

September 2023

## **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. When used in the treatment of depression, SJW is commonly dispensed in the form of a liquid extract standardized to either hypericin (0.1–0.3%) or hyperforin (1–6%) as the active ingredient. Therapeutic dosages range from 500 to 1800 mg with a typical starting dose of 900 mg daily. The full dosage is divided between three daily administrations (Klemow et al., 2011).

## **Q: What are the potential mechanisms of action underlying SJW for the treatment of major depressive disorder (MDD)?**

**A:** Research has suggested hyperforin compounds are responsible for the effect of SJW on mood by affecting neurotransmitter levels, including serotonin, norepinephrine, and dopamine (Klemow et al., 2011). SJW is an over-the-counter dietary supplement and is not regulated by the U.S. Food and Drug Administration (FDA). Given this limited oversight, SJW dosing and formulations may vary across different manufacturers.

## **Q: Is SJW recommended as a treatment for MDD in the Military Health System (MHS)?**

**A:** Yes. The 2022 VA/DoD *Clinical Practice Guideline for the Management of Major Depressive Disorder* suggests a standardized extract of SJW as medication monotherapy for patients with mild MDD who prefer herbal treatments with a “weak for” strength of recommendation. The guideline cautions against using SJW with 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. Recommendations for or against a treatment may be characterized as strong or weak based on a variety of factors (e.g., confidence in the quality of the evidence, weight of treatment benefits versus risks, feasibility). The CPGs also state if there is insufficient evidence to develop a 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 as a treatment for MDD?**

**A:** Yes. Other authoritative reviews have provided some evidence substantiating SJW for MDD. Other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using grading systems similar to the VA/DoD CPGs. Notable among these is Cochrane, an international network that conducts high-quality reviews of healthcare interventions.

- Cochrane: A 2008 systematic review of SJW for major depression included 29 trials comparing SJW to placebo or standard antidepressants (Linde, Berner, Kriston, 2008). The included studies varied with regard to country and type of SJW extract and included subjects with mostly mild to moderate depression. Overall, the authors found SJW to be superior to placebo and similarly effective to standard antidepressants with fewer side effects. The authors cautioned that studies from countries with a tradition of physicians prescribing SJW may report overly optimistic results.

**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 the FDA, and dosing and formulations may vary across different manufacturers. For additional guidance on selecting a treatment for MDD, please visit the PHCoE Clinician Resources section of the website and navigate to clinical support tools.

**References**

Department of Veterans Affairs/Department of Defense. (2022) VA/DoD clinical practice guideline for management of major depressive disorder. Version 4.0. Washington (DC): Department of Veterans Affairs/Department of Defense.

Klemow, K.M., Bartlow, A., Crawford, J., Kocher, N., Shah, J., & Ritsick, M. (2011). Medical attributes of st. john's wort (hypericum perforatum) In I.F.F. Benzie & S. Wachtel-Galor (Eds.). *Herbal Medicine: Biomolecular and Clinical Aspects* (2nd ed., chapter 11). CRC Press/Taylor & Francis. <https://www.ncbi.nlm.nih.gov/books/NBK92750/?report=reader>

Linde, K., Berner, M. M., & Kriston, L. (2008). St. John's wort for major depression. *Cochrane Database of Systematic Reviews*, Issue 4. Art. No.: CD000448. DOI: 10.1002/14651858.CD000448.pub3