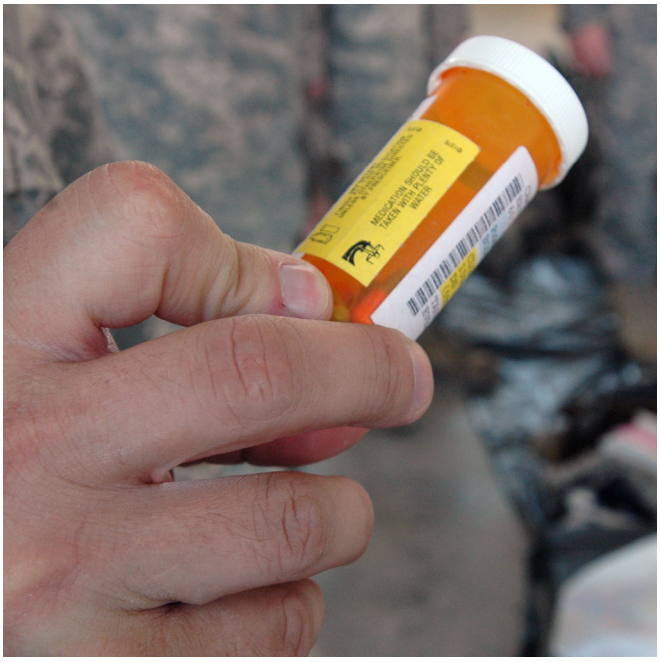
Effective Pharmacotherapies for the Treatment of Major Depressive Disorder

The Military Health System and the Department of Veterans Affairs offer several effective, evidence-based approaches for treating major depressive disorder (MDD). When treating uncomplicated MDD, the 2022 Department of Veterans Affairs/ Department of Defense Clinical Practice Guideline (CPG) for MDD states:

- We recommend that MDD be treated with either psychotherapy or pharmacotherapy as monotherapy, based on patient preference. (p. 33)[1]
- When choosing an initial pharmacotherapy, or for patients who have previously responded well to pharmacotherapy, we suggest one of the following (not rank ordered): bupropion; mirtazapine; a seratonin-norepinephrine reuptake inhibitor; Trazadone, vilazodone, or vortioxetine; a selective serotonin reuptake inhibitor. (p. 39)[1] With the choice of pharmacotherapy, the Work Group recommends selecting any of several agents with no evidence supporting one over another. (p. 35)[1]
- When choosing an initial pharmacotherapy, we suggest against using: esketamine, ketamine, monoamine oxidase inhibitors (MAOIs), nefazodone, tricyclic antidepressants (TCAs). (p. 39)[1]



What if my patient with MDD demonstrated a partial or no response to an adequate trial of a suggested initial pharmacotherapy?

We suggest (not rank ordered):

- switching to another antidepressant (including TCAs, MAOIs, eskatimine, ketamine, or nefazodone);
- switching to psychotherapy;
- augmenting with a psychotherapy;
- augmenting with a second-generation antipsychotic. (p. 24)[1]

Relapse Prevention/Continuation Phase

- For patients with MDD who achieve remission with antidepressant medication, we recommend continuation of antidepressants at the therapeutic dose for at least six months to reduce the risk of relapse. (p. 25)[1]
- For patients with MDD at high risk for relapse or recurrence (e.g., two or more prior episodes, unstable remission status), we suggest offering a course of cognitive behavioral therapy, interpersonal therapy, or mindfulness-based cognitive therapy during the continuation phase of treatment (i.e., after remission is achieved) to reduce the risk of subsequent relapse/recurrence. (p. 25)[1]
- The evidence does not support recommending one of these three evidence-based psychotherapies over another. (p. 25)[1]

Additional Considerations for Providers

- ✓ **For individuals with mild to moderate MDD who are breastfeeding or pregnant, we recommend offering an evidence-based psychotherapy as a first-line treatment. (p. 25)**[1]
- ✓ **In patients with a history of MDD prior to pregnancy who responded to antidepressant medications, and are currently stable on pharmacotherapy, weigh risk/benefit balance to both mother and fetus in treatment decisions. (p. 25)**[1]
- ✓ **For older adults (≥ 65 years) with mild to moderate MDD, we suggest offering a first-line psychotherapy. (p. 25)**[1]
- ✓ **Patient preference and the additional safety risks of pharmacotherapy should be considered when making this decision. (p. 25)**[1]
- ✓ **We suggest offering a combination of pharmacotherapy and evidence-based psychotherapy for the treatment of patients with MDD characterized as:**
  - **severe (e.g., PHQ-9 >20),**
  - **persistent major depressive disorder (duration greater than two years),**
  - **recurrent (with two or more episodes). (p. 43)**[1]

Disclaimer: No single treatment is right for everyone. Consult with colleagues about antidepressants and psychotherapy treatment options to determine which treatment is best for your patient based on the benefits, risks, and side effects of each treatment.

References

1 Veterans Affairs and Department of Defense. (2022). *VA/DOD Clinical Practice Guideline for the Management of Major Depressive Disorder.* Version 4.0. https://www.healthquality.va.gov/guidelines/MH/mdd/VADoDMDDCPGFinal508.pdf

Resources

Military/Veterans Crisis Line provides free, confidential support for service members and veterans in crisis. Dial 988, then press 1 to chat live with a counselor.
veteranscrisisline.net

Military OneSource provides 24/7 support and information on housing, financial, legal, medical and psychological services

- State-side: 800-342-9647
- Overseas: 800-342-9647
- Collect: 484-530-5908

www.militaryonesource.mil

inTransition offers specialized coaching and assistance for active-duty service members, National Guard members, reservists, veterans, and retirees to help them adapt to their transitions between systems of care.

- State-side: 800-424-7877
- Overseas: 800-748-81111 (in Australia, Germany, Italy, Japan, and South Korea only)

www.health.mil/inTransition