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

<table>
<thead>
<tr>
<th>Generic (Trade Name)</th>
<th>Food and Drug Administration Approved Indications</th>
<th>Dosage Form/Strength</th>
<th>Generic Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram (Celexa®)</td>
<td>Depression (includes major depressive disorder),</td>
<td>Solution: 10 mg/5 mL</td>
<td>✔</td>
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<tr>
<td></td>
<td></td>
<td>Tablet: 10 mg, 20 mg, 40 mg</td>
<td></td>
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<tr>
<td>Escitalopram (Lexapro®)</td>
<td>Depression (includes major depressive disorder), generalized anxiety disorder,</td>
<td>Solution: 5 mg/5 mL</td>
<td>✔</td>
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<td></td>
<td></td>
<td>Tablet: 5 mg, 10 mg, 20 mg</td>
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<tr>
<td>Fluoxetine (Prozac®, Prozac Weekly®)</td>
<td>Bulimia nervosa, depression (includes major depressive disorder), obsessive-compulsive disorder, panic disorder,</td>
<td>Delayed-release capsule: 90 mg</td>
<td>✔</td>
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<tr>
<td></td>
<td></td>
<td>Immediate-release capsule:</td>
<td></td>
</tr>
<tr>
<td>Generic (Trade Name)</td>
<td>Food and Drug Administration Approved Indications</td>
<td>Dosage Form/Strength</td>
<td>Generic Availability</td>
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<tr>
<td>Sarafem®</td>
<td>premenstrual dysphoric disorder,</td>
<td>10 mg, 20 mg, 40 mg</td>
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<td></td>
<td></td>
<td>Immediate-release tablet: 10 mg, 20 mg, 60 mg</td>
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<td></td>
<td></td>
<td>Solution: 20 mg/5 mL</td>
<td></td>
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<tr>
<td>Fluvoxamine</td>
<td>Obsessive-compulsive disorder,</td>
<td>Extended release capsule: 100 mg, 150 mg</td>
<td></td>
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<tr>
<td>(Luvox®, Luvox® CR)</td>
<td></td>
<td>Immediate release tablet: 25 mg, 50 mg, 100 mg</td>
<td>checkmark</td>
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<tr>
<td>Paroxetine hydrochloride (Paxil®, Paxil CR®)</td>
<td>Depression (includes major depressive disorder), generalized anxiety disorder*, obsessive-compulsive disorder*, panic disorder, premenstrual dysphoric disorder†, posttraumatic stress disorder*, social anxiety disorder</td>
<td>Extended release tablet: 12.5 mg, 25 mg, 37.5 mg</td>
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<tr>
<td></td>
<td></td>
<td>Suspension, oral: 10 mg/5 mL</td>
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<tr>
<td></td>
<td></td>
<td>Immediate release tablet: 10 mg, 20 mg, 30 mg, 40 mg</td>
<td>checkmark</td>
</tr>
<tr>
<td>Paroxetine mesylate (Brisdelle®, Pexeva®)</td>
<td>Depression (includes major depressive disorder), obsessive-compulsive disorder, panic disorder, vasomotor symptoms associated with menopause; (moderate to severe)¶</td>
<td>Immediate release capsule: 7.5 mg</td>
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<td></td>
<td></td>
<td>Immediate release tablet: 10 mg, 20 mg, 30 mg, 40 mg</td>
<td>checkmark</td>
</tr>
<tr>
<td>Sertraline (Zoloft®)</td>
<td>Depression (includes major depressive disorder), obsessive-compulsive disorder, panic disorder, premenstrual dysphoric disorder, posttraumatic stress disorder, social anxiety disorder</td>
<td>Oral concentrate: 20 mg/mL</td>
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<td></td>
<td></td>
<td>Tablet: 25 mg, 50 mg, 100 mg</td>
<td>checkmark</td>
</tr>
</tbody>
</table>

*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.\textsuperscript{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).\textsuperscript{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.\textsuperscript{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).\textsuperscript{31}
- A meta-analysis evaluated venlafaxine compared to SSRIs in treatment of major depressive disorder. Using a random effect model showed that venlafaxine was 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).\textsuperscript{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.\textsuperscript{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.\textsuperscript{18-27}
  - Antidepressants are recommended as first-line treatment for GAD, with the following agents considered treatment options: SSRIs, SNRIs, and nonsedating tricyclic antidepressants (TCAs).\textsuperscript{38}
- Other Key Facts:
  - Fluoxetine is the only agent within the class that carries indications for treating bulimia nervosa, while Brisdelle\textsuperscript{®} (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.\textsuperscript{1-16}
Therapeutic Class Overview: selective serotonin reuptake inhibitors

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