

Q. What is St. John's Wort?

A. St. John's Wort (SJW) or *Hypericum perforatum* is a flowering plant used for its antidepressant properties. SJW is most commonly used and studied for depression in the form of a liquid extract standardized to either hypericin (0.1–0.3%) or hyperforin (1–6%) as active ingredients.

Q. What are the potential mechanisms of action underlying SJW?

A. Research has suggested hyperforin compounds are responsible for the effect of SJW on mood by affecting neurotransmitter levels, including serotonin, norepinephrine and dopamine. SJW is an over the counter dietary supplement and is not regulated by the Food and Drug Administration (FDA). Given this limited oversight, SJW dosing and formulations may vary across different manufacturers.

Q. Is SJW recommended in the Military Health System (MHS)?

A. **Yes.** The 2016 VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder gives a Weak For recommendation for the use of SJW, and suggests considering standardized extract of SJW as medication monotherapy for patients with mild major depressive disorder (MDD) who prefer herbal treatments. The guideline cautions against using SJW for moderate to severe MDD, women who are pregnant or breastfeeding, or in combination with another antidepressant to avoid drug-herb interactions.

The MHS relies on the VA/DoD clinical practice guidelines (CPGs) to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

Q. Do other authoritative reviews recommend SJW for MDD?

A. **No.** Other authoritative reviews have not substantiated SJW for MDD.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) Systematic Review Repository and the Cochrane Database of Systematic Reviews.

- AHRQ: No reviews were found including SJW for MDD.
- Cochrane: A 2008 systematic review found that SJW is superior to placebo in patients with MDD and SJW is similarly effective as standard antidepressants, but that certain factors complicate the interpretation.

Q. Is there any recent research on SJW as a treatment for MDD?

A. A search conducted in January 2017 identified two meta-analyses on the efficacy of SJW for the treatment of depression published in the time period since the search conducted for the 2016 VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder. One meta-analysis (Cui & Zheng, 2016) included 27 trials and 3,126 patients with depression, finding that SJW was not significantly different from selective serotonin reuptake inhibitors (SSRIs) in treatment response or remission. SJW had a significantly lower rate of adverse events and fewer withdrawals. A second meta-analysis (Ng, Venkatanarayan, & Ho, 2017) of 27 trials, for a total of 3,808 patients, found that SJW showed comparable

treatment response and remission, with a significantly lower dropout rate compared to standard SSRIs. The authors note that the duration of the included studies ranged from 4 to 12 weeks, limiting any conclusions on long-term effectiveness.

Q. What conclusions can be drawn about the use of SJW as a treatment for MDD in the MHS?

A. SJW standardized extract is safe and effective as monotherapy for mild MDD, for patients who are not pregnant or breastfeeding. SJW is not recommended for moderate to severe forms of MDD. Providers should exercise caution when recommending SJW due to common drug-herb interactions. SJW is not regulated by FDA, and dosing and formulations may vary across different manufacturers.

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References

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