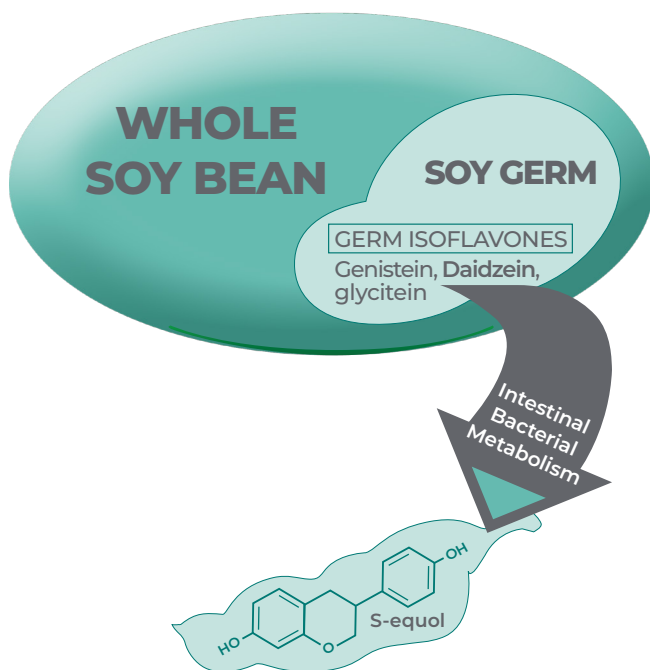


EQUELLE®

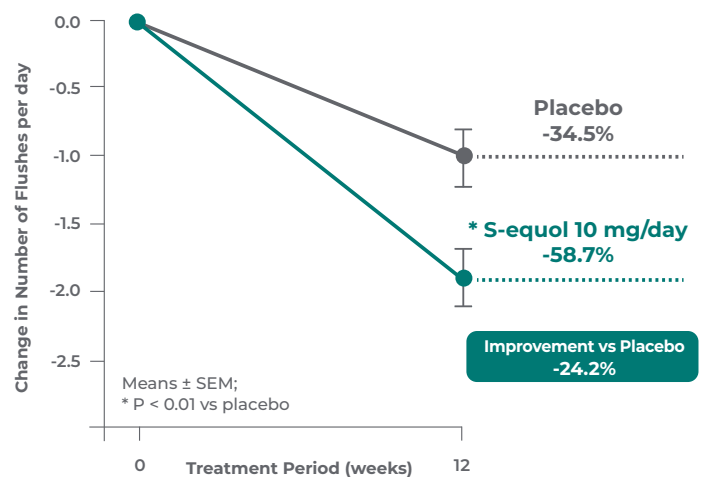
Efficacy of **S-equol** for Menopausal Symptom Relief†

Women want effective and safe options to manage their menopausal symptoms. A new option backed by basic science and controlled clinical studies is EQUELLE, a supplement that contains the soy-based compound called S-equol. A naturally fermented soy germ based ingredient, S-equol provides relief by reducing the frequency of hot flashes and muscle discomfort among post-menopausal women.† S-equol is a metabolite of the soy isoflavone daidzein that 20-30% of American women produce naturally. S-equol is currently being studied as a dietary supplement for menopausal symptom relief for the 70-80% of women who can not produce S-equol naturally.

Conversion from Soy Germ to S-equol



Reduction of Hot Flash Frequency



S-equol has been studied in double blind placebo controlled trials among menopausal women. S-equol significantly reduced frequency of hot flashes when given as a daily 10mg dose for 12 weeks.¹

Women taking a daily oral dose of 10mg (BID) of S-equol reduced their frequency of hot flashes by 58.7% after 12 weeks of treatment, significantly more than the 34.5% reduction experienced in women receiving a placebo (p=0.0092).¹

S-equol is rapidly absorbed and attains optimal concentrations in the blood stream, providing very high systemic bioavailability.

Takeshi Aso, et. al "A Natural S-Equol supplement alleviates hot flashes and other menopausal symptoms in Equol non-producer postmenopausal Japanese women." J Women's Health; January 2012.

EQUELLE is manufactured by Pharmavite® the makers of Nature Made®

† These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Safety of **S-equol** & Soy/Soy Isoflavones for Menopausal Symptom Relief

To date, no study shows that S-equol stimulates breast tumor growth and/or increases breast density and negatively affects endometrial health.

Soy/soy isoflavones safety evidence and breast health

- In a two year soy isoflavone intervention study in post menopausal women (n=135 per group), given 80 mg/day or 120 mg/day there were no differences in mammographic measures between the treatment groups and placebo.²
- 70 mg/day soy isoflavones for three years (n=235) also did not show any notable change in mammographic density from baseline in postmenopausal women.³
- Epidemiological data and meta-analyses of clinical trials in both Asian and Western populations conclude that soy isoflavones do not increase breast cancer incidence. Breast tissue in women consuming soy foods is less dense.^{4,5}

Soy/soy isoflavones safety evidence and breast cancer survivors

- A cohort study in US breast cancer survivors (N=3,088) showed a significant trend toward lower mortality as soy isoflavone intake increased.⁶
- An epidemiological study (N=5,042) in Chinese breast cancer survivors demonstrated that soy consumption was associated with decreased risk of death and no increased risk in recurrence of breast cancer, in both ER-positive and ER-negative women and in both tamoxifen users and nonusers.⁷

Soy/soy isoflavones safety evidence and endometrial health

- In a two year soy isoflavone (80mg/day or 120mg/day) intervention study (n=135 per group), soy isoflavones did not affect endometrial thickness.⁸
- 70mg/day soy isoflavones for three years (n=235) did not change endometrial thickness in postmenopausal women.³
- A case-control study suggests no increased risk of endometrial cancer associated with higher consumption of phytoestrogens, observed at levels commonly consumed in the typical American diet.⁹

S-equol safety evidence and breast health

- S-equol 10 or 30mg/day for 12 weeks did not increase breast density in post menopausal women.¹⁰
- Both SE5-OH* and purified S-equol from SE5-OH* alone did not cause tumor proliferation in the athymic mouse model using MCF-7 cell.¹¹
- R/S-Equol did not stimulate the growth of estrogen-dependent human breast tumor cell (MCF-7) growth in athymic mice.¹²
- S-equol did not stimulate tumors in the chemically induced mammary carcinogenesis in rats.¹³

S-equol evidence and endometrial health

- S-equol 10 or 30mg/day for 12 weeks did not increase endometrial thickness in post menopausal women.¹⁰
- Both SE5-OH* and pure S-equol did not affect uterine epithelial thickness or weight in ovariectomized rats.¹⁴
- S-equol did not affect uterine weight in the chemically induced mammary carcinogenesis in rats.¹³

**SE5-OH is the product of fermentation of soy germ by the bacterial strain Lactococcus 20-92 using a patented and proprietary process by Otsuka Pharmaceutical Co., Ltd.*

1. Aso T, Uchiyama S, Matsumura Y, et al. J Womens Health 2012; 21:92-100. 2. Maskarinec G, Verheus M, Steinberg FM, et al. J Nutr 2009;139:981-6.3. Palacios S, et al. Climacteric 2010;13:368-75. 4. Peeters PH, et al. Breast Cancer Res Treat 2003;77:171-83. 5. Trock BJ, et al. J Natl Cancer Inst 2006;98:459-71. 6. Caan BJ, Natarajan L, Parker B, et al. Cancer Epidemiol Biomarkers Prev 2011;20:854-8. 7. Shu XO, Zheng Y, Cai H, et al. Jama 2009;302:2437-43. 8. Steinberg FM, Murray MJ, Lewis RD, et al. Am J Clin Nutr 2011;93:356-67. 9. Horn-Ross PL, et al. J Natl Cancer Inst 2003;95:1158-64. 10. Oyama A, Ueno T, Uchiyama S, et al. Menopause 2012;19:202-10. 11. Onoda A, et al. Food Chem Toxicol 2011. 12. Ju YH, et al. Carcinogenesis 2006;27:856-63. 13. Brown NM, Belles CA, Lindley SL, et al. Carcinogenesis 2010;31:886-93. 14. Yoneda T, et al. Menopause 2011;18:814-20.