple St., Suite 301, New Haven, CT 06510; Tel: 203-764-6621; Fax: 203-764-6766; E-mail: kimberly.yonkers@yale.edu

direct comparative studies are warranted to better identify candidates for continuous vs intermittent SSRI treatment.

Findings from pilot studies also suggest that paroxetine and paroxetine CR reduce the frequency and severity of hot flashes in perimenopausal women and women with breast cancer. Again, additional studies are needed to assess the optimal duration of treatment of hot flashes, particularly in menopausal women. ♣

#### DISCLOSURE

This work was supported by an unrestricted educational grant from GlaxoSmithKline. Dr. Yonkers serves as a consultant and receives grant and research support from Eli Lilly, GlaxoSmithKline, and Berlex Laboratories. She receives grant and research support from Pherin Pharmaceuticals and serves as consultant for Pfizer and Wyeth.

#### REFERENCES

1. Michaud CM, Murray CJL, Bloom BR. Burden of disease: implications for future research. *JAMA*. 2001;285:535-539.
2. Kessler RC, McGonagle KA, Swartz M, Blazer DG, Nelson CB. Sex and depression in the National Comorbidity Survey, I: lifetime prevalence, chronicity, and recurrence. *J Affect Disord*. 1993;29:85-96.
3. Kornstein SG. The evaluation and management of depression in women across the life span. *J Clin Psychiatry*. 2001;62(suppl):11-17.
4. Deuster PA, Adera T, South-Paul J. Biological, social, and behavioral factors associated with premenstrual syndrome. *Arch Fam Med*. 1999;8:122-128.
5. Wittchen HU, Becker E, Lieb R, Krause P. Prevalence, incidence and stability of premenstrual dysphoric disorder in the community. *Psychol Med*. 2002;32:119-132.
6. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994.
7. Grady-Welky T. Premenstrual dysphoric disorder. *N Engl J Med*. 2003;348:433-438.
8. Yonkers KA. Antidepressants in the treatment of premenstrual dysphoric disorder. *J Clin Psychiatry*. 1997;58(suppl):4-10.
9. Endicott J. History, evolution, and diagnosis of premenstrual dysphoric disorder. *J Clin Psychiatry*. 2000;61(suppl):5-8.
10. Hylan TR, Sundell K, Judge R. The impact of premenstrual symptomatology on functioning and treatment-seeking-behavior: experience from the United States, United Kingdom, and France. *J Women's Health Gender-Based Med*. 1999;8:1043-1052.
11. Altshuler LL, Cohen LS, Moline ML, Kahn DA, Carpenter D, Docherty JP. The Expert Consensus Guideline Series: Treatment of Depression in Women. *Postgraduate Medicine Special Report*. 2001; March.
12. Frackiewicz EJ, Shiovitz TM. Evaluation and management of premenstrual syndrome and premenstrual dysphoric disorder. *J Am Pharm Assoc*. 2001;41:437-447.
13. Mitwally MF, Kahn LS, Halbreich U. Pharmacotherapy of premenstrual syndromes and premenstrual dysphoric disorder: current practices. *Expert Opin Pharmacother*. 2002;3:1577.
14. Freeman EW, Rickels K, Sondheimer SJ, Polanski M. Differential response to antidepressants in women with premenstrual syndrome/premenstrual dysphoric disorder: a randomized controlled trial. *Arch Gen Psychiatry*. 1999;56:932-939.
15. March D, Pearlstein TB, Yonkers KA. Treatment of premenstrual dysphoric disorder. *Psychiatr Clin North Am: Annu Drug Ther*. 2001;15:277.
16. Romano S, Judge R, Dilton J, et al. The role of fluoxetine in the treatment of premenstrual dysphoric disorder. *Clin Ther*. 1999;21:615-633.
17. Wikander I, Sunblad C, Andersch B, et al. Citalopram in premenstrual dysphoria: is intermittent treatment during luteal phases more effective than continuous medication throughout the menstrual cycle? *J Clin Psychopharmacol*. 1998;18:390-398.

18. Yonkers KA. Hot flashes in premenstrual dysphoric disorder with serotonergic antidepressants. *Collaborative Study*.
19. Dimmock PW, V. Hot flashes in premenstrual dysphoric disorder.
20. Eriksson E. Hot flashes in premenstrual dysphoric disorder: superior to the non-serotonergic antidepressants. *Neuropsychopharmacology*.
21. Landén M, Sörvi L. Hot flashes in premenstrual dysphoric disorder: the treatment of premenstrual dysphoric disorder. *Psychiatric Association*.
22. Sundblad C, Wikander I. Hot flashes in premenstrual dysphoric disorder: efficacy of treatment.
23. Yonkers KA, Gorman-Smith R. Hot flashes in premenstrual dysphoric disorder. *J Clin Psychiatry*.
24. Pearlstein TB, Benowitz D. Hot flashes in the treatment of premenstrual dysphoric disorder: a randomized controlled trial. *Fertil Steril*. December 10, 2001.
25. Burt VK, Altshuler LL. Hot flashes in premenstrual dysphoric disorder: guidelines for treatment.
26. Greendale GA, J. Hot flashes in premenstrual dysphoric disorder.
27. Manson JE, M. Hot flashes in premenstrual dysphoric disorder.
28. Pearlstein T, Rosenthal L. Hot flashes in premenstrual dysphoric disorder.
29. Berendsen HHG. Hot flashes in premenstrual dysphoric disorder.
30. Shanafelt TD. Hot flashes in premenstrual dysphoric disorder. *Mayo Clin Proc*.
31. Carpenter JS, A. Hot flashes in premenstrual dysphoric disorder. *Am J Obstet Gynecol*. 1998;82:1682-1687.
32. Women's Health Initiative. Hot flashes in premenstrual dysphoric disorder: principles of management. *Ann Intern Med*. 2002;288:321-326.
33. Stearns V, Isaacs L. Hot flashes in premenstrual dysphoric disorder: treatment with paroxetine. *Int J Psychiatry Med*.
34. Weitzner MA. Hot flashes in premenstrual dysphoric disorder: treatment with paroxetine.
35. Beebe K, Stearns V. Hot flashes in premenstrual dysphoric disorder: treatment with paroxetine. *CR*. October 28-31, 2001.