Prescribing Guidelines for Antidepressants

- Use of depression-focused psychotherapy is recommended as an initial treatment option for patients with mild to moderate major depressive disorder, or for women who are pregnant or are breastfeeding.[3]
- Psychotherapy always should be strongly considered in combination with pharmacotherapy for patients with moderate to severe major depressive disorder.[3]
- Electroconvulsive therapy (ECT) is recommended as a treatment of choice for patients with severe major depressive disorder who are not responsive to psychotherapy and/or pharmacological intervention.[3] Additionally, the portion of response and remission is higher with ECT than any other from of antidepressant medication.
- For treatment of depression with psychotic features, ECT or pharmacotherapy appear to be first-line treatment options.[1]
- The patient and caregiver should be informed about the medication therapy, including information on the delay in onset of therapeutic effect, potential side effects, dosing regimen, danger of overdose, any possible drug-drug or drug-food interactions, and early signs of relapse. The patient and caregiver should also understand the importance of taking the medication daily as prescribed and to continue taking it, regardless of symptomatic improvement.
- Effectiveness between and within classes of antidepressants is generally comparable.
- When choosing a first-line antidepressant, some of the factors that should be considered are:
    - Side effects
    - Safety and tolerability
    - Previous response in patient or family member
    - Patient comorbid conditions, other medications, clinical features and preference
    - Cost
- Providers should disclose the potential for the emergence and/or worsening of suicidal ideation during anti-depressant therapy, particularly for patients below 25 years of age.[4]
- Side effects should be monitored closely, especially for patients who have had their dose increased. If side effects are intolerable, a period of subtherapeutic treatment is acceptable. However the goal is to reach therapeutic target levels observed in evidence-

based studies. If the intolerable side effects persist, consider a change of medication.

- If at least a moderate response has not been seen after 2 to 4 weeks of therapy with a therapeutic dose, the treatment plan should be re-evaluated. Medication adherence should also be assessed. Options for non-responders include changing medications, adding psychotherapy, ECT, and augmentation.[4,6]

- If a patient is showing a partial response, extend the medication trial to 4 to 6 weeks. For patients on modest dosages or who have low serum drug levels despite usual doses, use of higher doses may be helpful. Augmentation per practice guidelines is acceptable. Patients should be treated to remission.

- Patients should continue therapy at the same dosage that produced the therapeutic response for an additional 4 to 9 months after remission (this is known as the "continuation phase treatment"). Schedule regular patient visits and monitor adherence and signs of relapse. Remission is the absence of depressive symptoms or the presence of minimal symptoms such as a score less than 7 on HAM-D or a less than 5 on the PHQ-9. Full remission is defined as a 2-month absence of symptoms. [7]

- Maintenance phase treatment should be considered for patients with multiple or severe episodes of depression, residual symptoms between episodes, and/or other comorbid psychiatric disorders. Side effects and patient preference also should be taken into account.

- Patients who do not require maintenance phase treatment should be slowly tapered off their medication over several weeks.

- Treatment resistance has been defined as "failure to achieve remission with an adequate trial of therapy and three different classes of antidepressants at adequate duration and dosage".[7]

- Augmentation of antidepressant therapy with second-generation antipsychotics has proven in some combinations to offer abatement of symptoms in as little as a week; however, more study is needed to show if this impacts long-term outcomes. Short-term studies of these combinations note more patients withdrawing from the treatment groups due to adverse events. More long-term and short-term studies are needed to prove overall effectiveness of these combinations. Augmentation therapies also carry risks which should be considered: weight gain and other metabolic complications, hyperprolactinemia, tardive dyskinesia, neuroleptic malignant syndrome, QTc prolongation and high cost of many agents.[1]

- **Monitor for suicide**:[1]
    - Educate patients and families on the warning signs of suicide, as well as general suicide prevention strategies (e.g., removal of weapons).
    - Closely monitor patients via weekly office visits in the first few months (supplemented by phone calls between visits for the first two weeks) of medication therapy and after any dosage changes.
    - Monitor for new or more frequent thoughts of suicide, increased anxiety, agitation, aggressiveness or impulsivity, and involuntary restlessness or hypomania.

- Contact all patients who miss appointments.

These guidelines are not intended to replace a practitioner's clinical judgment. They are designed to provide information and to assist practitioners with decisions regarding care. The guidelines are not intended to define a standard of care or exclusive course of treatment. Health care practitioners using these guidelines are responsible for considering their patient's particular situation in evaluating the appropriateness of these guidelines.

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