

Therapeutic Class Overview Selective Serotonin Reuptake Inhibitors

Therapeutic Class

- Overview/Summary:** The antidepressants are approved to treat a variety of mental disorders, including anxiety disorders, depressive disorders, eating disorders (bulimia nervosa), and premenstrual dysphoric disorder.¹⁻¹⁶ Anxiety disorders include agoraphobia, anxiety disorder due to another medical condition, generalized anxiety disorder, other specified anxiety disorder, panic disorder, selective mutism, separation anxiety disorder, social anxiety disorder or social phobia, specific phobia, substance/medication induced anxiety disorder, and unspecified anxiety disorder.¹⁷ Some antidepressants have also been used in nonpsychiatric conditions, such as chronic musculoskeletal pain, diabetic peripheral neuropathy, fibromyalgia, insomnia, moderate to severe vasomotor symptoms associated with menopause, nocturnal enuresis, and tobacco abuse.¹⁻¹⁷

Treatment for psychiatric disorders includes psychotherapy, pharmacotherapy or the combination of the two. The decision to implement psychotherapy is dependent upon patient willingness and severity of illness. Despite the variety of pharmacologic options available, all antidepressants appear to be equally efficacious for mood disorders. Therefore, initial treatment should depend on the individual's overall medical condition and current medication profile.¹⁸⁻²⁷ Pharmacology, tolerability and safety profiles differ among these classes and among individual agents. However, for all antidepressants, the Food and Drug Administration (FDA) requires manufacturers to include a black-box warning notifying prescribers of the potential for antidepressants to increase suicidal thoughts in children and adults.¹⁸⁻²⁷

The antidepressants can be classified in several ways, such as by chemical structure and/or presumed mechanism of activity. The agents included in this review belong to the category, selective serotonin-reuptake inhibitors (SSRIs). The SSRIs include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline. These agents are believed to exert their effects through potentiating the serotonergic activity in the central nervous system.¹⁻¹⁶ All but fluvoxamine are Food and Drug Administration (FDA)-approved for the treatment of major depressive disorder.¹⁻¹⁶

Table 1. Current Medications Available in the Therapeutic Class^{1-2,5-13}

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Citalopram (Celexa ^{®*})	Depression (includes major depressive disorder),	Solution: 10 mg/5 mL Tablet: 10 mg 20 mg 40 mg	✓
Escitalopram (Lexapro ^{®*})	Depression (includes major depressive disorder), generalized anxiety disorder,	Solution: 5 mg/5 mL Tablet: 5 mg 10 mg 20 mg	✓
Fluoxetine (Prozac ^{®*} , Prozac Weekly ^{®*} ,	Bulimia nervosa, depression (includes major depressive disorder), obsessive-compulsive disorder, panic disorder,	Delayed-release capsule: 90 mg Immediate-release capsule:	✓

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Sarafem [®])	premenstrual dysphoric disorder,	10 mg 20 mg 40 mg Immediate-release tablet: 10 mg 20 mg 60 mg Solution: 20 mg/5 mL	
Fluvoxamine (Luvox [®] , Luvox [®] CR)	Obsessive-compulsive disorder,	Extended release capsule: 100 mg 150 mg Immediate release tablet: 25 mg 50 mg 100 mg	✓
Paroxetine hydrochloride (Paxil [®] *, Paxil CR [®] *)	Depression (includes major depressive disorder), generalized anxiety disorder*, obsessive-compulsive disorder*, panic disorder, premenstrual dysphoric disorder [†] , posttraumatic stress disorder*, social anxiety disorder	Extended release tablet: 12.5 mg 25 mg 37.5 mg Suspension, oral: 10 mg/5 mL Immediate release tablet: 10 mg 20 mg 30 mg 40 mg	✓
Paroxetine mesylate (Brisdelle [®] , Pexeva [®])	Depression (includes major depressive disorder), obsessive-compulsive disorder, panic disorder, vasomotor symptoms associated with menopause; (moderate to severe) [#]	Immediate release capsule: 7.5 mg Immediate release tablet: 10 mg 20 mg 30 mg 40 mg	-
Sertraline (Zoloft [®])	Depression (includes major depressive disorder), obsessive-compulsive disorder, panic disorder, premenstrual dysphoric disorder, posttraumatic stress disorder, social anxiety disorder	Oral concentrate: 20 mg/mL Tablet: 25 mg 50 mg 100 mg	✓

*Immediate-release only

†Extended-release only

#Brisdelle[®] only; Brisdelle[®] is not indicated for the treatment of any psychiatric condition.

Evidence-based Medicine

- Clinical trials have demonstrated the safety and efficacy of the serotonin and norepinephrine reuptake inhibitors for their FDA-approved indications.²⁸⁻⁸²
- In one study which compared fluoxetine, imipramine and desipramine for duration of initial therapy, fluoxetine was taken for a longer period of time than desipramine or imipramine ($P < 0.001$ for either desipramine or imipramine).²⁸ Statistical comparisons between the two TCAs were not done but they were numerically similar. The difference in duration of therapy was due primarily to less tolerability of desipramine and imipramine. Only 9% of the patients switched from fluoxetine due to adverse events while 27% and 28% assigned to desipramine and imipramine respectively switched due to adverse events ($P < 0.001$ for both TCAs compared to fluoxetine).
- The overall length of antidepressant therapy (if the patient switched to another agent) was not different regardless of which agent was initiated first. In addition, response to medication as measured by the Hamilton Depression Rating Scale (HDRS) was equivalent.²⁹
- One study comparing health care costs of fluoxetine versus imipramine and fluoxetine versus desipramine compared outpatient costs to primary care and to mental health. The authors found no difference in primary care visit cost in either comparison (fluoxetine versus desipramine; $P = 0.19$ and fluoxetine versus imipramine; $P = 0.98$). There was also no difference in mental health outpatient visit cost in either comparison group (fluoxetine versus desipramine; $P = 0.33$ and fluoxetine versus imipramine; $P = 0.73$).³¹
- A meta-analysis evaluated venlafaxine compared to SSRIs in treatment of major depressive disorder. Using a random effect model showed that venlafaxine has statistically higher rates of achieving remission (odds ratio [OR], 1.13; 95% CI, 1.0 to 1.28; $P = 0.05$) and response (OR, 1.17; 95% CI, 1.03 to 1.34; $P = 0.02$). Subgroup analysis found that venlafaxine had a significantly better response rate than fluoxetine (OR, 1.28; 95% CI, 1.05 to 1.55; $P = 0.01$). There were no significant differences in response or remission between venlafaxine and other individual SSRIs. There was no significant difference in all cause discontinuation between venlafaxine and SSRIs (OR, 1.10; 95% CI, 0.97 to 1.25; $P = 0.15$). Venlafaxine had significantly higher discontinuation due to adverse events compared with SSRIs (OR, 1.41, 95% CI, 1.10-1.79, $P = 0.006$).³⁸

Key Points within the Medication Class

- According to Current Clinical Guidelines:
 - National and international treatment guidelines for the treatment of depression state that selecting an agent should be driven by anticipated side effects, tolerability, patient preference, and quantity and quality of available clinical data, and that the effectiveness of antidepressants is usually comparable within and between medication classes.¹⁸⁻²⁷
 - Guidelines also state that medications that can be considered first-line therapy for most patients include selective serotonin reuptake inhibitors (SSRIs), SNRIs, mirtazapine, or bupropion, while monoamine oxidase inhibitors (MAOIs) should be reserved for patients who are unresponsive to other available medications. These guidelines do not recommend one SSRI, SNRI or MAOI over another.¹⁸⁻²⁷
 - Antidepressants are recommended as first-line treatment for GAD, with the following agents considered treatment options: SSRIs, SNRIs, and non-sedating tricyclic antidepressants (TCAs).³⁸
- Other Key Facts:
 - Fluoxetine is the only agent within the class that carries indications for treating bulimia nervosa, while Brisdelle® (paroxetine mesylate) is the only SSRI that is FDA-approved for the treatment of vasomotor symptoms associated with menopause.
 - All of the SSRI products have a Black Box Warning regarding the potential for antidepressants to increase suicidal thoughts in children and young adults.¹⁻¹⁶

References

1. Micromedex® Healthcare Series [database on the internet]. Greenwood Village (CO): Thomson Reuters (Healthcare) Inc.; Updated periodically [cited 2016 Jan]. Available from: <http://www.thomsonhc.com/>.
2. Drug Facts and Comparisons 4.0 [database on the Internet]. St. Louis: Wolters Kluwer Health, Inc.; 2016 [cited 2016 Jan]. Available from: <http://online.factsandcomparisons.com>.
3. Celexa® [package insert]. St. Louis (MO): Forest Pharmaceuticals; 2014 Jul.
4. Citalopram solution [package insert]. Carmel (NY): Silarx Pharmaceuticals, Inc.; 2014 Jun.
5. Lexapro® [package insert]. St. Louis (MO): Forest Pharmaceuticals; 2014 Oct.
6. Prozac® [package insert]. Indianapolis (IN): Eli Lilly and Company; 2014 Oct.
7. Prozac Weekly® [package insert]. Indianapolis (IN): Eli Lilly and Company; 2014 Jul.
8. Fluoxetine solution [package insert]. Sellersville (PA): Teva Pharmaceuticals USA, Inc.; 2014 Sep.
9. Sarafem® [package insert]. Rockaway (NJ): Warner-Chilcott; 2014 Oct.
10. Fluvoxamine maleate tablet [package insert on the Internet]. Detroit (MI): Caraco Pharmaceutical Laboratories, Ltd; 2014 Jul [cited 2014 Sep 22]. Available from: <http://dailymed.nlm.nih.gov/dailymed/druginfo.cfm?id=5329>.
11. Luvox CR® [package insert]. Palo Alto (CA): Jazz Pharmaceuticals, Inc.; 2014 Jul.
12. Paxil® [package insert]. Research Triangle Parke (NC): GlaxoSmithKline; 2014 Jul.
13. Paxil CR® [package insert]. Research Triangle Parke (NC): GlaxoSmithKline; 2014 Jul.
14. Peveva® [package insert]. New York (NY): Noven Therapeutics, LLC; 2014 May.
15. Brisdelle® [package insert]. Miami (FL): Noven Therapeutics, LLC; 2014 Dec.
16. Zolof® [package insert]. New York (NY): Pfizer Inc; 2014 May.
17. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA, American Psychiatric Association, 2013.
18. American Psychiatric Association (APA). Practice guideline for the treatment of patients with major depressive disorder. 3rd ed. Arlington (VA): American Psychiatric Association (APA); 2010 Oct. 152 p. Available at: http://psychiatryonline.org/data/Books/prac/PG_Depression3rdEd.pdf. Accessed Dec 2015.
19. National Institute for Clinical Excellence. Depression in adults: recognition and management. National Institute for Clinical Excellence (NICE); October 2009. Available at: <http://guidance.nice.org.uk/CG90>. Accessed Dec 2015.
20. National Institute for Clinical Excellence. Generalized anxiety disorder and panic disorder in adults: management. National Institute for Clinical Excellence (NICE); January 2011. Available at: <http://www.nice.org.uk/nicemedia/live/13314/52599/52599.pdf>. Accessed Dec 2015.
21. Stein M, Goin M, Pollack M, et al. Practice guideline for the treatment of patients with panic disorder, second edition. American Psychiatric Association; 2009. Available at: http://psychiatryonline.org/data/Books/prac/PanicDisorder_2e_PracticeGuideline.pdf.
22. Koran L, Hanna G, Hollander E, Nestadt G, Simpson H; American Psychiatric Association. Practice guideline for the treatment of patients with obsessive-compulsive disorder. Arlington (VA): American Psychiatric Association, 2007 Jul [cited 2008 Nov 25]. Available from: http://www.psych.org/psych_pract/treatg/pg/OCDPracticeGuidelineFinal05-04-07.pdf.
23. Geller DA, March J, AACAP Committee on Quality Issues. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Obsessive-Compulsive Disorder. American Academy of Child and Adolescent Psychiatry (AACAP). J Am Acad Child Adolesc Psychiatry 2012; 51(1):98-113.
24. Benedek D, Friedman M, Zatzick D, Ursano R. Guideline Watch (March 2009): Practice guideline for the treatment of patients with acute stress disorder and posttraumatic stress disorder. American Psychiatric Association; 2005. Available at: http://psychiatryonline.org/data/Books/prac/AcuteStressDisorder-PTSD_GuidelineWatch.pdf. Accessed Dec 2015.
25. Cohen JA, AACAP Work Group on Quality Issues. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Posttraumatic Stress Disorder. American Academy of Child and Adolescent Psychiatry (AACAP). J Am Acad Child Adolesc Psychiatry 2010;49(4):414-430.
26. American College of Obstetricians and Gynecologists (ACOG). Premenstrual syndrome. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2000:1-9.
27. Yager J, Devlin MJ, Halmi KA, et al. American Psychiatric Association (APA). Practice guidelines for the treatment of patients with eating disorders. Arlington, VA: American Psychiatric Association; 2006 Jun:1-128. [cited 2008 Nov 25]. Available from: http://www.psych.org/psych_pract/treatg/pg/EatingDisorders3ePG_04-28-06.pdf.
28. Claxton A, de Klerk E, Parry M, Robinson JM, Schmidt ME. Patient compliance to a new enteric-coated weekly formulation of fluoxetine during continuation treatment of major depressive disorder. J Clin Psychiatry. 2000 Dec;61(12):928-32.
29. Walsh BT, Seidman SN, Sysko R, et al. Placebo response in studies of major depression: variable, substantial, and growing. JAMA. 2002;287:1840-7.
30. Simon GE, VonKorff M, Heiligenstein JH, et al. Initial antidepressant choice in primary care. Effectiveness and cost of fluoxetine vs tricyclic antidepressants. JAMA. 1996 Jun 26;275(24):1897-902.
31. Simon GE, Heiligenstein J, Revicki D, et al. Long-term outcomes of initial antidepressant drug choice in a "real world" randomized trial. Arch Fam Med. 1999 Jul-Aug;8(4):319-25.
32. Geddes JR, Carney SM, Davies C, et al. Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. Lancet. 2003;361:653-61.
33. Dunner DL, Lipshitz A, Pitts C, Davies JT. Efficacy and tolerability of controlled-release paroxetine in the treatment of severe depression; post hoc analysis of pooled data from a subset of subjects in four double-blind clinical trials. Clin Ther. 2005;27:1901-11.
34. Weihs KL, Settle EC Jr, Batey SR, et al. Bupropion sustained release versus paroxetine for the treatment of depression in the elderly. J Clin Psychiatry. 2000 Mar;61(3):196-202.

35. Kavoussi RJ, Segraves RT, Hughes AR, et al. Double-blind comparison of bupropion sustained release and sertraline in depressed outpatients. *J Clin Psychiatry*. 1997;58(12):532-7.
36. Rocca P, Calvarese P, Faggiano F, Marchiaro L, Mathis F, Rivoira E, Taricco B, Bogetto F. Citalopram versus sertraline in late-life nonmajor clinically significant depression: a 1 year follow-up clinical trial. *J Clin Psychiatry* 2005;66:360-9.
37. Kerber KB, Wisniewski SR, Luther JF, Leuchter AF, D'Empaire I, Trivedi MH, et al. Effects of heart disease on depression treatment: results from the COMED study. *General Hospital Psychiatry*. 2012;34:24-34.
38. Morris DW, Budhwar N, Husain M, Wisniewski SR, Kurian BT, Luther JF, et al. Depression treatment in patients with general medical conditions: results from the CO-MED trial. *Ann Fam Med*. 2012;10:23-33.
39. de Silva VA, Hanwella R. Efficacy and tolerability of venlafaxine vs specific serotonin reuptake inhibitors in treatment of major depressive disorder: a meta-analysis of published studies. *International Clinical Psychopharmacology*. 2012 Jan;27(1):8-16.
40. Moore N, Verdoux H, Fantino B. Prospective, multicentre, randomized, double-blind study of the efficacy of escitalopram versus citalopram in outpatient treatment of major depressive disorder. *Int Clin Psychopharmacol*. 2005 May;20(3):131-7.
41. Lam RW, Andersen HF. The influence of baseline severity on efficacy of escitalopram and citalopram in the treatment of major depressive disorder: an extended analysis. *Pharmacopsychiatry*. 2006 Sep;39(5):180-4.
42. Colonna L, Andersen HF, Reines EH. A randomized, double-blind, 24-week study of escitalopram (10 mg/day) versus citalopram (20 mg/day) in primary care patients with major depressive disorder. *Curr Med Res Opin*. 2005 Oct;21(10):1659-68.
43. Gorman JM, Korotzer A, Su G. Efficacy comparison of escitalopram and citalopram in the treatment of major depressive disorder: pooled analysis of placebo-controlled trials. *CNS Spectr*. 2002 Apr;7(4 Suppl 1):40-4.
44. Boulenger JP, Huusom AK, Florea I, Baekdal T, Sarchiapone M. A comparative study of the efficacy of long-term treatment with escitalopram and paroxetine in severely depressed patients. *Curr Med Res Opin*. 2006 Jul;22(7):1331-41.
45. Ventura D, Armstrong EP, Skrepnek GH, Haim Erder M. Escitalopram versus sertraline in the treatment of major depressive disorder: a randomized clinical trial. *Curr Med Res Opin*. 2007 Feb;23(2):245-50.
46. Mathews M, Gommoll C, Chen D, Nunez R, Khan A. Efficacy and safety of vilazodone 20 and 40 mg in major depressive disorder: a randomized, double-blind, placebo-controlled trial. *Int Clin Psychopharmacol*. 2015 Mar;30(2):67-74.
47. Thase ME, Rush AJ, Howland RH, et al. Double-blind switch study of imipramine or sertraline treatment of antidepressant-resistant chronic depression. *Arch Gen Psychiatr*. 2002;59:233-9.
48. Le Noury J, Nardo JM, Healy D, et al. Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence. *BMJ*. 2015 Sep 16;351:h4320.
49. Versiani M, Moreno R, Ramakers-van Moorsel CJ, Schutte AJ. Comparative Efficacy Antidepressants Study Group. Comparison of the effects of mirtazapine and fluoxetine in severely depressed patients. *CNS Drugs*. 2005;19(2):137-46.
50. Wheatley D, Kremer CME. A randomized, double-blind comparison of mirtazapine and fluoxetine in patients with major depression. *J Clin Psychiatry*. 1998 Jun;59(6):306-12.
51. Behke K, Sogaard J, Martin S, et al. Mirtazapine orally disintegrating tablet versus sertraline. *J Clin Psychopharmacol*. 2003 Aug;23:4.
52. Rossini D, Serretti A, Franchini L, Mandelli L, Smeraldi E, Ronchi DD, Zanardi R. Sertraline versus fluvoxamine in the treatment of elderly patients with major depression. *J Clin Psychopharmacol* 2005;25:471-5.
53. Llorca PM, Azorin JM, Despiegel N, Verpillat P. Efficacy of escitalopram in patient with severe depression: a pooled analysis. *Int J Clin Pract*. 2005 Mar;59(3):268-75.
54. Burke WJ, Gergel I, Bose A. Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients. *J Clin Psychiatry*. 2002;63:331-6.
55. Goldstein DJ, Lu Y, Detke MJ, et al. Duloxetine in the treatment of depression a double-blind placebo-controlled comparison with paroxetine. *J Clin Psychopharmacol*. 2004;24:389-99.
56. Fava M, Hoog SL, Judge RA, Kopp JB, Nilsson ME, Gonzales JS. Acute efficacy of fluoxetine versus sertraline and paroxetine in major depressive disorder including effects of baseline insomnia. *J Clin Psychopharmacol*. 2002;22(2):137-47.
57. Saveanu R, Etkin A, Duchemin AM, et al. The international Study to Predict Optimized Treatment in Depression (iSPOT-D): outcomes from the acute phase of antidepressant treatment. *J Psychiatr Res*. 2015 Feb;61:1-12.
58. Chuang HY, Chang YH, Cheng LY, et al. Venlafaxine, paroxetine and milnacipran for major depressive disorder: a pragmatic 24-week study. *Chin J Physiol*. 2014 Oct 31;57(5):265-70.
59. Cipriani A, Brambilla P, Furukawa T, et al. Fluoxetine versus other types of pharmacotherapy for depression. *Cochrane Database Syst Rev*. 2005 Oct 19;(4):CD004185.
60. Bull SA, Hu XH, Hunkeler EM, et al. Discontinuation of use and switching of antidepressants: influence of patient-physician communication. *JAMA*. 2002 Sep 18;288(11):1403-9.
61. Anderson IM. Selective serotonin reuptake inhibitors versus tricyclic antidepressants: a meta-analysis of efficacy and tolerability. *J Affect Disord*. 2000 Apr;58(1):19-36.
62. MacGillivray S, Arroll B, Hatcher S, et al. Efficacy and tolerability of selective serotonin reuptake inhibitors compared with tricyclic antidepressants in depression treated in primary care: systematic review and meta-analysis. *BMJ*. 2003;326:1014-9.
63. Steffens DC, Ranga K, Krishnan MD, et al. Are SSRIs better than TCAs? Comparison of SSRIs and TCAs: a meta-analysis. *Depress Anxiety*. 1997;6:10-8.
64. Davidson JR, Bose A, Wang Q. Safety and efficacy of escitalopram in the long-term treatment of generalized anxiety disorder. *J Clin Psychiatry* 2005;66:1441-6.
65. Goodman WK, Bose A, Wang Q. Treatment of generalized anxiety disorder with escitalopram: pooled results from double-blind, placebo-controlled trials. *J Affect Disord*. 87;2005:161-7.
66. Dahl AA, Ravindran A, Allgulander C, Kutcher SP, Austin C, Burt T. Sertraline in generalized anxiety disorder: efficacy in treatment in psychic and somatic anxiety factors. *Acta Psychiatr Scand* 2005;111:429-35.

67. Bielski RJ, Bose A, Chang CC. A double-blind comparison of escitalopram and paroxetine in the long-term treatment of generalized anxiety disorder. *Ann Clin Psychiatry*. 2005 Apr;17(2):65-9.
68. Ball S, Kuhn A, Wall D, Shekhar A, Goddard AW. Selective serotonin reuptake inhibitor for generalized anxiety disorder: a double-blind, prospective comparison between paroxetine and sertraline. *J Clin Psychiatry* 2005;66:94-9.
69. Schmitt R, Gazalle FK, Lima MS, Cunha A, Souza J, Kapczinski F. The efficacy of antidepressants for generalized anxiety disorder: a systematic review and meta-analysis. *Rev Bras Psiquiatr*. 2005 Mar;27(1):18-24.
70. Mundo E, Bianchi L, Bellodi L. Efficacy of Fluvoxamine, paroxetine, and Citalopram in the treatment of obsessive-compulsive disorder: A single-blind study. *J Clin Psychopharmacol*. 1997;17(4):267-71.
71. Sheehan DV, Burnham DB, Iyengar MK, Perea P. Efficacy and tolerability of controlled-release paroxetine in the treatment of panic disorder. *J Clin Psychiatry* 2005;66:34-40.
72. Stahl SM, Gergel I, Li D. Escitalopram in the treatment of panic disorder: a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry*. 2003 Nov;64(11):1322-7.
73. Rampello L, Alvano A, Raffaele R, Malaguarnera M, Vecchio I. New possibilities of treatment for panic attacks in elderly patients: escitalopram versus citalopram. *J Clin Psychopharmacol*. 2006 Feb;26(1):67-70.
74. Bandelow B, Behnke K, Lenoir S, et al. Sertraline versus paroxetine in the treatment of panic disorder: An acute, double-blind noninferiority comparison. *J Clin Psych*. 2004;65(3):405-13.
75. Ballenger JC, Wheadon DE, Steiner M, Bushnell W, Gergel IP. Double-blind, fixed-dose, placebo-controlled study of paroxetine in the treatment of panic disorder. *Am J Psychiatry*. 1998;155:36-42.
76. Davidson JR, Connor KM, Hertzberg MA, Weisler RH, Wislon WH, Payne VM. Maintenance therapy with fluoxetine in posttraumatic stress disorder. *J Clin Psychopharmacol* 2005;25:166-9.
77. Friedman MJ, Marmar CR, Baker DG, Sikes CR, Farfel GM. Randomized, double-blind comparison of sertraline and placebo for posttraumatic stress disorder in a department of veterans affairs setting. *J Clin Psychiatry* 2007;61:711-20.
78. Pearlstein TB, Bellew KM, Endicott J, Steiner M. Paroxetine controlled release for premenstrual dysphoric disorder: Remission analysis following a randomized, double-blind, placebo-controlled trial. *Prim Care Companion J Clin Psychiatry*. 2005;7:53-60.
79. Steiner M, Hirschberg AL, Bergeron R, Holland F, Gee M, Van Erp E. Luteal phase dosing with paroxetine controlled release in the treatment of premenstrual dysphoric disorder. *Am J Obstet Gynecol*. 2005;193:352-60.
80. Yonkers KA, Kornstein SG, Gueorguieva R, Merry B, Van Steenburgh K, Altemus M. Symptom-Onset Dosing of Sertraline for the Treatment of Premenstrual Dysphoric Disorder: A Randomized Clinical Trial. *JAMA Psychiatry*. 2015 Oct;72(10):1037-44.
81. Mullins CD, Shaya FT, Meng F, Wang J, Harrison D. Persistence, switching, and discontinuation rates among patients receiving sertraline, paroxetine, and citalopram. *Pharmacotherapy*. 2005;25(5):660-7.
82. Stein DJ, Ipser JC, van Balkom AJ. Pharmacotherapy for social anxiety disorder. *Cochrane Database Syst Rev*. 2000 (4):CD001206. doi: 10.1002/14651858.CD001206.pub2.