

## SERTRALINE: HOT FLASHES (WOMEN)

Drug	Off-Label Use	Evidence	Documentation
Sertraline (eg, Zoloft)	<ul style="list-style-type: none"><li>■ Indication</li><li><input type="checkbox"/> Dose</li><li><input type="checkbox"/> Route/Dosage Form</li><li><input type="checkbox"/> Population</li></ul>	<ul style="list-style-type: none"><li>■ Controlled Trials</li><li><input type="checkbox"/> Noncontrolled Trials</li><li><input type="checkbox"/> Guidelines</li><li><input type="checkbox"/> Case Reports</li><li><input type="checkbox"/> Other</li></ul>	<b>5</b>

1=GOOD 2=FAIR 3=SAFETY CONCERNS 4=INSUFFICIENT 5=POOR

**Background:** Hot flashes often occur during and after menopause (either spontaneous or surgically induced) and in breast cancer survivors. Although the etiology of hot flashes is multifactorial, decreased estrogen levels may play a role in lowering serotonin levels.<sup>1</sup> Although hot flashes are not life-threatening, they can be disruptive and may affect ability to function and quality of life. Estrogens have been widely used to treat vasomotor symptoms associated with menopause, but alternative therapies are often needed for women with positive estrogen-receptor breast cancer. In addition, recent information regarding the benefit-risk ratio of estrogens in postmenopausal therapy has caused many clinicians to examine alternative therapies. Other serotonin reuptake inhibitors have also been used to treat hot flashes (see Venlafaxine: Hot Flashes; Paroxetine: Hot Flashes; Fluoxetine: Hot Flashes).

### Study Design:

*Controlled trials –*

*Hot flashes in breast cancer survivors:* One randomized, double-blind, placebo-controlled, crossover trial: 62 patients.

*Menopausal hot flashes:* One randomized, double-blind, placebo-controlled, parallel group trial: 99 post- and perimenopausal women.

One randomized, double-blind, placebo-controlled, crossover trial: 199 post- and perimenopausal women.

**Patient Population:** Breast cancer survivors or menopausal women.

### Dosage and Duration:

*Breast cancer patients –* 50 mg daily.

*Menopausal patients –* 50 to 100 mg daily.

**Results:** The use of sertraline in the treatment of hot flashes has been limited to one randomized trial in patients with breast cancer and 3 controlled trials in menopausal women. Data on the treatment of hot flashes of both etiologies is variable.

*Breast cancer patients –* In a double-blind, placebo-controlled, crossover trial, there was no difference between sertraline and placebo in the percentage of women who had at least a 50% reduction in hot flash frequency at the end of the first treatment period (36% vs 27%;  $P = 0.7$ ). However, significantly more patients in the sertraline group preferred sertraline treatment compared with placebo (56% vs 17%;  $P = 0.003$ ); approximately 28% had no preference. Each treatment phase lasted 6 weeks without a washout period in between. At 12 weeks, patients who received sertraline first and crossed over to placebo had a 1% change in hot flash frequency compared with levels at 6 weeks. Although there was no statistically significant difference in hot flash frequency and score at 6 and 12 weeks when compared with baseline, women crossing from placebo to sertraline had a decrease in hot flash frequency and score, whereas those who crossed from sertraline to placebo had an increase. No woman had total resolution of hot flashes. Measures of depression and quality of life were within normal levels and did not change significantly between the treatment groups.<sup>2</sup>

*Menopausal women –* Variable results were also noted in 3 controlled trials evaluating the use of sertraline in women with menopause-related hot flashes. Although one controlled cross-over study demonstrated a significant reduction in the median number of hot flashes with sertraline and, thus, an improvement in the overall hot flash score (severity  $\times$  frequency), there was no difference between sertraline and placebo in the severity of flashes.<sup>3</sup>

In another controlled crossover trial of 102 postmenopausal women not taking hormonal therapy, there was a substantial variability in response to treatment. Although both sertraline and placebo significantly reduced the severity of hot flashes when compared with baseline, there was no difference between the 2 groups. The percentage of reduction in hot flashes was not related to the number of hot flashes at baseline but to a reduction in their reported severity, and only in women with clinically significant reduction. Possible factors associated with this vigorous reduction included a higher level of education, increased activity level, and menstrual status (more than 1 year postmenopause).<sup>4</sup>

In an additional controlled trial in 99 adult peri- or postmenopausal women experiencing at least 14 hot flashes per week, sertraline was not more effective than placebo in relieving severity or frequency and was associated with more side effects, including decreased sexual function.<sup>5</sup>

**Safety:** In the limited number of studies to date, the most commonly cited side effects have included dry mouth, nausea, sexual dysfunction, gastro-

intestinal symptoms, headache, and upper respiratory infection. Although it does not appear that the side effect profile demonstrated in these studies is different than the expected side effects when sertraline is used for the treatment of depression, it should be noted that the product labeling for antidepressants, including sertraline, has recently been revised to include a black box warning regarding a possible increased risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults with major depressive disorders and other psychiatric disorders.<sup>6</sup>

**Therapy Considerations:** Initial data suggest that there is a varied response to the use of sertraline in the management of hot flashes related to tamoxifen use in breast cancer patients or to menopausal changes. At this time, several other drugs in this class have demonstrated better efficacy for this use.

Summary of the Clinical Literature on the Use of Sertraline for the Treatment of Hot Flashes in Women

Citation	Indication	Study design	Patient population/profile	Drug (Route) Dose (Duration)	Results	Safety	Author conclusions																																																								
<b>Breast cancer therapy</b>																																																															
Kimmick, et al. 2006 <sup>2</sup>	Hot flashes associated with tamoxifen in breast cancer patients	Randomized Double-blind Placebo-controlled Crossover	<p>62 adult breast cancer patients who were receiving adjuvant tamoxifen therapy and having at least 1 hot flash/day or more than 7 per week</p> <p>MAOI and SSRI use discontinued 14 d prior to study enrollment.</p> <p><i>Sertraline: 33 patients</i> Median age: 56.7 y (range, 36.6 to 77 y) Postmenopausal: 84.8% Mean BSL hot flashes: Per day: 6.1 Score: 12.8</p> <p><i>Placebo: 29 patients</i> Median age: 52.3 y (range, 41.1 to 77.1 y) Postmenopausal: 93.1% Mean BSL hot flashes: Per day: 5.5 Score: 11.2</p>	<p><b>Sertraline (PO):</b> 50 mg every morning × 6 wk</p> <p>or</p> <p><b>Placebo (PO):</b> Each morning × 6 wk</p> <p><i>Study design</i></p> <p>BSL assessment: 1 wk Treatment 1: 6 wk Treatment 2: 6 wk</p> <p>No washout period provided.</p>	<p><i>Clinical outcomes:</i></p> <p>Patient completors</p> <table border="1"> <tr><td>Enrolled</td><td>62</td></tr> <tr><td>Baseline assessment</td><td>54</td></tr> <tr><td>First 6-wk period</td><td>47</td></tr> <tr><td>Both 6-wk periods</td><td>39</td></tr> </table> <p><u>Mean data</u></p> <table border="1"> <tr><td>50% reduction in hot flash frequency at the end of first treatment period<sup>a</sup></td><td>SER</td><td>PLB</td></tr> <tr><td></td><td>36%</td><td>27%</td></tr> <tr><td>Patient rated as best<sup>b</sup> (28% had no preference)</td><td>56%</td><td>17%</td></tr> </table> <p>At 12 wk, patients who received sertraline first and crossed over to placebo had a 1% change in hot flash frequency compared with level at 6 wk.</p> <p>Although there was no statistically significant difference in hot flash frequency and score at 6 and 12 wk when compared with baseline, the authors stated that women crossing from placebo to sertraline had a decrease in hot flash frequency and score, whereas those who crossed from sertraline to placebo had an increase. No woman had total resolution of hot flashes.</p> <p>Measures of depression and quality of life were within normal levels and did not change significantly within the treatment groups.</p> <p><sup>a</sup><i>P</i> = 0.7; SER vs PLB <sup>b</sup><i>P</i> = 0.003; SER vs PLB</p>	Enrolled	62	Baseline assessment	54	First 6-wk period	47	Both 6-wk periods	39	50% reduction in hot flash frequency at the end of first treatment period <sup>a</sup>	SER	PLB		36%	27%	Patient rated as best <sup>b</sup> (28% had no preference)	56%	17%	<p><i>ADR profile:</i></p> <table border="1"> <tr><td><u>ADR</u></td><td><u>PLB</u></td><td><u>SER</u></td></tr> <tr><td>Nausea</td><td>2</td><td>7</td></tr> <tr><td>Heartburn</td><td>1</td><td>1</td></tr> <tr><td>Fatigue/malaise</td><td>0</td><td>3</td></tr> <tr><td>Diarrhea</td><td>0</td><td>5</td></tr> <tr><td>Anxiety</td><td>0</td><td>3</td></tr> <tr><td>Constipation</td><td>2</td><td>1</td></tr> <tr><td>Abdominal cramps</td><td>1</td><td>1</td></tr> <tr><td>Dry mouth</td><td>0</td><td>1</td></tr> <tr><td>Headache</td><td>1</td><td>1</td></tr> <tr><td>Insomnia</td><td>0</td><td>0</td></tr> <tr><td>Weight gain</td><td>0</td><td>0</td></tr> <tr><td>Loss of appetite</td><td>1</td><td>0</td></tr> </table>	<u>ADR</u>	<u>PLB</u>	<u>SER</u>	Nausea	2	7	Heartburn	1	1	Fatigue/malaise	0	3	Diarrhea	0	5	Anxiety	0	3	Constipation	2	1	Abdominal cramps	1	1	Dry mouth	0	1	Headache	1	1	Insomnia	0	0	Weight gain	0	0	Loss of appetite	1	0	Sertraline decreased hot flashes in breast cancer survivors taking tamoxifen and women preferred sertraline to placebo.
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## Summary of the Clinical Literature on the Use of Sertraline for the Treatment of Hot Flashes in Women

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<i>Menopausal hot flashes</i>							
Kerwin, et al. 2007 <sup>4</sup>  <i>Sponsored by manufacturer</i>	Menopausal hot flashes	Randomized Double-blind Placebo-controlled Crossover	102 adult postmenopausal women having hot flashes and not taking hormonal therapy	<b>Sertraline (PO):</b> 50 mg daily × 4 wk  or <b>Placebo (PO):</b> daily × 4 wk  <b>Study design</b> BSL assessment: 1 wk Treatment 1: 4 wk Washout: 1 wk Treatment 2: 4 wk	<i>Clinical outcomes:</i>  Study completors 87  <u>Change in hot flashes from BSL in median severity</u> Reductions Clinically significant (≥ 30%) <sup>a,b</sup> 2.1 1.6 1.5 Nonsignificant (< 30% to 0) 2.2 2 1.8 Increase (0 to 100%) 1.7 1.6 1.8  <sup>a</sup> <i>P</i> = 0.002; BSL vs PLB <sup>b</sup> <i>P</i> < 0.001; BSL vs SER  There was a substantial variability in response to treatment. The percentage of reduction in hot flashes was not related to the number of hot flashes at baseline but to a reduction in the reported severity of hot flashes at baseline, but only in the women who had clinically significant reductions. Possible factors associated with vigorous reduction in hot flashes included a higher level of education, increased activity level, and menstrual status (> 1 y postmenopause).	<i>ADR profile:</i>  ADR data not provided.	This study demonstrated that the treated population had a varied response to treatment.

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Grady, et al. 2007 <sup>5</sup>	Menopausal hot flashes	Randomized Double-blind Placebo-controlled	<p>99 adult women who were either perimenopausal or postmenopausal and had at least 14 hot flashes/week</p> <p><i>Sertraline: 50 patients</i> Mean age: 50.5 y Time since menopause: 3.9 y BDI score: 6 Estrogen use: 2.5 y PSQI: 8.7</p> <p><i>Placebo: 49 patients</i> Mean age: 52.6 y Time since menopause: 3.1 y BDI score: 5.1 Estrogen use: 1.5 y PSQI: 8.3</p>	<p><b>Sertraline (PO):</b> Weeks 1 to 2: 50 mg daily If no side effects, then Weeks 3 to 6: 100 mg daily</p> <p>or</p> <p><b>Placebo (PO):</b> Daily × 6 wk</p>	<p><i>Clinical outcomes:</i></p> <p><i>Primary outcome</i> Percentage change in mean daily hot flash frequency and score from baseline to 6 wk.</p> <p><i>Secondary outcomes</i> Change in scores for quality of life, menopausal symptoms, sleep quality, sexual function, mood, and side effects.</p> <table border="1"> <thead> <tr> <th>Mean daily data</th> <th>SER</th> <th>PLB</th> </tr> </thead> <tbody> <tr> <td>Hot flashes/day<sup>a</sup></td> <td></td> <td></td> </tr> <tr> <td>BSL</td> <td>8.6</td> <td>9.3</td> </tr> <tr> <td>Week 2</td> <td></td> <td></td> </tr> <tr> <td>Mean</td> <td>6.6</td> <td>7.8</td> </tr> <tr> <td>Mean % change</td> <td>-22.1</td> <td>-18.5</td> </tr> <tr> <td>Week 6</td> <td></td> <td></td> </tr> <tr> <td>Mean</td> <td>5.1</td> <td>5.8</td> </tr> <tr> <td>Mean % change</td> <td>-39.01</td> <td>-38.3</td> </tr> <tr> <td>Hot flash score<sup>a</sup></td> <td></td> <td></td> </tr> <tr> <td>BSL</td> <td>16.4</td> <td>18.4</td> </tr> <tr> <td>Week 2</td> <td></td> <td></td> </tr> <tr> <td>Mean</td> <td>11.7</td> <td>14.4</td> </tr> <tr> <td>Mean % change</td> <td>-25.4</td> <td>-23</td> </tr> <tr> <td>Week 6</td> <td></td> <td></td> </tr> <tr> <td>Mean</td> <td>8.8</td> <td>10.3</td> </tr> <tr> <td>Mean % change</td> <td>-42.2</td> <td>-40.6</td> </tr> <tr> <td>Mean score changes</td> <td>SER</td> <td>PLB</td> </tr> <tr> <td>GCS</td> <td>-0.7</td> <td>-1</td> </tr> <tr> <td>MOSSF-36 QOL</td> <td></td> <td></td> </tr> <tr> <td>Physical component<sup>b</sup></td> <td>-2.3</td> <td>0.8</td> </tr> <tr> <td>Mental component</td> <td>0.1</td> <td>-0.3</td> </tr> <tr> <td>PSQI</td> <td>-1.2</td> <td>-1.3</td> </tr> <tr> <td>FSFI<sup>c</sup></td> <td>-2.2</td> <td>2.4</td> </tr> </tbody> </table> <p><sup>a</sup>P = NS; SER vs PLB <sup>b</sup>P = 0.05; SER vs PLB <sup>c</sup>P = 0.001; SER vs PLB</p>	Mean daily data	SER	PLB	Hot flashes/day <sup>a</sup>			BSL	8.6	9.3	Week 2			Mean	6.6	7.8	Mean % change	-22.1	-18.5	Week 6			Mean	5.1	5.8	Mean % change	-39.01	-38.3	Hot flash score <sup>a</sup>			BSL	16.4	18.4	Week 2			Mean	11.7	14.4	Mean % change	-25.4	-23	Week 6			Mean	8.8	10.3	Mean % change	-42.2	-40.6	Mean score changes	SER	PLB	GCS	-0.7	-1	MOSSF-36 QOL			Physical component <sup>b</sup>	-2.3	0.8	Mental component	0.1	-0.3	PSQI	-1.2	-1.3	FSFI <sup>c</sup>	-2.2	2.4	<p><i>ADR profile:</i></p> <table border="1"> <thead> <tr> <th>ADRs</th> <th>SER</th> <th>PLB</th> </tr> </thead> <tbody> <tr> <td>URI</td> <td>19</td> <td>14</td> </tr> <tr> <td>GI</td> <td>19</td> <td>12</td> </tr> <tr> <td>Headache</td> <td>11</td> <td>11</td> </tr> <tr> <td>Dry mouth<sup>a</sup></td> <td>10</td> <td>1</td> </tr> <tr> <td>Fatigue</td> <td>7</td> <td>5</td> </tr> <tr> <td>Mood change</td> <td>7</td> <td>4</td> </tr> <tr> <td>Dizziness</td> <td>7</td> <td>1</td> </tr> <tr> <td>Pain</td> <td>5</td> <td>4</td> </tr> <tr> <td>Decreased libido</td> <td>4</td> <td>0</td> </tr> <tr> <td>Insomnia</td> <td>4</td> <td>1</td> </tr> <tr> <td>Rash</td> <td>3</td> <td>5</td> </tr> </tbody> </table> <p><sup>a</sup>P = 0.005; SER vs PLB</p>	ADRs	SER	PLB	URI	19	14	GI	19	12	Headache	11	11	Dry mouth <sup>a</sup>	10	1	Fatigue	7	5	Mood change	7	4	Dizziness	7	1	Pain	5	4	Decreased libido	4	0	Insomnia	4	1	Rash	3	5	When compared with placebo, sertraline was not more effective in relieving the severity and frequency of hot flashes in peri- and postmenopausal women.
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Gordon, et al. 2006 <sup>3</sup>	Menopausal hot flashes	Randomized Double-blind Placebo-controlled Crossover	97 adult women having hot flashes who were not receiving hormonal therapy  Mean age: 52.6 y Mean number of hot flashes/week: 47.3 Median severity of hot flashes at BSL: 2	<b>Sertraline (PO):</b> 50 mg daily × 4 wk  or  <b>Placebo (PO):</b> daily × 4 wk  <u>Study design</u> BSL assessment: 1 wk Treatment 1: 4 wk Washout period: 1 wk Treatment 2: 4 wk	<i>Clinical outcomes:</i>  Ten patients dropped out prior to completion of the study.  <u>Median hot flash score</u> BSL 81 Sertraline phase <sup>a</sup> 42 Placebo phase 57  <sup>a</sup> <i>P</i> = 0.001; SER vs PLB  The severity of hot flashes was not significantly different between the 2 groups.	<i>ADR profile:</i>  During the first week of active treatment, 49% of the sertraline group experienced some nausea compared with 19% of patients on placebo ( <i>P</i> < 0.001). The proportion experiencing nausea declined in subsequent weeks: week 2 (24%), week 3 (16%), and week 4 (19%). Weeks 2 through 4 were not significantly different than rates for placebo. There was no significant difference between active drug and placebo for sexual functioning or libido.	Sertraline reduced the number of hot flashes and improved hot flash score when compared with placebo.

**ABBREVIATIONS****BDI** = Beck Depression Inventory**FSFI** = Female Sexual Function Index**GCS** = Greene Climacteric Scale**MAOI** = monoamine oxidase inhibitor**MOSSF-36 QOL** = Medical Outcomes Study Short Form Health Survey**PSQI** = Pittsburgh Sleep Quality Index**SER** = sertraline**SSRI** = selective serotonin reuptake inhibitor**URI** = upper respiratory infection**SCALES****Beck Depression Inventory:** A 21-item scale to detect depressive features. Each item is ranked on a scale of zero to 4. A score less than 10 = no depression, 10 to 16 = mild depression, 17 to 29 = moderate depression, and 30 to 60 = severe depression.**Female Sexual Function Index:** A 19-question assessment tool that assesses desire, arousal, lubrication, orgasm, satisfaction, and pain. Minimum score is 2 (worst) and maximum score is 36 (best).**Greene Climacteric Scale:** A 21-item scale used to assess core menopausal symptom severity, including hot flashes, night sweats, somatic symptoms, and sexual interest, with a score that ranges from 0 (best) to 63 (worst).**Hot Flash score:** The number of hot flashes per week and average severity multiplied to calculate the hot flash score for the week.**Hot Flash Severity:** A 4-point scale used to assess severity of hot flashes. 1 = mild, 2 = moderate, 3 = severe, and 4 = very severe.**Mean Daily Hot Flash score:** Sum of all severity scores for all hot flashes divided by the number of hot flashes.**Pittsburgh Sleep Quality Index:** A 19-item scale that assesses sleep patterns, quality, and disturbances over a 1-month time frame, with a score that ranges from 0 (best) to 3 (worst).**Short Form Health Survey-36:** A 36-question survey that assesses physical and mental health, each with a score that ranges from 0 (worst) to 100 (best).**REFERENCES**<sup>1</sup> Shaver JL. Beyond hormonal therapies in menopause. *Exp Gerontol.* 1994;29(3-4):469-476.<sup>2</sup> Kimmick GG, Lovato J, McQuellon R, Robinson E, Muss HB. Randomized, double-blind, placebo-controlled, crossover study of sertraline (*Zoloft*) for the treatment of hot flashes in women with early stage breast cancer taking tamoxifen. *Breast J.* 2006;12(2):114-122.

- <sup>3</sup> Gordon PR, Kerwin JP, Boesen KG, Senf J. Sertraline to treat hot flashes: a randomized, controlled, double-blind, crossover trial in a general population. *Menopause*. 2006;13(4):568-575.
- <sup>4</sup> Kerwin JP, Gordon PR, Senf JH. The variable response of women with menopausal hot flashes when treated with sertraline. *Menopause*. 2007;14(5):1-5.
- <sup>5</sup> Grady D, Cohen B, Tice J, Kristof M, Olyaie A, Sawaya GF. Ineffectiveness of sertraline for treatment of menopausal hot flushes: a randomized controlled trial. *Obstet Gynecol*. 2007;109(4):823-830.
- <sup>6</sup> US Food and Drug Administration. Center for Drug Evaluation and Research. Antidepressant use in children, adolescents, and adults. <http://www.fda.gov/cder/drug/antidepressants/default.htm>. Published March 22, 2004. Updated May 2, 2007. Accessed July 10, 2007.
- Carpenter JS, Andrykowski MA, Cordova M, et al. Hot flashes in postmenopausal women treated for breast carcinoma: prevalence, severity, correlates, management, and relation to quality of life. *Cancer*. 1998;82(9):1682-1691.
- Charig CR, Rundle JS. Flushing. Long-term side effect of orchiectomy in treatment of prostatic carcinoma. *Urology*. 1989;33(3):175-178.
- Fugate SE, Church CO. Nonestrogen treatment modalities for vasomotor symptoms associated with menopause. *Ann Pharmacother*. 2004;38(9):1482-1499.
- Nelson HD, Vesco KK, Haney E, et al. Nonhormonal therapies for menopausal hot flashes: systematic review and meta-analysis. *JAMA*. 2006;295(17):2057-2071.
- North American Menopause Society. Treatment of menopause associated vasomotor symptoms: position statement of The North American Menopause Society. *Menopause*. 2004;11(1):11-33.
- Sicat BL, Brokaw DK. Nonhormonal alternatives for the treatment of hot flashes. *Pharmacotherapy*. 2004;24(1):79-93.

### SUGGESTED READINGS

Berendsen HH. The role of serotonin in hot flushes. *Maturitas*. 2000;36(3):155-164.