

Identification and Treatment of Major Depressive Disorder (MDD) for Adults

Antidepressant Management Tips

- The characteristics of the depressive episode, associated comorbid diagnoses and patient specific factors that influence safety, tolerability, ease of use and cost all influence the choice of antidepressant. Serotonin Specific Reuptake Inhibitor (SSRI) class antidepressants have become the mainstay of initial treatment of MDD, especially in the primary care community, because of their relatively good tolerability and safety profile, and familiarity with the agents. It is important to recognize that other classes of antidepressants may be indicated for depressive episodes with certain features (for example, MAOI class for MDD with atypical features) or when comorbid conditions may also be a target (for example bupropion in MDD and tobacco use disorder), and in cases that do not respond to an adequate trial of an SSRI. Choosing an antidepressant is an exercise in balancing these factors: safety, tolerability, efficacy, price, and simplicity of use.
- It is important to prescribe an antidepressant at adequate dose and duration before considering it a failed trial and switching or augmentation is considered.
- Switching and augmenting have similar rates of efficacy in research trials. Switching may be a less complicated choice in a primary care setting (exceptions being generic triiodothyronine and **buspirone**, which have few side effects and no significant monitoring demands). Lithium has the strongest efficacy evidence base, but drug interactions and monitoring demands for toxicity, thyroid and renal side effects may be limiting. The atypical antipsychotics (Abilify and Seroquel) have good efficacy data, but also risks for metabolic syndrome and tardive dyskinesia and incur higher cost.
- When switching, typically it is better to switch between rather than within antidepressant class, though some studies have shown that a single switch to another SSRI is an acceptable option.
- Treatment of depression in pregnancy and lactating women requires special considerations that are beyond the scope of this guideline. (See resource section on page 12 in MDD Guideline for further information.)
- All antidepressants: inform and discuss common and potential high-risk side effects including risk of agitation, precipitation of manic episode and/or provocation of suicidal ideation. Most antidepressants should be tapered to avoid a discontinuation syndrome and to give better odds of avoiding a recurrence of depression.
- Patients 24 and younger: highlight risk of provocation of suicidal ideation. The risk of provocation of suicidal ideation (small signal in research studies) must be balanced against the risk of untreated depression (greater risk according to most authorities).

Drug-drug Interactions

It is important to consider potential drug-drug interaction to ensure safe and effective antidepressant prescribing. Both inhibition and induction as well as protein binding effects can result in unexpected and sometimes dramatic differences in expected blood levels resulting in toxicity (e.g., like elevating Warfarin levels or beta blocker levels) or otherwise affecting the effectiveness of the drug. When prescribing antidepressants, it is a best practice to run a drug-drug interaction check using a program such as Epocrates (www.Epocrates.com).

Selected High-risk Antidepressant Side Effects

1. Effexor, Cymbalta and Pristiq: warn about hypertension (check baseline and follow-up blood pressure)
2. Cymbalta: warn about heavy drinking and about pre-existing liver disease (check baseline LFTs prior to prescription if risk factors for liver disease)
3. nefazodone: hepatotoxicity (check baseline and follow-up LFTs)
4. Wellbutrin: seizure provocation (highlight safe dosing parameters)
5. TCA: warn about orthostatic hypotension and overdose risk
6. MAOI: highlight dietary and medication restrictions (For further information, refer to patient education on page 11 in MDD Guideline - MAOI Diet and Medication Restrictions)