# Psychotropic Medication Utilization Parameters for Children and Youth in Texas Public Behavioral Health (6th Version)

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**June 2019**

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# Introduction and General Principles

The Psychotropic Medication Utilization Parameters were initially developed in 2004 to provide evidence-informed guidance on the use of psychotropic medication with children and youth and suggest parameters for utilization review. While the most recent versions have focused primarily on children within the Texas foster care system, this sixth iteration of the Psychotropic Medication Utilization Parameters has been refocused to address the treatment of all children and adolescents served by the public behavioral health system in Texas. It has long been recognized that the Parameters are based upon sound psychiatric principles and scientific evidence that apply to all children and adolescents who are treated with these medications. Additionally, the development of the Parameters has returned to the public behavioral health section that sponsored the first edition in 2004. Currently the professionals responsible for the sixth version constitute a Workgroup of the Psychiatric Executive Formulary Committee (PEFC) of the Health and Specialty Division of the Texas Health and Human Services Commission. The PEFC addresses the formulary and prescribing parameters that are used in the Texas state mental hospitals, state supported living centers, local mental health authorities, local intellectual disability health authorities, and their contractors.

The use of psychotropic medications in children and adolescents is an issue confronting parents, other caregivers, and health care professionals across the United States. This population has multiple and complex care needs relating to rapid developmental changes, incomplete brain maturation, diagnostic uncertainty, incomplete long-term evidence base for most medication classes, impact of ecological systems such as family and school, and issues of self-determination. Additionally, children and youth, especially those in foster care for whom the Parameters were originally developed, may have treatment complexity related to emotional or psychological stress. They may have experienced abusive, neglectful, serial or chaotic caretaking environments. Birth family history may not be available. These traumatized children often present with a fluidity of different symptoms over time reflective of past traumatic events that may mimic or underlie many psychiatric disorders and result in difficulties with attachment, mood regulation, behavioral control, and other areas of functioning. In view of these considerations, the American Academy of Child and Adolescent Psychiatry (AACAP) emphasizes the importance of holistic and collaborative mental health treatment, recommending prescribers of psychotropic medication in child-serving systems utilize a biopsychosocial perspective guided by trauma-informed and system of care principles. A trauma-informed approach involves understanding the prevalence and impact of trauma, recognizing trauma signs and symptoms, responding with trauma-sensitive procedures and practices, and endeavoring to minimize re-traumatization. The system of care framework includes providing effective services that are family-driven and youth-guided, home and community-based, strengths-based and individualized and culturally and linguistically appropriate.

**Additionally, it is important that a comprehensive evaluation be performed before beginning treatment for a mental or behavioral disorder. Except in the case of an emergency, a child should receive a thorough health history, psychosocial assessment, mental status exam, and physical exam before prescribing a psychotropic medication.** The physical assessment should be performed by a physician or another healthcare professional qualified to perform such an assessment. It is recognized that in some emergency situations, it may be in the best interest of the child to prescribe psychotropic medications before a physical exam can be performed. In these situations, a thorough health history should be performed to assess for significant medical disorders and past response to medications, and a physical evaluation should be performed as soon as possible. A thorough psychosocial assessment should be performed by an appropriately qualified mental health clinician (licensed masters or doctoral level), a psychiatrist/ child

psychiatrist, or a primary care physician with experience in providing mental health care to children and youth. The child's symptoms and functioning should be assessed across multiple domains and multiple informants when possible, and the assessment should be developmentally age appropriate. It is very important that information about the child's history, including history of trauma and current functioning be made available to the treating physician in a timely manner, either through an adult who is well-informed about the child or through a comprehensive medical record. It is critical to meet the individual needs of patients and their families in a culturally competent manner. This requirement indicates a need to address communication issues as well as differences in perspectives on issues such as behavior and mental functioning. Interpretation of clinical symptoms and decisions concerning treatment should, whenever possible, be informed by the child's current level of biopsychosocial developmental as well as history of trauma, neglect or abuse and the timing of these stressors. In general, optimal outcomes are achieved with well-coordinated team-based care with members of different professions (e.g., child psychiatrist, child psychologist, social worker, primary care physician, etc.) each contributing their particular expertise to the treatment plan and follow- up. **Note well: At present there are no biomarkers to assist with the diagnosis of mental disorders, and imaging (e.g., MRI) and other tests (e.g., EEG) are not generally helpful in making a clinical diagnosis of a mental disorder. Consequently, the diagnosis is based on a comprehensive clinical assessment.**

Prescribers should be mindful of the important role of nonpharmacological, psychosocial treatments in remediating behavioral and emotional disturbances among youth. In many instances, especially with milder presentations, it is prudent to undertake psychotherapy or environmental changes before beginning pharmacotherapy. In other situations, pharmacotherapy may help attenuate symptoms and distress so that psychosocial treatment may be successfully implemented. For instance, youth with more severe anxieties may benefit from anxiolytic medications to enable their participation in evidence-based treatments that involve exposure and skills development. Similarly, children with highly disruptive or aggressive conduct with comorbid ADHD may first need pharmacotherapy that reduces ADHD-related impulsivity before behavioral therapies can gain traction. Therefore, whenever possible and appropriate, psychotherapy should generally begin before or concurrent with prescription of a psychotropic medication. Equally important, the role of the health care provider and the health care environment's potential to exacerbate a child's symptoms, given their respective trauma history, should be considered and minimized through trauma-informed approaches to care. Patient and caregiver education should be provided about the condition to be treated, treatment options (non-pharmacological and pharmacological), treatment expectations, and potential side effects that may occur during the prescription of psychotropic medications.

**It is recognized that many psychotropic medications do not have Food and Drug Administration (FDA) approved labeling for use in children.** The FDA has a statutory mandate to ensure that approved product labeling accurately reflects pharmaceutical company sponsored research on safety and efficacy for the indications listed. that. The FDA does not regulate physician and other health provider practice. In fact, the FDA has stated that it does "not limit the way a practitioner may prescribe an approved drug." Studies and expert clinical experience often support the use of a medication for an "off-label" use. This practice is particularly relevant in child psychiatry as there is a dearth of FDA-registration trials in youth. Physicians therefore must use the available evidence, expert opinion, their own clinical experience, and exercise their clinical judgment in prescribing what is best for each individual patient. To that end, clear documentation of the physician's rationale in the medical record facilitates continuity of care and minimizes misinterpretation.

## Role of Primary Care Providers

Primary care providers play a valuable role in the care of youth with mental disorders. Not only are they the clinicians most likely to initially interact with children who are in distress due to an emotional or psychiatric disorder, but also an inadequate number of child psychiatrists are available to meet children's mental health needs. Primary care clinicians are in an excellent position to perform screenings of children for potential mental disorders, and they can diagnose and treat relatively straightforward situations such as uncomplicated ADHD, anxiety, or depression. Primary care providers should provide advice to youth, including those in foster care, and their care givers about handling feelings and behaviors, recognizing the need for help, making decisions regarding healthy life styles, and the available treatments for childhood mental disorders. As always, consideration should be given regarding the need for referral for counseling, psychotherapy, or behavioral therapy. Primary care providers vary in their training, clinical experience, and confidence to address mental disorders in children. Short courses and intensive skills-oriented seminars may be beneficial in assisting primary care clinicians in caring for children with mental disorders. Active liaisons with child psychiatrists who are available for phone consultation or referral can be beneficial in assisting primary care clinicians to meet the mental health needs of children. For children and youth in foster care, the American Academy of Pediatrics has provided a policy statement ("Health Care Issues for Children and Adolescents in Foster Care and Kinship Care") which can be found at: http://pediatrics.aappublications.org/con- tent/136/4/e1131

## General Principles

A DSM-5 psychiatric diagnosis should be made whenever possible before the prescribing of psychotropic medications. If a diagnosis cannot be reached, rational pharmacology based on specific symptom management may be necessary while additional clinical information is gathered.

Clearly defined target symptoms and treatment goals for the use of psychotropic medications should be identified and documented in the medical record at the time of or before beginning treatment. These target symptoms and treatment goals should be assessed at each clinic visit with the child and caregiver in a culturally and linguistically appropriate manner. Whenever possible, standardized clinical rating scales (clinician, patient, primary caregiver, teachers, and other care providers) or other measures should be used to quantify the response of the child's target symptoms to treatment and the progress made toward treatment goals.

In deciding whether to prescribe a psychotropic medication in a specific child, the clinician should carefully consider potential side effects, including those that are uncommon but potentially severe, and evaluate the overall benefit to risk ratio of pharmacotherapy. Except in the case of an emergency, informed consent should be obtained from the appropriate party(s) and assent from the child or adolescent before beginning psychotropic medication. Informed consent to treatment with psychotropic medication entails diagnosis, expected benefits and risks of treatment, including common side effects, discussion of laboratory findings, and uncommon but potentially severe adverse events. Alternative treatments, the risks associated with no treatment, and the overall potential benefit to risk ratio of treatment should be discussed.

Medication management should be collaborative. Youth, as well as caregivers, should be involved in decision- making about treatment, in accordance with their developmental level. Parents providing informed consent should be engaged, and where applicable, other caregivers, family, and child related agencies should be involved. Whenever possible,

trauma-informed, evidence-based psychotherapy, should begin before or concurrent with the prescription of psychotropic medication.

Before starting psychopharmacological treatment in preschool-aged children even more emphasis should be placed on treatment with non-psychopharmacological interventions, as this age group has few FDA-approved psychiatric treatments and even less of a clinical research base than older youth. Assessment of parent functioning and mental health needs, in addition to training parents in evidence-based behavior management can also reduce the need for the use of medication. During the prescription of psychotropic medication, the presence or absence of medication side effects should be documented in the child's medical record at each visit. Appropriate monitoring of indices such as height, weight, blood pressure, or laboratory findings should be documented.

Monotherapy regimens for a given disorder or specific target symptoms should usually be tried before polypharmacy regimens. While the goal is to use as few psychotropic medications as can be used to appropriately address the child's clinical status, it is recognized that the presence of psychiatric comorbidities may affect the number of psychotropic medications that are prescribed. When polypharmacy regimens are needed, addition of medications should occur in a systematic orderly process, accompanied by on-going monitoring, evaluation, and documentation. The goal remains to minimize polypharmacy while maximizing therapeutic outcomes.

Medications should be initiated at the lower end of the recommended dose range and titrated carefully as needed. Only one medication should be changed at a time, unless a clinically appropriate reason to do otherwise is documented in the medical record. (Note: starting a new medication and beginning the dose taper of a current medication is considered one medication change).

The use of "prn" or as needed prescriptions is discouraged. If they are used, the situation indicating need for the administration of a prn medication should be clearly indicated as well as the maximum dosage in a 24-hour period and in a week. The frequency of administration should be monitored to assure that these do not become regularly scheduled medications unless clinically indicated. The frequency of clinician follow-up should be appropriate for the severity of the child's condition and adequate to monitor response to treatment, including: symptoms, behavior, function, and potential medication side effects. At a minimum, a child receiving psychotropic medication should be seen by the clinician at least once every ninety days.

The potential for emergent suicidality should be carefully evaluated and monitored, particularly in depressed children and adolescents as well as those beginning antidepressant treatment, those having a history of suicidal behavior or deliberate self-harm, and those with a history of anxiety or substance abuse disorders. Youth at risk of suicide should have a written, collaborative safety plan that is regularly monitored. If the prescribing clinician is not a child psychiatrist, referral to or consultation with a child psychiatrist, or a general psychiatrist with significant experience in treating children, should occur if the child's clinical status has not shown meaningful improvement within a timeframe that is appropriate for the child's diagnosis and the medication regimen being used.

Before adding additional psychotropic medications to a regimen, the child should be assessed for adequate medication adherence, appropriateness of medication daily dosage, accuracy of the diagnosis, the occurrence of comorbid disorders (including substance abuse and general medical disorders), and the influence of psychosocial stressors. If a medication has not resulted in improvement in a child's target symptoms (or rating scale score), discontinue that medication rather than adding a second medication to it.

If a medication is being used in a child for a primary target symptom of aggression associated with a DSM-5 non-psychotic diagnosis (e.g., conduct disorder, oppositional defiant disorder, intermittent explosive disorder), and the behavior disturbance has been in remission for six months, then serious consideration should be given to slow tapering and discontinuation of the medication. If the medication is continued in this situation, the necessity for continued treatment should be evaluated and documented in the medical record at a minimum of every six months. The clinician should clearly document care provided in the child's medical record, including history, mental status assessment, physical findings (when relevant), impressions, rationale for medications prescribed, adequate laboratory monitoring specific to the drug(s) prescribed at intervals required specific to the prescribed drug and potential known risks, medication response, presence or absence of side effects, treatment plan, and intended use of prescribed medications.

## Use of Psychotropic Medication in Preschool Age Children

The use of psychotropic medication in young children of preschool ages is a practice that is limited by the lack of evidence available for use of these agents in this age group. The Preschool Psychopharmacology Working Group (PPWG) published guidelines (Gleason 2007) summarizing available evidence for use of psychotropic medications in this age group. The PPWG was established in response to the clinical needs of preschoolers being treated with psychopharmacological agents and the absence of systematic practice guidelines for this age group, with its central purpose to attempt to promote an evidence-based, informed, and clinically sound approach when considering medications in preschool-aged children.

The PPWG guidelines emphasize consideration of multiple different factors when deciding on whether to prescribe psychotropic medications to preschool-aged children. Such factors include the assessment and diagnostic methods utilized in evaluating the child for psychiatric symptoms/illness, the current state of knowledge regarding the impact of psychotropic medication use on childhood neurodevelopmental processes, the regulatory and ethical contexts of use of psychotropic medications in small children (including available safety information and FDA status), and the existing evidence base for use of psychotropic medication in preschool aged children. It should be noted here that although the FDA many decades ago approved marketing of chlorpromazine for use in children down to the age of 6 months, this approval was based on clinical practice and not on a rigorous demonstration of efficacy and safety that would be required for approval today. Essentially this use was "grandfathered" in and current prescription for children and adolescents is limited, the evidence base is not current and very thin despite the long history of use in the past.

Very limited information is available regarding the use of antipsychotics in the preschool age population, and no information is available regarding the use of long-acting injectable (LAI) antipsychotics in this population. Not having information to describe the effects of antipsychotics on growth and development in preschoolers is of concern. Many antipsychotics produce significant weight gain in children, and this should be of concern in the preschool population. Akathisia may also be an issue in the preschool population. The use of antipsychotics in preschoolers should be limited to the most severe situations, and the goal should be for it to be of short duration. For these reasons, antipsychotic LAIs are not recommended in the preschool population.

The publication includes specific guidelines and algorithm schematics developed by the PPWG to help guide treatment decisions for several psychiatric disorders that may present in preschool-aged children, including Attention-Deficit Hyperactivity Disorder, Disruptive Behavioral Disorders, Major Depressive Disorder, Bipolar Disorder, Anxiety Disorders, Post-Traumatic Stress Disorder, Obsessive-Compulsive Disorder, Pervasive Developmental Disorders, and Primary Sleep

Disorders. The working group's key points and guidelines are like the general principles regarding the use of psychotropic medication in children already detailed in this paper. However, the working group's algorithms put more emphasis on treating preschool-aged children with non-psycho- pharmacological interventions (for up to 12 weeks) before starting psychopharmacological treatment, to be very cautious in introducing psychopharmacological interventions to rapidly developing preschoolers.

The working group also emphasizes the need to assess parent functioning and mental health needs, in addition to training parents in evidence-based behavior management, since parent behavior and functioning can have a large impact on behavior and symptoms in preschool-aged children.

## Treatment of Opioid Use Disorders in Adolescents

Unfortunately, the opioid crisis in the US extends into the adolescent population and physicians are being confronted with the need to make recommendations and treatment decisions in this area. Although extensive discussion is beyond the scope of this document, there are 3 available options for Medication Assisted Treatment (MAT) in adolescents: buprenorphine, naltrexone and methadone. A good overview can be found in The ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use (2015). This guideline makes the following recommendations which have not changed in the face of more recent albeit scant literature:

(1) Clinicians should consider treating adolescents who have opioid use disorder using the full range of treatment options, including pharmacotherapy that are available for adults. NB: Prescription of buprenorphine and/or methadone requires special provider qualifications. Further information may be found at https://www.samhsa.gov/medication-assisted-treatment/treatment.

(2) Opioid agonists (methadone and buprenorphine) and antagonists (naltrexone) may be considered for treatment of opioid use disorder in adolescents. Age is a consideration in treatment, and Federal laws and US FDA approvals need to be considered for patients under age 18. See 42 CFR 8.12 (.) (2): "Maintenance treatment for persons under age 18. A person under 18 years of age is required to have had two documented unsuccessful attempts at short-term detoxification or drug-free treatment within a 12-month period to be eligible for maintenance treatment. No person under 18 years of age may be admitted to maintenance treatment unless a parent, legal guardian, or responsible adult designated by the relevant State authority consents in writing to such treatment."

(3) Psychosocial treatment is recommended in the treatment of adolescents with opioid use disorder and required under federal law for those receiving methadone.

(4) Concurrent practices to reduce infection (e.g., sexual risk reduction interventions) are recommended as components of comprehensive treatment for the prevention of sexually transmitted infections and blood-borne viruses.

(5) Adolescents may benefit from treatment in hospitals or other specialized treatment facilities that provide multidimensional services.

## Levels of Warnings Associated with Medication Adverse Effects

Psychotropic medications have the potential for adverse effects. Some adverse effects are time-limited and remit with continued treatment; others require intervention for effective management, and in some situations compel

discontinuation of the medication that causes them. Some adverse effects are detected prior to marketing and are included in the FDA approved product labeling provided by the manufacturers. When looking at product labeling, these adverse effects will be listed in the "Warnings and Precautions" section. As well, the "Adverse Reactions" section of the product labeling will outline those adverse effects reported during clinical trials, as well as those discovered during post-marketing evaluation. Many tertiary drug information resources also list common adverse effects and precautions for use with psychotropic medications.

At times, post-marketing evaluation may detect critical adverse effects associated with significant morbidity and mortality. The Food and Drug Administration (FDA) may require manufacturers to revise product labeling to indicate these critical adverse effects. If found to be particularly significant, these effects are demarcated by a box outlining the information at the very beginning of the product labeling, and have, in turn, been named boxed warnings. Boxed warnings are the strongest warning required by the FDA. It is important for clinicians to be familiar with all medication adverse effects, including boxed warnings, to appropriately monitor patients and minimize the risk of their occurrence. The medication tables include boxed warnings as well as other potential adverse effects. The list of potential adverse effects in the tables should not be considered exhaustive, and the clinician should consult the FDA approved product labeling and other reliable sources for information regarding medication adverse effects.

The FDA has in recent years taken additional measures to try to help patients avoid serious adverse events. New guides called Medication Guides have been developed and are specific to medication and medication classes. Medication Guides advise patients and caregivers regarding possible adverse effects associated with classes of medications and include pre- cautions that they or healthcare providers may take while taking/prescribing certain classes of medications. The FDA requires that Medication Guides be issued with certain prescribed medications and biological products when the Agency determines that certain information is necessary to prevent serious adverse effects, that patient decision-making should be informed by information about a known serious side effect with a product, or when patient adherence to directions for the use of a product are essential to its effectiveness. During the drug distribution process, if a Medication Guide has been developed for a certain class of medications, then one must be provided with every new prescription and refill of that medication.

Copies of the Medication Guides for psychotropic medications can be accessed on the FDA website at: http://www.fda.gov/Drugs/DrugSafety/ ucm085729.htm.

## Criteria Indicating Need for Further Review of a Child's Clinical Status

The following situations indicate a need for review of a patient's clinical care. These parameters do not necessarily indicate that treatment is inappropriate, but they do indicate a need for further review. For a child being prescribed a psychotropic medication, any of the following suggests the need for additional review of a patient's clinical status:

- Absence of a thorough assessment for the DSM-5 diagnosis(es) in the child's medical record.
- Four (4) or more psychotropic medications prescribed concomitantly (side effect medications are not included in this count).
- Prescribing of:
    - Two (2) or more concomitant stimulants*
    - Two (2) or more concomitant alpha agonists*

- Two (2) or more concomitant antidepressants
- Two (2) or more concomitant antipsychotics
- Three (3) or more concomitant mood stabilizers

*The prescription of a long-acting and an immediate-release stimulant or alpha agonist of the same chemical entity does not constitute concomitant prescribing.

Note: When switching psychotropic medications, overlaps and cross taper should occur in a timely fashion, generally within 4 weeks.

- The prescribed psychotropic medication is not consistent with appropriate care for the patient's diagnosed mental disorder or with documented target symptoms usually associated with a therapeutic response to the medication prescribed.
- Psychotropic polypharmacy (2 or more medications) for a given mental disorder is prescribed before utilizing psychotropic monotherapy.
- The psychotropic medication dose exceeds usual recommended doses (literature based maximum dosages in the following tables).
- Psychotropic medications are prescribed for children of very young age, including children receiving the following medications with an age of:
  - Stimulants: Less than three (3) years of age
  - Alpha Agonists: Less than four (4) years of age
  - Antidepressants: Less than four (4) years of age
  - Mood Stabilizers: Less than four (4) years of age
  - Antipsychotics: Less than five (5) years of age
- Prescribing by a primary care provider who has not documented previous specialty training for a diagnosis other than the following (unless recommended by a psychiatrist consultant):
  - Attention Deficit Hyperactive Disorder (ADHD)
  - Uncomplicated anxiety disorders
  - Uncomplicated depression
- Antipsychotic medication(s) prescribed continuously without appropriate monitoring of glucose and lipids at least every 6 months.

# Usual Recommended Doses

The attached medication charts are intended to reflect usual doses and brief medication information for commonly used psychotropic medications. The tables contain two columns for maximum recommended doses in children and adolescents – the maximum recommended in the FDA approved product labeling, and the maximum recommended in medical and pharmacological literature sources. The preferred drug list of medications potentially prescribed for foster children is the same as for all other Texas Medicaid recipients.

The tables are intended to serve as a resource for clinicians. The tables are not intended to serve as comprehensive drug information references or a substitute for sound clinical judgment in the care of individual patients. Circumstances may dictate the need for the use of higher doses in specific patients. In these cases, careful documentation of the rationale

for the higher dose should occur, and careful monitoring and documentation of response to treatment should be performed. If the use of higher medication doses does not result in improvement in the patient's clinical status within a reasonable time period (e.g., 2-4 weeks), then the dosage should be decreased, and other treatment options considered.

Not all medications prescribed by clinicians for psychiatric diagnoses in children and adolescents are included in the following tables. However, in general, medications not listed do not have adequate efficacy and safety information available to support a usual maximum dose recommendation.

## Stimulants for Treatment of ADHD

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children and Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Amphetamine mixed salts | Adderall®* (immediate-release tablet) | Age 3-5 years: 2.5 mg/day<br>Age ≥ 6 years: 5mg once or twice daily | Age 3-5 years: 30 mg/day<br>Age ≥ 6 years and ≤50 kg: 40 mg/day<br>Age ≥ 6 years and >50 kg: 60 mg/day | Approved for age ≥ 3 years: 40 mg/day | One to three times daily | Baseline and ongoing: height, weight, heart rate, and blood pressure<br>Baseline: Assessment using a targeted cardiac history of the child and the family, and a physical examination of the child with an EKG and/ or a pediatric cardiology consult as indicated | Abuse potential<br>Sudden death and serious cardiovascular events (boxed warning for amphetamine products and dextroamphetamine) | • Risk of sudden death in those with pre- existing structural cardiac abnormalities or other serious heart problems<br>• Hypertension<br>• Potential for psychiatric adverse events (hallucinations, delusional thinking, mania, aggression, etc.)<br>• Current evidence is unclear regarding a definitive answer as to whether extended use of stimulants leads to a permanent reduction in ultimate adult height; however, a small statistically significant reduction is possible. If mild growth suppression occurs, it is likely reversible upon discontinuation of stimulant<br>• Tics<br>• Decreased appetite and weight<br>• Sleep disturbance/ insomnia<br>• Serotonin Syndrome: Increased risk when co-administered with serotonergic agents (e.g., SSRIs, SNRIs, triptans)<br>• Peripheral vasculopathy, including Raynaud's phenomenon, and associated signs and symptoms: Instruct patients to report any numbness, pain, or color change in fingers or toes. |
| | Adderall®XR* (capsule with 50% IR: 50% ER beads) | Age 6-12 years: 5-10 mg/day<br>Age ≥13 years: 10 mg/day | Age ≥ 6 years and ≤50 kg: 30 mg/day<br>Age ≥ 6 years and >50 kg: 60 mg/day | Approved for age ≥ 6 years: 30 g/day | Once daily | | | |
| | Mydayis® ER (capsule with triple-release beads; 16-hour duration) | Age 13-17 years: 12.5 mg/day | Age ≥ 13 years: 25 mg/day | Approved for age ≥13 years: 25 mg/day | Once daily | | | |
| Amphetamine sulfate | Evekeo® (immediate-release tablet) | Age 3-5 years: 2.5 mg once or twice daily<br>Age ≥ 6 years: 5mg once or twice daily | Age ≥ 3 years: 40 mg/day | Approved for age ≥ 3 years: 40 mg/day | 1-3 times daily | | | |
| Amphetamine base | Adzenys®XR-ODT (oral disintegrating tablet; 50% IR: 50% ER; orange flavor)<br>Must be fully dissolved on tongue before swallowing | Age ≥ 6 years: 6.3 mg/day (3.1 mg = 5 mg Adderall®XR) | Age 6-12 years: 18.8 mg/day<br>Age 13-17 years: 12.5 mg/day | Approved for age ≥ 6 years<br>Ages 6-12 years: 18.8 mg/day (= to 30 mg Adderall®XR)<br>Ages 13-17 years: 12.5 mg/day (= to 20 mg Adderall®XR); no evidence that higher doses conferred additional benefit in this age group | Once daily | | | |
| | Adzenys®ER (extended-release oral suspension; 50% IR: 50% ER; orange flavor) | | | | | | | |
| | Dyanavel® XR (extended-release oral suspension; bubblegum flavor) | Age ≥6 years: 2.5-5 mg/day (2.5 mg = 4 mg Adderall®XR) | Age ≥6 years: 20 mg/day | Approved for age ≥ 6: 20 mg/day | Once daily | | | |
| Dextroamphetamine | Dextroamphetamine immediate-release tablet* (Dexedrine brand name not available) | Age 3-5 years: 2.5 mg/day<br>Age ≥ 6 years: 5 mg once or twice daily | Age 3-5 years: 30 mg/day<br>Age ≥ 6 years and ≤50 kg: 40 mg/day<br>Age ≥ 6 years and >50 kg: 60 mg/day | Approved for age ≥3 years: 40 mg/day | Once or twice daily | | | |
| | Zenzedi® (immediate-release tablet) | | | | | | | |
| | Procentra® (immediate-release oral suspension; bubblegum flavor) | | | | | | | |
| | Dexedrine* Spansule® (capsule with 50% IR: 50% ER beads) | Age 3-5 years: not recommended<br>Age ≥ 6 years: 5 mg/day | Age ≥ 6 years and ≤50 kg: 40 mg/day<br>Age ≥ 6 years and >50 kg: 60 mg/day | Age ≥ 6 years: 40 mg/day | | | | |

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children and Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Lisdexamfetamine | Vyvanse® (long-lasting prodrug capsule)<br><br>Vyvanse® (long-lasting chewable tablets; strawberry flavor) Chewable tabs must be chewed completely before swallowing | Age 3-5 years: No data<br><br>Age ≥ 6 years: 30 mg/day | Age 3-5 years: No data<br><br>Age ≥ 6 years: 70 mg/day | Approved for age ≥ 6 years: 70 mg/day | Once daily | | | |

Symbols and abbreviations: IR, immediate-release; ER, extended-release, XR, extended-release; ODT, orally disintegrating tablet.
*Generic available.
Amphetamine Table Footnotes:
See FDA-approved product labeling for each individual medication for complete boxed warnings.
Many extended-release stimulants have been found to have higher plasma exposure for patients ≤ 12 years at the same dose as adolescents, and higher rates of adverse effects.
Clinicians may choose whichever stimulant formulation (IR/SR/ER, etc.) they deem appropriate. Monitor more closely for dose titrations in younger patients and consider reducing dose of medications should adverse events arise.
It is generally recommended to adjust stimulant doses in weekly increments, until desired clinical effect is achieved
If switching between stimulant formulations/products, it is recommended to discontinue the previous treatment, and then initiate and titrate using recommended titration schedule for the new agent; increase stimulant dose in weekly increments.
Beaded formulations enclosed in capsules may be helpful for children with difficulty swallowing tablets or capsules, as the capsules may be opened and sprinkled on cold or room temperature applesauce or other soft foods. Contents of the entire capsule should be consumed immediately, not stored. Beads should be swallowed whole, and not chewed.
In rare instances, it may be necessary to exceed the FDA-based maximum dose of stimulant medication to achieve optimal clinical efficacy; however, this should be done on a case-by-case basis with careful monitoring for treatment-emergent adverse effects.

# Stimulants for Treatment of ADHD Continued

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children and Adolescents | Schedule | Baseline/ Monitoring | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Methylphenidate | Ritalin®* (immediate-release tablet) | Age 3-5 years: 2.5 mg twice daily<br><br>Age ≥ 6 years: 5mg twice daily | Age 3-5 years: 22.5 mg/day<br><br>Age ≥ 6 years: ≤50 kg: 60 mg/day >50 kg: 100 mg/day<br><br>Any dose of methylphenidate exceeding 60mg/day should be used with caution, and with attentive monitoring | Approved for children >6 years: 60 mg/day | One to three times daily | Baseline and ongoing: height, weight, heart rate, and blood pressure<br><br>Baseline: Assessment using a targeted cardiac history of the child and the family, and a physical examination of the child with an EKG and/ or a pediatric cardiology consult as indicated | Abuse potential | • Risk of sudden death in those with pre- existing structural cardiac abnormalities or other serious heart problems<br>• Hypertension<br>• Potential for psychiatric adverse events (hallucinations, delusional thinking, mania, aggression, etc.)<br>• Conflicting data exist regarding whether extended use of stimulants leads to a reduction in ultimate adult height. However, if stimulant treatment is persistent until growth is complete, a small statistically significant reduction is possible.<br>• Tics<br>• Decreased appetite and weight<br>• Sleep disturbance<br>• Serotonin Syndrome: Increased risk when co-administered with serotonergic agents (e.g., SSRIs, SNRIs, triptans)<br>• Peripheral vasculopathy, including Raynaud's phenomenon, and associated signs and symptoms: Instruct patients to report any numbness, pain, or color change in fingers or toes<br>• Daytrana®TD patch: Post marketing reports of acquired skin depigmentation or hypopigmentation of the skin |
| | Methylin®* (immediate-release chewable tab; grape flavor)<br><br>Methylin®* (immediate-release oral solution; grape flavor) | | | | | | | |
| | Ritalin®SR* (intermediate-release tablet) | Age ≥ 3 years: 10 mg/day | | | Once daily | | | |
| | Methylin®ER* (intermediate-release tablet) | | | | | | | |
| | Metadate®ER* (intermediate-release tablet) | | | | | | | |
| | Ritalin®LA* (extended-release capsule; 50% IR: 50% ER) | Age ≥ 6years: 10 -20 mg/day | | | Once daily | | | |
| | Metadate®CD* (extended-release capsule; 30% IR: 70% ER) | Age ≥ 6years: 20 mg/day | | | Once daily | | | |
| | Quillivant®XR (extended-release oral suspension; 20% IR: 80% ER; banana flavor) | | | | Once daily Shake vigorously for at least 10 seconds for accurate dosing | | | |
| | QuilliChew®ER (chewable extended-release tablet; 30% IR: 70% ER; cherry flavor) | | | | Once daily | | | |
| | Aptensio®XR (extended-release capsule; 40% IR: 60% ER) | Age ≥ 6years: 10 mg/day | | | Once daily | | | |
| | Cotempla XR-ODT (oral disintegrating tablet; 25% IR: 75% ER; grape flavor) | Age ≥ 6 years: 17.3 mg/day | Age 6-17 years: 51.8 mg/day | Approved for children 6 years and older: 51.8 mg/day | Once daily | | | |

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children and Adolescents | Schedule | Baseline/ Monitoring | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| | Concerta®* (extended-release osmotic release oral tablet; 22% IR: 78% ER) | Age ≥ 6 years: 18 mg/day | Age 3-5 years: 36 mg<br><br>Age ≥ 6 years: 72 mg/day | Approved for children ≥ 6 years<br><br>Age 6-12 years: 54 mg/day<br><br>Age 13-17 years: 72mg/day or 2 mg/kg/day, whichever is less | Once daily | | | |
| | Daytrana®TD patch (extended-release) | Age ≥ 6 years: 10 mg/day | Age 3-5 years: 20 mg/day<br><br>Age ≥ 6 years: 30 mg/day | Approved for children ≥ 6 years | Once daily<br><br>Note: Patch is designed to be worn for 9 hrs. Removing the patch early leads to a clinical effect, ending 2-3 hours after the patch is removed | | | |
| | Jornay PM (extended-release capsule containing beads with delayed-release coating and extended-release coating)<br><br>Note: This is the ONLY stimulant formulation designed to be administered IN THE EVENING. Recommended time of administration is 8:00 pm (range: 6:30pm-9:30pm). Time of onset is approximately 10 hours following administration. | Age ≥ 6 years: 20 mg once a day given in the EVENING | Age ≥ 6 years: 100 once a day given in the EVENING | Approved for children ≥ 6 years: 100mg/day | Once daily in the EVENING | | | |
| | Focalin®* (immediate-release tablet) | Age ≥ 6 years: 2.5 mg twice daily | Age ≥ 6 years: 50 mg/day | Approved for children ≥ 6 years: 20 mg/day | Twice daily | | | |
| | Focalin®XR* (extended-release capsule; 50% IR: 50% ER) | Age ≥ 6 years: 5-10 mg/day | | Approved for children ≥ 6 years: 30 mg/day | Once daily | | | |

Symbols and abbreviations: IR, immediate-release; ER, extended-release, XR, extended-release; SR, sustained-release; CD, controlled delivery; LA, long-acting; TD, transdermal; ODT, orally disintegrating tablet

* Generic available.

Methylphenidate Table Footnotes:

See FDA-approved product labeling for each individual medication for complete boxed warnings.

Many extended-release stimulants have been found to have higher plasma exposure for patients ≤ 12 years at the same dose as adolescents, and higher rates of adverse effects.

Clinicians may choose whichever stimulant formulation (IR/SR/ER, etc.) they deem appropriate. Monitor more closely for dose titrations in younger patients and consider reducing dose of medications should adverse events arise.

It is generally recommended to adjust stimulant doses in weekly increments, until desired clinical effect is achieved

If switching between stimulant formulations/products, it is recommended to discontinue the previous treatment, and then initiate and titrate using recommended titration schedule for the new agent.

Beaded formulations enclosed in capsules may be helpful for children with difficulty swallowing tablets or capsules, as the capsules may be opened and sprinkled on cold or room temperature applesauce or other soft foods. Contents of the entire capsule should be consumed immediately, not stored. Beads should be swallowed whole, and not chewed.

In rare instances, it may be necessary to exceed the FDA-based maximum dose of stimulant medication to achieve optimal clinical efficacy; however, this should be done on a case-by-case basis with careful monitoring for treatment-emergent adverse effects.

# Other ADHD Treatments

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Baseline/ Monitoring | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Atomoxetine | Strattera®* | Age ≥ 6 years and weight ≤70 kg: 0.5 mg/kg/day | Age ≥ 6 years: 1.8 mg/kg/day or 100 mg/day, whichever is less | Approved for treatment of ADHD (age 6-17 years): 1.4 mg/kg/day or 100 mg/ day, whichever is less | Once or twice daily | Baseline and ongoing: height, weight, heart rate, and blood pressure | Suicidal ideation in children and adolescents being treated for ADHD | • Severe liver injury<br>• Contraindicated to use within 14 days of an MAOI<br>• Increased blood pressure and heart rate<br>• Psychiatric adverse events |

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Baseline/ Monitoring | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| | | Age ≥ 6 years and weight >70 kg: 40 mg/day | | | | Onset of therapeutic effect typically delayed 3 weeks | | • Priapism (rare) |
| Clonidine | Catapres® (IR)* | Age ≥ 6 years and weight <45 kg: 0.05 mg/day<br>Age ≥ 6 years and weight >45 kg: 0.1 mg/day | Age ≥ 6 years AND<br>Weight 27-40.5 kg: 0.2 mg/day<br>Weight 40.5-45 kg: 0.3 mg/day<br>Weight >45 kg: 0.4 mg/day | Not approved for treatment of ADHD in children and adolescents | One to four times daily | Baseline and ongoing: heart rate and blood pressure<br>Personal and family cardiovascular history | None | • Hypotension<br>• Bradycardia<br>• Syncope<br>• Sedation/Somnolence<br>• When tapering, total daily dose should be reduced in decrements of no more than 0.1mg for clonidine and 1mg for guanfacine every 3-7 days to avoid rebound hypertension<br>• See product labeling for Kapvay® and Intuniv® for information about clinically significant drug interactions<br>• Swallow ER tablets whole. Do not chew or break. |
| | Kapvay® (ER)* | Age ≥ 6 years: 0.1 mg/day | Age ≥ 6 years: 0.4 mg/day | Approved for monotherapy and adjunctive therapy to stimulants for treatment of ADHD (age 6-17 years): 0.4 mg/day | Once or twice daily | | | |
| Guanfacine | Tenex® (IR)* | Age ≥ 6 years and weight <45 kg: 0.5 mg/day<br>Age ≥ 6 years and weight > 45 kg: 1 mg/day | Age ≥ 6 years AND Weight 27-40.5 kg: 2 mg/day<br>Weight 40.5-45 kg: 3 mg/day<br>Weight >45 kg: 4 mg/day | Not approved for children and adolescents | One to four times daily | | | CAUTION IF USED WITH ANTIPSYCHOTICS (↓ BP) |
| | Intuniv® (ER)* | Age ≥ 6 years: 1 mg/day | Age 6-12 years: 4 mg/day<br>Age 13-17 years: 7 mg/day | Approved for monotherapy and adjunctive therapy to stimulants for treatment of ADHD<br>Age 6-12 years: 4 mg/day<br>Age 13-17 years: 7 mg/day<br>**Doses > 4mg/day have not been studied in adjunctive trials. | Once daily Do not administer with high fat meals. | | | |
| Bupropion | Wellbutrin®* | Age ≥ 6 years: 3 mg/kg/day or 150 mg/day, whichever is less | Age ≥ 6 years: 6 mg/kg/day or 300 mg/day with no single dose >150 mg, whichever is less | Not approved for children and adolescents | One to three times daily | Blood pressure and Pulse<br>Mental status exam and suicide assessment | Increased risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders | • Lowers seizure threshold (use caution with other agents that may lower seizure threshold-e.g. antipsychotics, TCA's, excessive alcohol)<br>• Discontinuation syndrome<br>• Activation of mania/ hypomania<br>• Suicidal ideation potential<br>• Contraindicated for use within 14 days of an MAOI |
| | Wellbutrin®SR* | | 400 mg/day | | Once or twice daily | | | |
| | Wellbutrin®XL* | | 450 mg/day | | Once daily | | | |
| Imipramine | Tofranil®* | Reviewed but not included/recommended | | | | | | • Caution with cardiac disease<br>• Cardiac conduction abnormalities<br>• Orthostatic hypotension<br>• Activation of mania/ hypomania<br>• Anticholinergic and cognitive adverse effects<br>• Lowers seizure threshold<br>• Discontinuation syndrome<br>• Suicidal ideation potential<br>• Use caution in those with history of suicide attempts; may be cardiotoxic in overdose<br>• Contraindicated for use within 14 days of an MAOI |
| Tricyclic Antidepressant | Multiple Individual medications | Reviewed but not included/recommended | | | | | | |

*Generic available.

Symbols and Abbreviations: IR, immediate release; SR, sustained-release formulation; ER, extended-release; XL, extended-length; BP, blood pressure; TCA, tricyclic antidepressant; MAOI, monoamine oxidase inhibitor.

# Antidepressants - SSRIs

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning** | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Citalopram | Celexa®*oral tablet<br>Citalopram*<br>oral solution (mint flavor) | Age 6-11 years: 10 mg/day<br>Age ≥ 12 years: 20 mg/day | Age ≥ 6 years: 40 mg/day | Not approved for children and adolescents | Once daily | • Pregnancy test<br>• as clinically indicated | Increased risk compared to placebo of suicidal thinking and behavior | • Suicidal ideation<br>• Activation of mania/hypomania |

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning** | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Escitalopram | Lexapro®*oral tablet<br><br>Escitalopram*<br>oral solution (mint flavor) | Age 6-11 years:<br>5 mg/day<br><br>Age ≥ 12 years (MDD): 10 mg/day | Age 6-11 years:<br>20mg/day<br><br>Age ≥ 12 years:<br>30 mg/day | Not approved for children<br>Approved for treatment of MDD in adolescents (age 12-17 years): 20 mg/day | | • Monitor for emergence of suicidal ideation or behavior<br>• Monitor weight and growth<br>• Obtain serum sodium if symptoms of hyponatremia occur (e.g. headaches, confusion, etc.) | (suicidality) in children, adolescents, and young adults in short- term studies of major depressive disorder (MDD) and other psychiatric disorders | • QTc prolongation potential (citalopram, escitalopram, sertraline, fluoxetine)<br>• Discontinuation syndrome<br>• Abnormal bleeding<br>• Contraindicated to use within 14 days of an MAOI; Do not start MAOI for 5 weeks after fluoxetine discontinuation<br>• Serotonin Syndrome<br>• Hyponatremia risk |
| Fluoxetine | Prozac®*oral capsule<br><br>Fluoxetine*<br>oral solution; (mint flavor) | Age 6-11 years:<br>5-10 mg/day<br><br>Age ≥ 12 years:<br>10 mg/day | Age ≥ 6 years:<br>60/day | Approved for treatment of MDD (age 8-18 years):<br>20 mg/day<br><br>Approved for treatment of OCD (age 7-17 years):<br>60 mg/day | | | | |
| Paroxetine | Paxil®*<br>oral tablet<br>Paxil®*<br>oral suspension (orange flavor)<br>Paxil®CR* | Reviewed but not included/recommended – evidence of possible harm | | | | | | |
| Fluvoxamine | Luvox®* *Brand name unavailable | Age ≥ 8 years:<br>25 mg/day | Age 8-11 years:<br>200 mg/day<br><br>Age 12-17 years:<br>300 mg/day | Approved for treatment of OCD (age 8-17 years):<br><br>Ages 8-11 years:<br>200 mg/day<br><br>Ages 12-17 years:<br>300 mg/day | Immediate-release: daily doses >50 mg should be divided -CR tablets: once daily | | | |
| | Luvox®CR* | Lowest available dose (100mg) may not be an appropriate initial dose for pediatric patients | | | | | | |
| Sertraline | Zoloft®*oral tablet<br>Zoloft®*oral solution (menthol flavor)<br>solution must be diluted before use | Age 6-12 years:<br>12.5-25 mg/day<br><br>Age 13-17 years:<br>25-50 mg/day | Age ≥ 6 years:<br>200 mg/day | Approved for treatment of OCD (age 6-17 years):<br>200 mg/day | Once daily | | | |
| Vilazodone<br>SSRI and 5-HT1A receptor partial agonist | Viibryd® | Age 12-17 years:<br>5mg/day on days 1-3, then 10mg/day on days 4-7 | Age 12-17 years:<br>30mg/day | Not approved for children and adolescents | Once daily | | | |

* Generic available.

Symbols and Abbreviations: CR, controlled-release; MDD, major depressive disorder; OCD, obsessive compulsive disorder, MAOI, monoamine oxidase inhibitor

** From Boxed Warning in FDA approved labeling for Antidepressants (SSRIs, SNRIs and Other Mechanisms): Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Both patients and families should be encouraged to contact the clinician if depression worsens, the patient demonstrates suicidal behavior or verbalizations, or if medication side effects occur. The appropriate utilization of non-physician clinical personnel who are knowledgeable of the patient population can aid in increasing the frequency of contact between the clinic and the patient/parent.

Footnote:

Unless there are concerns regarding specific issues, such as drug interactions, etc., fluoxetine has the most efficacy and safety data in the pediatric depression literature. Fluoxetine should be tried as the first-line option in children and adolescents aged 8 and older to treat moderate-to-severe major depressive disorder for which psychological therapy is insufficient to relieve symptoms after a reasonable trial (4-6 sessions).

# Antidepressants - SNRIs

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Venlafaxine* | Effexor®*<br>Effexor®XR* | Reviewed but not included/recommended – evidence of possible harm | | | | • Pregnancy test as clinically indicated<br>• Monitor for emergence of suicidal ideation or behavior<br>• Blood pressure during dosage titration and as clinically indicated<br>• Monitor weight and growth<br>Hepatic function testing baseline and as clinically indicated<br>• CBC and EKG at baseline and as clinically indicated for Clomipramine | Increased risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders | • Suicidal ideation<br>• Abnormal bleeding<br>• Severe skin reactions<br>• Discontinuation syndrome<br>• Activation of mania/ hypomania<br>• Hepatotoxicity<br>• Elevated blood pressure and pulse<br>• Serotonin Syndrome<br>• Seizures<br>• Hyponatremia<br>• Contraindicated for use within 14 days of an MAOI<br>• Rare cases of drug rash with eosinophilia and systemic symptoms (DRESS) |
| Duloxetine | Cymbalta®* | Age 7-17 years:<br>30 mg/day | Age 7-17 years:<br>120 mg/day | Approved for treatment of Generalized Anxiety Disorder<br>Age 7-17 years:<br>120 mg/day<br>Target dose 30-60mg/day | Once or twice daily | | | |
| Desvenlafaxine | Pristiq®* | Age 7-17 years<br>20 - <35 kg:<br>25mg<br><br>35 - <70 kg:<br>35mg<br><br>≥70 kg:<br>50mg | Age 7-17 years:<br>50mg/day | Not approved for children and adolescents | Once daily | | | |
| Levomilnacipran | Fetzima® | Reviewed but not included/recommended - insufficient evidence | | | | | | |
| Clomipramine | Anafranil®* | Age 10-17 years:<br>25 mg/day | Age 10-17 years:<br>3 mg/kg/day or 200 mg/ day, whichever is less | Approved for treatment of OCD<br>Age 10-17 years:<br>3 mg/kg/day or 200 mg/ day, whichever is less | Once daily | | | |

# Antidepressants – Other Mechanisms

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Mirtazapine | Remeron®*<br>Remeron® Soltab ODT (orange flavor) | Age 7-17 years: 7.5 mg/day<br>See comments – age of 3 based on one open label study, n=26 | Age ≥ 3 years: 45 mg/day | Not approved for children & adolescents | Once daily | • Pregnancy test – as clinically indicated<br>• Monitor for emergence of suicidal ideation or behavior<br>• Blood pressure during dosage titration and as clinically indicated<br>• Monitor weight and height<br>• Serum cholesterol levels<br>• CBC baseline and<br>• periodically<br>• Activation of Mania/Hypomania<br>• Selegiline: Monitor for tyramine induced hypertensive crisis | Increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short term studies of major depressive disorder (MDD) and other psychiatric disorders<br>In addition: EMSAM is contraindicated in patients less than 12 years of age (due to potential for hypertensive crisis) | • Suicidal ideation<br>• Abnormal bleeding<br>• Weight gain<br>• Discontinuation syndrome<br>• Activation of mania/ hypomania<br>• Orthostatic hypotension and syncope<br>• Serotonin Syndrome<br>• Hyponatremia<br>• Contraindicated for use within 14 days of an MAOI<br>• Mirtazapine: Rare cases of hepatotoxicity, seizures, and neutropenia<br>• Selegiline TD: tyramine rich foods and beverages should be avoided with doses of selegiline patch ≥ 9 mg per 24 hours or greater |
| Vortioxetine | Trintellix® | Reviewed but not included/recommended - insufficient evidence | | | | | | |
| Selegiline | Emsam® (transdermal system) | Age ≥ 12 years: 6 mg per 24 hours | Age ≥ 12 years: 12 mg per 24 hours | Approved for treatment of Major Depressive Disorder: Age ≥ 12 maximum dose of 12 mg per 24 hours | One patch daily | | | |
| Monoamine oxidase inhibitors (MAOIs) oral formulations | Reviewed but not included/recommended – increased risk of adverse events possible; risk of safety issues in youth given drug-food interactions, drug-drug interactions, etc. | | | | | | | |
| St. John's Wort | Reviewed but not included/recommended - insufficient evidence | | | | | | | |

* Generic available.

Symbols and Abbreviations: CR, controlled-release; MDD, major depressive disorder; OCD, obsessive compulsive disorder, MAOI, monoamine oxidase inhibitor; ODT = orally disintegrating tablet; TD = transdermal

** From Boxed Warning in FDA approved labeling for Antidepressants (SSRIs, SNRIs and Other Mechanisms): Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Both patients and families should be encouraged to contact the clinician if depression worsens, the patient demonstrates suicidal behavior or verbalizations, or if medication side effects occur. The appropriate utilization of non-physician clinical personnel who are knowledgeable of the patient population can aid in increasing the frequency of contact between the clinic and the patient/parent.

Footnote:

Unless there are concerns regarding specific issues, such as drug interactions, etc., fluoxetine has the most efficacy and safety data in the pediatric depression literature. Fluoxetine should be tried as the first-line option in children and adolescents aged 8 and older to treat moderate-to-severe major depressive disorder for which psychological therapy is insufficient to relieve symptoms after a reasonable trial (4-6 sessions).

# Antipsychotics: Second Generation (Atypical)

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Aripiprazole | Abilify® oral tablet*<br>Abilify Discmelt®* (oral disintegrating tablet; vanilla flavor)<br>Abilify® oral solution* (orange flavor) | Age ≥ 4 years: 2 mg/day | Age 4-11 years: 15 mg/day<br>Age ≥12 years: 30 mg/day | Approved for treatment of Bipolar Mania or Mixed Episodes (age 10-17 years) and Schizophrenia(13-17 years): 30 mg/day<br>Approved for treatment of irritability associated with Autistic Disorder (age 6-17 years): 15 mg/day<br>Approved for Tourette's Disorder (6-18 years): weight < 50 kg 10mg/day; weight ≥ 50 kg 20mg/day | Once daily | • Fasting plasma glucose level or HbA1c – at baseline, at 12 weeks, then annually.<br>• Lipid screening - at baseline, at 12 weeks, and as clinically indicated<br>• Blood pressure, pulse – at baseline, 12 weeks, and annually<br>• Weight (BMI) – at baseline, at 4 weeks, at 8 weeks, 12 weeks, and annually. BMI should be compared against growth charts www.cdc.gov/growthcharts Weight gain exceeding 90th percentile for age or a change of 5 BMI units for youths obese at treatment initiation should have weight management intervention and increased frequency of glucose and lipid monitoring | Increased the risk of suicidal thoughts and behavior in short-term studies in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders | • Extrapyramidal side effects<br>• Neuroleptic Malignant<br>• Syndrome<br>• Tardive Dyskinesia<br>• Hyperglycemia and Diabetes Mellitus<br>• Prolactinemia and gynecomastia (most common with risperidone and paliperidone)<br>• Weight gain<br>• Dyslipidemia<br>• Orthostatic Hypotension<br>• Leukopenia, neutropenia, and agranulocytosis<br>• Lowers seizure threshold<br>• Cognitive and motor impairment potential<br>• Hyperthermia<br>• Dysphagia |
| Quetiapine | Seroquel® *<br>Seroquel®XR* | Age 5- 9 years: 12.5-25 mg/day<br>Age 10-17 years: 25 mg twice day | Age 5- 9 years: 400mg/day<br>Age 10-17 years: 800 mg/day | Approved for treatment of Bipolar Mania (age 10-17 years): 600 mg/day<br>Approved for treatment of Schizophrenia (13-17 years): 800 mg/day | IR: One to three times daily<br>XR: Once daily | | | |

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Olanzapine<br><br>*Not recommended to try as a first-line treatment option due to risk of significant weight gain* | Zyprexa®*<br><br>Zyprexa Zydis®* (oral disintegrating tablet; unflavored, sweetened) | Age 4-5 years: 1.25 mg/day<br><br>Age 6-12years: 2.5 mg/day<br><br>Age ≥ 13years: 2.5-5 mg/day | Age 4-5 years: 12.5 mg/day<br><br>Age 6-17 years: 20 mg/ day | Approved for treatment of Bipolar Mania or Mixed Episodes<br>Schizophrenia (age 13-17 years):<br>20 mg/day<br><br>Approved for treatment of depressive episodes associated with Bipolar I Disorders (age 10-17 years): 12 mg/day in combination with 50mg/day fluoxetine | Once daily | • CBC as clinically indicated.<br>• Pregnancy test – as clinically indicated<br>• EPS evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase<br>• Tardive Dyskinesia evaluation (AIMS or NRS) at regular intervals throughout treatment (at least every 3 months)<br>• Sexual function– inquire for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males (priapism has been reported with SGAs); This inquiry should be done at each visit for the first 12 months and every 6 months thereafter.<br>• Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision-yearly<br>• Cardiovascular – obtain family history at baseline. In patients with family history of cardiac abnormalities or sudden death, personal history of syncope, palpitations, or cardiovascular abnormalities, baseline EKG and subsequent monitoring is recommended<br>• For patients with resting HR > 130 bpm, PR interval > 200 msec, QRS > 120 msec, or QTc > 460 msec, consider alternate therapy (AACAP Practice Parameter for the use of atypical antipsychotic medications in children and adolescents 2011)<br>• **Clozapine** Monitoring Parameters: Clozapine is associated with severe neutropenia (absolute neutrophil count (ANC) less than 500/µL). The requirements to prescribe, dispense, and receive clozapine are incorporated into a single, shared program called the Clozapine Risk Evaluation and Mitigation Strategy (REMS). Must follow specific requirements for CBC monitoring as per product labeling and clozapine REMS website.<br>• Prescribers and pharmacies must certify the | Increased the risk of suicidal thoughts and behavior in short-term studies in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders | • Rare cases of DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) Presence of a fever with a rash and swollen lymph glands, or swelling to the face. Requires immediate medical attention.<br>• Possible increase in the risk of unexplained sudden death. However, this is still rare, and causality has not been established. |
| Risperidone | Risperdal®*<br><br>Risperdal M-Tab®*(oral disintegrating tablet; peppermint flavor)<br><br>Risperdal® (oral solution; unflavored) | Age 4-5 years: <20 kg: 0.25 mg/day<br>>20 kg: 0.5 mg/day<br><br>Age ≥6 years: 0.5 mg/day | Age 4-11 years: 3 mg/day<br><br>Age ≥12 years: 6 mg/day | Approved for treatment of Schizophrenia (age 13-17 years) and Bipolar Mania or Mixed Episodes (age 10-17 years):<br>6mg/day<br><br>Approved for treatment of irritability associated with autistic disorder (age 5-16 years):<br>3 mg/day | Once or twice daily | | None related to youth | |
| Clozapine<br><br>*Reserved for treatment-resistant psychosis, following 2 failed trials of antipsychotic medications with adequate dose/duration* | Clozaril®*<br><br>FazaClo®* (oral disintegrating tablet; mint flavor)<br><br>Versacloz® oral suspension (unflavored, sweetened) | Age 8-11 years: 6.25-12.5 mg/day<br><br>Age ≥ 12 years: 6.25-25 mg/day | Age 8-11 years: 150-300 mg/day<br>Age ≥ 12 years: 600 mg/day<br><br>Target serum clozapine level of 350 ng/mL for optimal efficacy | Not approved for children and adolescents | Once or twice daily | | • Severe neutropenia<br>• Seizures<br>• Orthostasis, bradycardia, syncope<br>• Myocarditis, cardiomyopathy, mitral valve incompetence | |
| Asenapine | Saphris® (sublingual tablet; black cherry flavor) | Age ≥ 10 years: 2.5 mg twice daily | Age ≥ 10 years: 10 mg twice daily | Approved for acute treatment of Bipolar Mania and Mixed Episodes (age 10-17 years):<br>10 mg twice daily | Twice daily. Avoid eating or drinking for 10 minutes after sublingual administration | | None related to youth | |

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| | | | | | | use of Clozapine at www.clozapinerems.com | | |
| Iloperidone | Fanapt® | Reviewed but not included/recommended - insufficient evidence | | | | | None related to youth | |
| Paliperidone | Invega®* | Children: Insufficient Evidence<br>Adolescent: (Age ≥ 12years): 3 mg/day | Children: Insufficient Evidence<br><br>Adolescents (Age ≥ 12 years), Schizophrenia: Weight < 51 kg: 6 mg/day<br>Weight ≥ 51 kg: 12 mg/day | Approved for treatment of Schizophrenia (age 12-17 years):<br>Weight < 51 kg: 6 mg/day<br>Weight ≥ 51 kg: 12 mg/day | Once daily | | None related to youth | |
| Ziprasidone | Geodon®* | Bipolar Disorder (age 10-17 years): 20 mg/day | Bipolar Disorder (age 10-17 years)<br>Weight ≤ 45 kg: 80 mg/day<br>Weight > 45 kg: 160 mg/day | Not approved for children and adolescents | Twice daily; take with ≥500 calorie meal | | None related to youth | |
| Lurasidone | Latuda® | Schizophrenia (age 13-17 years): 40 mg/day<br><br>Bipolar I Depression monotherapy (age 10-17 years): 20 mg/day | Schizophrenia (age 13-17 years) 80 mg/day<br>Bipolar I Depression (age 10-17 years) 80 mg/day | Approved for treatment of Schizophrenia (age 13- 17 years) and Bipolar I Disorder, depressed phase, as monotherapy: 80 mg/day | Insufficient Evidence<br><br>Once daily taken with >350 calorie meal | | Increased the risk of suicidal thoughts and behavior in short-term studies in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders | |
| Brexpiprazole | Rexulti® | Reviewed but not included/recommended - insufficient evidence<br>Not approved for children and adolescents | | | | | None related to youth | |
| Cariprazine | Vraylar® | Reviewed but not included/recommended - insufficient evidence<br>Not approved for children and adolescents | | | | | None related to youth | |
| Combination Antipsychotic-Antidepressant Formulation(s) | | | | | | | | |
| Olanzapine/ Fluoxetine | Symbyax®* | Age 10-17 years: 3 mg olanzapine/25 mg fluoxetine once daily | Age 10-17 years: 12 mg olanzapine/50 mg fluoxetine once daily | Acute Depressive Episodes Associated with Bipolar I Disorder for age 10-17 years:<br>12 mg olanzapine/50 mg fluoxetine | Once Daily | | Increased the risk of suicidal thoughts and behavior in short-term studies in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders | |

Symbols and Abbreviations: XR, extended-release; HbA1c, hemoglobin A1c; BMI, body mass index; kg, kilograms; HR, heart rate; msec, milliseconds; AACAP, American Academy of Child and Adolescent Psychiatry; AIMS, Abnormal Involuntary Movement Scale; NRS, Neurological Rating Scale.

*Generic available.

+ XR, extended-release

** While iloperidone alone can cause QTc prolongation, concomitant administration with a CYP2D6 inhibitor (e.g., paroxetine) or a CYP3A4 inhibitor (e.g., ketoconazole) can double QTc prolongation compared with administering iloperidone alone. No long-acting injectable antipsychotic formulations are FDA-approved for use in children and adolescents.

Note: A cohort study found an increase of an additional 5.9 deaths/10,000-person years (7.7 – 1.8 deaths/10,000 person years) in children and youth receiving antipsychotics as compared with the control group. Their sample size was not adequate to compare potential risk of different antipsychotics (Ray 2019).

# Antipsychotics: First Generation (Typical)

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| Chlorpromazine* | Thorazine® (Brand name discontinued) | Age > 6 months: 0.25 mg/lb. every 4-6 hours, as needed<br><br>Adolescents: 10-25 mg/dose every 4-6 hours | Age < 5 years: 40 mg/day<br><br>Age 5-12 years: 75 mg/day<br><br>Age > 12 years: 800 mg/day | Approved for treatment of severe behavioral problems (age 6 months-12 years)<br><br>Outpatient Children: 0.55 mg/kg every 4-6 hours, as needed<br><br>Approved for the management of manifestations of Psychotic Disorders (age> 12 years): 1000 mg/day | 1-6 times daily | • Fasting plasma glucose level or HbA1c – at baseline, at 12 weeks, then annually.<br>• Lipid screening - at baseline, at 12 weeks, and as clinically indicated<br>• Blood pressure, pulse – at baseline, 12 weeks, and annually<br>• Weight (BMI) – at baseline, at 4 weeks, at 8 weeks, 12 weeks, and annually. BMI should be compared against growth charts www.cdc.gov/growthcharts Weight gain exceeding 90th percentile for age or a change of 5 BMI units for youths obese at treatment initiation should have weight management intervention and increased | None related to youth | • Tardive Dyskinesia<br>• Neuroleptic Malignant Syndrome<br>• Leukopenia, neutropenia, and agranulocytosis<br>• Drowsiness<br>• Orthostatic hypotension<br>• EKG changes<br>• EEG changes and seizures possible<br>• Extrapyramidal symptoms<br>• Ocular changes<br>• Hyperprolactinemia<br>• Anticholinergic effects (constipation, dry mouth, blurred vision, urinary retention)<br>• Risk of prolonged QTc interval and torsades de pointes (particularly with pimozide) |
| Haloperidol* | Haldol® (Brand name discontinued) | Age 3-12 years: Weight 15-40 kg: 0.025-0.05 mg/kg/day<br>Weight ≥ 40 kg: 1 mg/day | Age 3-12 years: 0.15 mg/kg/day or 6 mg/day, whichever is less | Approved for treatment of Psychotic Disorders, Tourette's Disorder, and severe behavioral problems (age ≥3 years). | One to three times daily | | None related to youth | |

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|
| | | Age > 12 years: 1 mg/day | Age >12 years: Acute agitation: 10 mg/dose Psychosis: 15 mg/day Tourette's Disorder: 15 mg/ day | Psychosis: 0.15 mg/kg/day<br><br>Tourette's Disorder and severe behavioral problems: 0.075 mg/kg/day<br><br>Severely disturbed children: 6 mg/day | | frequency of glucose and lipid monitoring<br>• CBC as clinically indicated.<br>• Pregnancy test – as clinically indicated<br>• EPS evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase<br>• Tardive Dyskinesia evaluation (AIMS or NRS) at regular intervals throughout treatment (at least every 3 months)<br>• Sexual function– inquire for evidence of galactorrhea/ gynecomastia, menstrual disturbance, libido disturbance or erectile/ ejaculatory disturbances in males (priapism has been reported with SGAs); This inquiry should be done at each visit for the first 12 months and every 6 months thereafter.<br>• Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision- yearly<br>• Cardiovascular – obtain family history at baseline. In patients with family history of cardiac abnormalities or sudden death, personal history of syncope, palpitations, or cardiovascular abnormalities, baseline EKG and subsequent monitoring is recommended for patients with resting HR > 130 bpm, PR interval > 200 msec, QRS > 120 msec, or QTc > 460 msec, consider alternate therapy (AACAP Practice Parameter for the use of atypical antipsychotic medications in children and adolescents 2011) EKG required at baseline and as clinically indicated for pimozide (use with other medications with QTc prolongation potential is contraindicated e.g., escitalopram, citalopram, macrolides, etc.) | | |
| Perphenazine* | Trilafon®* (Brand name discontinued) | Age 6-12 years: Insufficient Evidence<br><br>Age > 12 years: 4-16 mg two to four times daily | Age 6-12 years: Insufficient Evidence<br><br>Age > 12 years: 64 mg/day | Approved for treatment of psychotic disorders (age≥12 years).<br><br>Outpatient: 24 mg/day<br><br>Inpatient: 64 mg/day | Two to four times daily | | None related to youth | |
| Pimozide | Orap®* | Age ≥7 years: 0.05 mg/kg once a day<br><br>At doses > 0.05mg/kg/day CYP2D6 genotyping should be performed. In poor 2D6 metabolizers, dose should not exceed 0.5mg/kg/day | Age 7-12 years: 6 mg/day or 0.2 mg/kg/day, whichever is less<br><br>Age ≥ 12 years: 10 mg/day or 0.2 mg/kg/day, whichever is less | Approved for treatment of Tourette's Disorder (age ≥12 years): 10 mg/day or 0.2 mg/kg/ day, whichever is less | Once or twice daily | | None | |

*Generic available.

Symbols and Abbreviations: HbA1c, hemoglobin A1c; BMI, body mass index; kg, kilograms; HR, heart rate; msec, milliseconds; AACAP, American Academy of Child and Adolescent Psychiatry.

# Mood Stabilizers

| Drug (generic) | Drug (brand) | Initial Dosage | Target Dosage Range | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children& Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|---|
| Carbamazepine | Epitol®* tablet<br>Tegretol®* tablet<br><br>Tegretol®* (oral suspension; citrus vanilla flavor)<br><br>Tegretol®* (chewable tab, cherry flavor some generic formulations)<br>Tegretol®XR* tablet | Age 4-5 years: 10-20 mg/ kg/day in 2-3 divided doses<br><br>Age 6-12 years: 100mg twice daily<br><br>Age ≥ 13 years: 200mg twice daily | Age 4-5 years: 35 mg/kg/day<br><br>Ages 6-12 years: 400-800 mg/day<br><br>Age ≥ 13 years: 800- 1200 mg/day | Age 4-5 years: 35 mg/ kg/day<br><br>Ages 6-12 years: 800 mg/day<br><br>Age 13-15 years: 1000 mg/day<br><br>Age >15 | Approved for treatment of Seizure Disorders in all ages<br><br>Age < 6 years: 35 mg/kg/day<br><br>Age 6-12 years: 1000 mg/day<br><br>Age >15 years: 1200 mg/day | Two to four times daily<br><br>Twice daily | • CBC with differential - baseline and 1 to 2 weeks after each dose increase, annually, and as clinically indicated<br>• Electrolytes - baseline and 1 to 2 weeks after each dose increase, annually, and as clinically indicated | Serious dermatological reactions and HLA-B*1502 allele<br><br>Aplastic anemia and agranulocytosis | • Stevens-Johnson Syndrome<br>• Aplastic anemia<br>• Suicidality<br>• Teratogenicity<br>• Neutropenia and<br>• agranulocytosis<br>• Hyponatremia<br>• Induces metabolism of itself and many other drugs (strong CYP 3A4 inducer) |

| Drug (generic) | Drug (brand) | Initial Dosage | Target Dosage Range | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children& Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|---|
| | Carbatrol®* (extended release capsule)<br>Equetro® (extended release capsule) | | | years:<br>1200 mg/day | The safety and effectiveness of EQUETRO in pediatric and adolescent patients have not been established. | | • Hepatic function - baseline, monthly for first three months, annually and as clinically indicated.<br>• Pregnancy Test --- baseline as appropriate, and as clinically indicated<br>• Carbamazepine levels ---obtain 1 week after initiation and 3-4 weeks after dose adjustment, then as clinically indicated<br>• For patients with Asian descent, genetic test for HLA- B*1502 at baseline (prior to the initiation of carbamazepine). May use results of previously completed testing. Patients testing positive for the allele should not use carbamazepine unless benefit outweighs the risk<br>• Consider HLA-A*3101 genetic testing at baseline for those to be considered at high risk (most common in Asian, Native American, European, and Latin American descents)<br>• Monitor for the emergence of suicidal ideation or behavior<br>• Usual therapeutic trough level is between 4-12 mcg/ml | | • Decreased efficacy of oral contraceptives<br>• Withdrawal seizures<br>• Contraindicated to use within 14 days of an MAOI |
| Divalproex Sod | Depakote®* delayed-release tablets<br><br>Depakote® ER* extended- release tablets<br><br>Depakote® sprinkle capsules* | Age ≥6 years: 10-15 mg/kg/d | Age ≥6 years: 30-60mg/kg/day | Age ≥6 years: Serum level: 125 µg/mL, or 60 mg/kg/day | Approved for treatment of Seizure Disorders (age ≥ 10 years)<br>Maximum dose based upon serum level:<br>50-100 µg/mL, or 60 mg/kg/day | One to three times daily | • CBC - with differential and platelet count - baseline then 1 to 2 weeks after each dosage increase, every 3 months for the first year of treatment, then annually and as clinically indicated<br>• Comprehensive Metabolic Panel (hepatic function, serum creatinine, BUN and electrolytes) – baseline, every 3 months for the first year of treatment, then annually and as clinically indicated.<br>• Pregnancy Test – baseline as appropriate, and as clinically indicated<br>• Trough Valproic acid level – 1-2 weeks after initiation and dosage change, then as clinically indicated.<br>• Weight – baseline, quarterly for the first year of treatment, then annually and as clinically indicated<br>• Monitor for the emergence of suicidal ideation or behavior | • Hepatotoxicity (increased risk with young children)<br>atients (i.e., between 3 months and 10 years) have 50% higher clearances (i.e., mL/min/kg) than do adults. Over the age of 10 years, children have pharmacokinetic parameters that approximate those of adults.<br>• Teratogenicity<br>• Pancreatitis | • Hepatotoxicity<br>• Pancreatitis<br>• Urea cycle disorders<br>• Teratogenicity<br>• Suicidal ideation<br>• Neutropenia and leukopenia (significant increased risk with quetiapine co-administration)<br>• Thrombocytopenia<br>• Hyperammonemia<br>• Multi-organ hypersensitivity reaction<br>• Withdrawal seizures<br>• Polycystic ovarian syndrome<br>• Weight gain potential<br>• Aecia |

| Drug (generic) | Drug (brand) | Initial Dosage | Target Dosage Range | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children& Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Usual therapeutic trough levels:<br><br>Bipolar disorder:<br>50- 125 mcg/ml for valproic acid and Divalproex delayed release (Depakote®).<br><br>Acute mania:<br>85-125 mcg/ml for divalproex extended release (Depakote ER®). A lower therapeutic trough level may be needed with divalproex extended release for maintenance treatment.<br><br>For extended release products, a trough level is considered to be 18 to 24 hours after the last dose. | | |
| Lithium | Lithium carbonate capsules<br>Eskalith® CR (450 mg) extended-release tablet)<br>Lithobid® ER (300 mg extended-release tablet)<br>Lithium citrate* (oral solution, 300mg/5mL, raspberry flavor) | Age 6-11 years: 150mg twice per day<br><br>Age ≥12 years: 300 mg twice per day | Dose adjustment based upon serum level; increase in weekly increments 12-hour post dose serum level: 0.6-1.2 mEq/L | Age ≥12 years: Serum level: 1.2 mEq/L, or 1800 mg | Approved for treatment of manic episodes and maintenance of Bipolar Disorder (age ≥ 7 years)<br><br>Maximum dose:<br>20-30 kg:<br>acute: 1500 mg<br>maintenance: 1200 mg<br><br>>30 kg: 1800 mg<br>12-hour post dose serum level:<br>acute: 0.8-1.2 mEq/L<br>maintenance: 0.8-1 mEq/L | One to four times daily | • EKG – baseline, yearly<br>• CBC – baseline, yearly<br>• Thyroid studies – baseline; then TSH every 6 months<br>• Comprehensive Metabolic Panel, baseline, 3 months, annually. Caution: BUN: serum creatinine ratio >20 may be an indication of dehydration.<br>• UA - baseline<br>• Pregnancy Test<br>• Trough Lithium Levels – one week (i.e., 5-7 days) after initiation or dosage change, 3 months after initiation; for maintenance treatment every 6 months<br>• Weight – baseline, every 6 months<br>• Usual trough therapeutic level: 0.6-1.2 meq/L (12 hrs. post dose) | Toxicity above therapeutic serum levels | • Toxicity above therapeutic serum levels; narrow therapeutic index<br>• Chronic renal function impairment<br>• Increased risk of toxicity possible for patients with significant renal disease, dehydration, sodium depletion, concomitant drug interactions (ACEI, ARBS, NSAIDs, COXII inhibitors, diuretics, etc.)<br>• Polyuria<br>• Tremor<br>• Diarrhea<br>• Nausea<br>• Hypothyroidism<br>• Teratogenicity |

*Generic Available.

Symbols and Abbreviations: CR, controlled-release; ER and XR, extended-release; CYP, cytochrome P450; MAOI, monoamine oxidase inhibitor; ODT = orally disintegrating tablet; ACEI, Ace Inhibitor antihypertensive medication; ARP, Angiotensin Receptor Blocker antihypertensive medication, NSAIDs, non-steroidal anti-inflammatory drug; COX II inhibitors, cyclooxygenase II inhibitor pain medication; EKG, electrocardiogram; CBC, complete blood count; BUN, blood urea nitrogen; UA, urinalysis.

| Drug (generic) | Drug (brand)+ | Initial Dosage | Target Dosage Range | Literature Based Maximum Dosage | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Patient Monitoring Parameters | Boxed Warning | Warnings & Precautions |
|---|---|---|---|---|---|---|---|---|---|
| Lamotrigine | Lamictal® *<br><br>Lamictal® CD*<br>(chewable dispersible tablets)<br><br>Lamictal® ODT*<br>(oral disintegrating tablet; blackcurrant flavor) | Age 6-11 years: 2-5 mg/ day<br><br>Age ≥12 years:<br>25 mg/day (increase by 25 mg every 2 weeks) | Epilepsy dosing Age 6-11 years<br>Monotherapy: 4.5-7.5 mg/kg/day<br>With Valproate: 1-3 mg/kg/day<br>With Valproate and EIAEDs: 1-5 mg/kg/day<br>With EIAED's: 5-15 mg/kg/day<br><br>Age ≥12 years<br>Monotherapy: 225-375 mg/day<br>With Valproate: 100-200 mg/day<br>With Valproate and EIAEDs: 100-400 mg/day<br>With EIAEDs: 300-500 mg/day<br>See product labeling for detailed charts for alternate dosing in the presence of drug interactions i.e., divalproex/valproic acid OR EIAEDs (carbamazepine, phenytoin, phenobarbital, primidone) | See dosing tables below main table for recommended lamotrigine titration for 10-12-year-old and 13-17 year olds for pediatric bipolar disorder. Dosing is from a t randomized, placebo-controlled study conducted by Findling and colleagues for youth with bipolar disorder | Approved for adjunctive therapy for Seizure Disorders:<br>Age 2-12:<br>400 mg/ day<br><br>Age >12: 500 mg/day<br>Use of doses > 200mg/day in adults with bipolar depression has not conferred additional efficacy)<br>Not FDA-approved for treatment of Bipolar Disorder in patients younger than 18 years | Once or twice daily | • Renal Function - baseline and as clinically indicated<br>• Hepatic Function - baseline and as clinically indicated<br>• Pregnancy Test - baseline and as clinically indicated<br>• CBC – baseline and as clinically indicated<br>• Monitor for the emergence of suicidal ideation or behavior<br>• Monitor for rash, especially during the first two months of therapy | Serious rashes including Stevens-Johnson syndrome | • Dermatological reactions<br>• Potential Stevens-Johnson Syndrome; risk increased with too-rapid titration<br>• Drug reaction with eosinophilia and systemic symptoms (DRESS) reactions have occurred<br>• Suicidal ideation<br>• Aseptic meningitis<br>• Concomitant use with divalproex increases serum lamotrigine levels significantly (increased risk of rash/SJS without lamotrigine dose adjustment)<br>• Concomitant use with enzyme inducing AEDs (carbamazepine, phenytoin, phenobarbital, primidone) reduces serum lamotrigine levels significantly (reduced lamotrigine efficacy possible without lamotrigine dose adjustment)<br>• Concomitant use with oral contraceptives increases lamotrigine clearance<br>• Withdrawal seizure potential |
| | Lamictal XR® * (extended-release tablet) | Age ≥ 13 years:<br>25 mg/day | Age ≥13 years (without concomitant drug interactions):<br>25mg once daily for 2 weeks, then 50mg once daily for 2 weeks, then 100mg once daily for 1 week, then 150mg once daily for 1 week, then 200mg once daily for 1 week, then increase to maintenance dose of 300-400mg/day thereafter.<br>(Use of doses > 200mg/day in adults with bipolar depression has not conferred additional efficacy)<br>See product labeling for detailed charts for alternate dosing in the presence of drug interactions i.e., divalproex/valproic acid OR EIAEDs (carbamazepine, phenytoin, phenobarbital, primidone) | Lamictal XR® has no published data for mood stabilization in pediatrics | Approved for adjunctive therapy for Seizure Disorder 13 years or older<br>Maximum dose depends on presence of concomitant drug interactions, see product labeling<br>Not FDA-approved for treatment of Bipolar Disorder in patients younger than 18 years | Once daily | | | |
| Oxcarbazepine | Trileptal®<br>(film coated tablet)<br>Trileptal® oral suspension*<br>(plum-lemon flavor)<br>Oxtellar XR® extended-release tablet | Reviewed but not included/recommended - insufficient evidence | | | | | | None related to youth | |

*Generic Available.

Symbols and Abbreviations: CD, chewable dispersible; ER and XR, extended-release; ODT, oral disintegrating tablet; kg, kilograms; XR, extended-release; EIAED's - Enzyme Inducing Anti-Epileptic Drugs (e.g. Carbamazepine, Phenobarbital, Phenytoin, Primidone).

# Lamotrigine Dosing

**Lamotrigine Dose Titration for Adolescents 10-12 years of age.**

| | For Patients Taking Valproate[a] (mg/kg/day) | For Patients not Taking Carbamazepine (or Other Enzyme-Inducing Drugs) and not Taking Valproate[b] (mg/kg/day) | For Patients Taking Carbamazepine (or Other Enzyme-Inducing Drugs) and not Taking Valproate[b] (mg/kg/day) |
|---|---|---|---|
| Study Week | | | |
| Weeks 1 and 2 | 0.15 | 0.3[a] | 0.6 |
| Weeks 3 and 4 | 0.3 | 0.6 | 1.2 |
| Week 5 | 0.6 | 1.2 | 2.4 |
| Week 6 | 0.9 | 1.8 | 3.6 |
| Week 7 | 1.2 | 2.4 | 4.8 |
| Week 8 | 1.5 | 3.0 | 6.0 |
| Week 9 | 1.8 | 3.6 | 7.2 |
| Week 10 | 2.1 | 4.2 | 8.4 |
| Week 11 | 2.4 | 4.8 | 9.6 |
| Week 12 | 2.7 | 5.4 | 10.8 |
| Weeks 13–18 | 3.0 | 6.0 | 12.0 |
| Maximum Dose | 3 mg/kg/day or 100 mg/day[a] whichever occurred first | 6 mg/kg/day or 200 mg/day[b] whichever occurred first | 12 mg/kg/day or 300 mg/day[b] whichever occurred first |

*Note: [a]In 1 or 2 divided doses.*
*[b]In 2 divided doses (unless noted otherwise).*

**Lamotrigine Dose Titration for Adolescents 13-17 years of age.**

| Study Week | For Patients Taking Valproate | For Patients not Taking Carbamazepine (or Other Enzyme-Inducing Drugs) and not Taking Valproate | For Patients Taking Carbamazepine (or Other Enzyme-Inducing Drugs) and not Taking Valproate |
|---|---|---|---|
| Weeks 1 and 2 | 25 mg every other day | 25 mg/day | 50 mg/day |
| Weeks 3 and 4 | 25 mg/day | 50 mg/day | 100 mg/day[a] |
| Week 5 | 50 mg/day (minimum dose) | 100 mg/day (minimum dose) | 150 mg/day[a] |
| Week 6 | 75 mg/day | 150 mg/day | 200 mg/day[a] (minimum dose) |
| Week 7 | 100 mg/day (target dose) | 200 mg/day (target dose) | 250 mg/day[a] |
| Week 8 | 125 mg/day | 250 mg/day[a] | 300 mg/day[a] (target dose) |
| Week 9 | 150 mg/day (maximum dose) | 300 mg/day[a] (maximum dose) | 350 mg/day[a] |
| Weeks 10–18 | 150 mg/day | 300 mg/day[a] | 400 mg/day[a] (maximum dose) |

*Note: [a]In two divided doses.*

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Reprinted from the Journal of the American Academy of Child and Adolescent Psychiatry, Volume 52 (Edition 12), Findling RL, Chang K, Robb A, et al. Adjunctive Maintenance Lamotrigine for Pediatric Bipolar I Disorder: A Placebo-Controlled, Randomized Withdrawal Study, pages 1020-1031.e3, Copyright (2015), with permission from Elsevier.
https://www.sciencedirect.com/journal/journal-of-the-american-academy-of-child-and-adolescent-psychiatry http://www.elseevier.com

# Sedatives/Hypnotics

| Drug (generic) | Drug (brand) | Initial Dosage | Literature Based Maximum Dosage** | FDA Approved Maximum Dosage for Children & Adolescents | Schedule | Black Box Warning** | Warnings & Precautions |
|---|---|---|---|---|---|---|---|
| Diphenhydramine | Benadryl®* | Age 3-5 years: 6.25-12.5 mg (1mg/kg max)<br><br>Age 5-11 years: 12.5-25 mg<br><br>Age ≥12 years: 25-50 mg | 25-37 lbs: 12.5 mg<br>38-49 lbs: 19 mg<br>50-99 lbs: 25 mg<br>≥100 lbs: 50 mg<br><br>Evidence suggests that tolerance develops to the hypnotic effects of diphenhydramine within 5-7 nights of continuous use. | Approved for treatment of insomnia (age ≥12 years): 50 mg at bedtime | Once at bedtime | None | • Drowsiness<br>• Dizziness<br>• Dry mouth<br>• Nausea<br>• Nervousness<br>• Blurred vision<br>• Diminished mental<br>• alertness<br>• Paradoxical excitation<br>• Respiratory disease<br>• Hypersensitivity reactions<br>• May lower seizure threshold (avoid in epilepsy) |
| Trazodone* | Desyrel®* | Children: Insufficient Evidence<br><br>Adolescents: 25 mg | Children: Insufficient Evidence<br><br>Adolescents: 100 mg/day | Not approved for use as a hypnotic. | Once at bedtime | Increased the risk compared to placebo of suicidal thinking and behavior (Suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders | • Serotonin Syndrome<br>• Use Contraindicated within 14 days of an MAOI<br>• Suicidal ideation<br>• Activation of mania/hypomania<br>• Discontinuation syndrome<br>• Abnormal bleeding<br>• QT prolongation and risk of sudden cardia death<br>• Orthostatic hypotension and syncope<br>• Abnormal bleeding<br>• Priapism<br>• Hyponatremia<br>• Cognitive and motor impairment |
| Eszopiclone | Lunesta®* | Reviewed but not included/recommended - insufficient evidence/increased rate of adverse events in pediatric patients | | | | None | • Complex sleep behaviors possible<br>• Abnormal thinking and behavior changes<br>• Withdrawal effects<br>• Drug abuse and dependence<br>• Tolerance |
| Melatonin | No brand name | Age 3-5 years: 0.5mg<br><br>Age ≥6 years: 1mg | Age 3-5 years: 0.15 mg/kg or 3 mg, whichever is less<br><br>Age ≥6 years: 0.15mg/kg or 6mg, whichever is less | Regulated by FDA as a dietary supplement and not as a medication (no FDA approved indications) | Once at bedtime or alternatively, give 5-6 hrs before Dim Light Melatonin Onset (DLMO) | None | • Sedation<br>• Should be given directly before onset of sleep is desired due to short half-life |
| Ramelteon | Rozerem® | Reviewed but not included/recommended - insufficient evidence | | | | None | • Hypersensitivity reactions<br>• Need to evaluate for comorbid diagnoses<br>• Abnormal thinking and behavioral changes<br>• CNS depression<br>• Decreased testosterone possible<br>• Hyperprolactinemia possible |
| Hydroxyzine* | Vistaril®* | Age 3-5 years: 25 mg<br><br>Age ≥6 years: 50mg | Age 3-5 years: 25 mg<br><br>Age 6-11 years: 50mg<br><br>Age 12 years and older: 100 mg | Approved for treatment of anxiety and tension:<br>Age <6 years: 50 mg/day in divided doses<br><br>Age = 6 years: 50-100 mg/day in divided doses<br><br>Approved as a sedative when used as a premedication and following general anesthesia: 0.6 mg/kg | Once at bedtime | None | • Drowsiness<br>• Dry mouth<br>• Involuntary motor activity<br>• Blurred vision, dizziness, diminished mental alertness<br>• Paradoxical excitation associated with a small but definite risk of QT interval prolongation and torsades de pointes |
| Suvorexant | Belsomra® | Reviewed but not included/recommended - insufficient evidence | | | | None related to youth | • Sleep paralysis<br>• Somnolence |
| Zolpidem | Ambien®* | Reviewed but not included/recommended – evidence of possible harm | | | | None related to youth | • Hallucinations in children 6-17 have been reported<br>• Complex sleep behaviors possible<br>• Abnormal thinking and behavior changes<br>• Withdrawal effects<br>• Drug abuse and dependence<br>• Tolerance |
| Benzodiazepines | Alprazolam/ Xanax®*<br>Clonazepam/ Klonopin®*<br>Diazepam/ Valium®*<br>Lorazepam/ Ativan®*<br>Oxazepam/ Serax®*<br>(brand name unavailable)<br>Temazepam/ Restoril®* | Reviewed but not included/recommended – evidence of possible harm/increased incidence of adverse effects and potential for abuse and/or addiction | | | | Risks from concomitant use with opioids | • Withdrawal effects<br>• Drug abuse and dependence<br>• Tolerance<br>• Sedation potential |

*Generic Available

# Special Considerations

It is best to optimize the dose of psychotropic medication and allow an adequate trial (usually 4-8 weeks, depending on medication class) before a switch in psychotropic medication is performed, unless adverse effects prohibit or limit the current treatment.

## Titration of Antidepressant Medications

For most antidepressant medications, start at the recommended initial dose and wait approximately one week in between dose increases (as tolerated) until the target dose is achieved. It is recommended to start low and go slow to reduce treatment-emergent anxiety and potential activation. Guidelines suggest weekly contact with the young patient and their parent/caregiver for the first 4 weeks of treatment and bi-weekly thereafter. (NICE 2005; AACAP 2007; FDA) As with other medications treatments for Major Depressive Disorder and anxiety disorders, symptom improvement/response may be delayed until 4 weeks of treatment or longer.

## Taper of Antidepressant Medications

For antidepressant treatment duration >4-6 weeks, taper is recommended to avoid withdrawal symptoms (flu-like symptoms, anxiety, irritability, nausea, 'electric shock' sensation, etc.) and to reduce potential for symptom worsening and relapse. The taper schedule should be tailored depending on patient diagnosis and individual characteristics.

Abrupt discontinuation of antidepressant medications is generally NOT recommended. For significant or severe adverse effects, abrupt discontinuation may be advised; however, withdrawal adverse effects and relapse/symptom exacerbation are possible. A number of strategies for switching or discontinuing antidepressant medications have been studied in adults. A paucity of evidence exists to guide best practice for antidepressant tapering and discontinuation in youth. The following is based on review of available data, clinical experience, and expert consensus.

Tapering to discontinue: Antidepressant taper should occur slowly over at least 4 weeks [Example taper schedule: 10-20-25% dose reduction (from initial dose) each week until discontinuation is complete].

For patients achieving remission on antidepressant medications for a significant duration of time OR if significant withdrawal symptoms/symptom recurrence occur(s) during taper, a longer and slower taper can be considered (up to 12 weeks).

Switching between antidepressant classes: Cross-taper should occur over no longer than 4 weeks. Use caution using two antidepressant medications in higher doses to reduce the risk of serotonin syndrome (symptoms include: hyperthermia, hyperreflexia, agitation, tremor, sweating, altered mental status, tachycardia, etc.). An example taper schedule is: 25-50% dose reduction each week of previous antidepressant with titration of new antidepressant starting at 25% of target dose, then increasing over 2-4 weeks to target dose.

Switching between SSRIs: In cases of switching between SSRI medications, a direct switch can be performed (i.e., take the last dose of one SSRI medication one day, and then start an equivalent/therapeutic dose of a different SSRI the next day and discontinue previous SSRI). Taper is also possible, with a taper duration not to exceed approximately 2 weeks.

Individual medication considerations for tapering:

Fluoxetine: Due to the long half-life of fluoxetine (and active metabolite norfluoxetine), if dose is less than 40 mg/day, you may consider taper and discontinuation over 7-14 days [e.g., reduce to 20mg for 7 days, then 10mg for 7 days, then stop] depending on individual clinical factors. A longer taper is recommended if withdrawal symptoms occur or if clinical presentation worsens during taper.

Paroxetine: Due to the short half-life of paroxetine, a longer and slower taper may be necessary with a goal of discontinuation to prevent withdrawal and symptom exacerbation.

## Titration of Antipsychotic Medications

| Medication | Indication | Initial Dose | Titration Increments | Target Dose | Effective Daily Dose Range |
|---|---|---|---|---|---|
| Risperidone<br>Usual dosing is once daily, but can change to twice daily for persistent somnolence | Schizophrenia adolescents | 0.5 mg/day | 0.5-1 mg; no more often than daily* | 3 mg | 1-6 mg |
| | Bipolar mania children and adolescents | 0.5mg/day | 0.5-1mg; no more often than daily* | 1-2.5 mg | 1-6 mg |
| | Irritability in autistic disorder body weight < 20 kg | 0.25mg/day | Can ↑ to 0.5mg on Day 4; then ↑ by 0.25mg every 2+ weeks | 0.5mg | 0.5 – 3mg |
| | Irritability in autistic disorder body weight ≥ 20 kg | 0.5 mg/day | Can ↑ to 1mg on Day 4; then ↑ by 0.5mg every 2+ weeks | 1 mg | 0.5 – 3mg |
| Aripiprazole<br>Once daily dosing is recommended | Schizophrenia adolescents | 2 mg/day | 2mg x2 days; then 5mg x2 days; then 10 mg target; can ↑ in 5mg increments thereafter every 2+ weeks | 10 mg | 30 mg |
| | Bipolar mania children and adolescents | 2 mg/day | 2mg x2 days; then 5mg x2 days; then 10 mg target; can ↑ in 5mg increments thereafter every 2+ weeks | 10 mg | 30 mg |
| | Irritability in autistic disorder body weight < 20 kg | 2 mg/day | 2mg x2 days; then 5mg; can ↑ in 5mg increments gradually at intervals of no less than 1 week | 5-10 mg | 15 mg |
| | Tourette's<br>body weight < 50 kg | 2 mg/day | 2mg x2 days; then 5mg; can ↑ in 5mg increments gradually at intervals of no less than 1 week | 5 mg | 10 mg |
| | Tourette's<br>body weight ≥ 50 kg | 2 mg/day | 2mg x2 days; then 5mg x5 days, with a target dose of 10mg/d on Day 8; can ↑ in 5mg increments gradually at intervals of no less than 1 week | 10 mg | 20 mg |
| Quetiapine<br>Usual dosing is twice daily, but can change to three times daily dosing for tolerability (sedation/somnolence); | Schizophrenia adolescents | 25mg twice daily | Day 1: 50mg total dose, divided twice daily<br>Day 2: 100mg total dose, divided twice daily<br>Day 3: 200mg total dose, divided twice daily<br>Thereafter, can gradually ↑ in increments of no more than 100mg/day; not to exceed the max recommended daily dose | 400-800 mg/day | 800 mg |
| | Bipolar mania children and adolescents | 25mg twice daily | Same titration as above | 400-600 mg/day | 600 mg |
| Olanzapine<br>Once daily dosing in the evening is recommended | Schizophrenia adolescents | 2.5-5mg/day | Titration increments of 2.5-5 mg are recommended | 12.5 mg | 10-20mg |
| | Bipolar mania children and adolescents | 2.5-5mg/day | Titration increments of 2.5-5 mg are recommended | 10 mg | 10-20mg |
| Asenapine<br>Twice daily dosing is recommended<br>Sublingual (SL) administration only; fully dissolve tablet under tongue, then wait 10 minutes to eat or drink | Bipolar mania in 10-17 year- olds | 2.5 mg SL twice daily | 2.5 mg SL twice daily x3 days, then 5mg SL twice daily x3 days. Thereafter can ↑ to 10mg SL twice daily if desired after no more than 3 days.<br>Note: Faster titration may increase risk of dystonia. | 2.5 – 10mg SL twice daily (5mg – 20mg total daily dose) | 10mg SL twice daily |
| Paliperidone<br>Once daily dosing is recommended | Schizophrenia adolescents<br>body weight < 51 kg | 3 mg/day | Initial dose titration is not required. Dose adjustments can be made in increments of 3mg, at intervals of 5+ days. | 3-6 mg | 6mg |
| | Schizophrenia adolescents<br>body weight ≥ 51 kg | 3 mg/day | Initial dose titration is not required. Dose adjustments can be made in increments of 3mg, at intervals of 5+ days. | 3-12 mg | 12mg |
| Lurasidone<br>Once daily dosing is recommended<br>Take with food ~ at least 350 calories | Schizophrenia adolescents | 40mg/day | Initial dose titration is not required | 40-80mg | 80mg |
| | Depressive episode in Bipolar I disorder in children and adolescents | 20mg/day | Initial dose titration is not required. The dose may be ↑ after 1 week based on response & tolerability. | 20-40mg | 80mg |
| Olanzapine (O) /fluoxetine (F) combination<br>Once daily dosing in the evening is recommended | Depressive episode in Bipolar I disorder in children and adolescents | 2.5mg (O) +20mg (F) once a day | Titration increments of 2.5-5 mg (O) are recommended; Titration increments of 10-20 mg (F) are recommended | 2.5-10 (O)/ 20-50 (F) | 12mg (O)/50mg (F) |

Recommended titration for antipsychotic medications with FDA-approved indications in children and adolescents (based on individual product labeling/package inserts).
Abbreviations/symbols: ↑ = increase(d); QD = once daily dosing; BID = twice daily dosing (usually morning and evening, 10-12 hours apart); TID = three times daily dosing (usually 6-8 hours apart); kg = kilograms (1 kg is equivalent to 2.2 pounds); SL = sublingual; O = olanzapine/F = fluoxetine
*Slower titration may be advisable for some patients, particularly those with a history of adverse events or EPS with antipsychotic medications.

## Taper of Antipsychotic Medications

Several strategies for switching or discontinuing antipsychotic medications have been studied in adults. A paucity of evidence exists to guide best practice for antipsychotic tapering and discontinuation in youth. The following is based on review of available data, clinical experience, and expert consensus.

In patients with antipsychotic use > 4 weeks, psychotic disorders, patients with a history of repeated relapse, or treatment resistant symptoms, abrupt antipsychotic discontinuation is generally not advised. Withdrawal adverse effects and relapse/symptom exacerbation are possible. For dangerous or severe adverse effects, abrupt discontinuation may be necessary to reduce the risk of potential harm to the patient. Neuroleptic malignant syndrome (NMS) is a life-threatening reaction to antipsychotic medications, which typically presents with high fever, muscle rigidity, confusion, autonomic instability, etc. In the case of neuroleptic malignant syndrome, abrupt discontinuation of the antipsychotic is required, as well as emergency management to reduce body temperature and blood pressure. For patients experiencing less-severe treatment-emergent adverse effects for which discontinuation is desired, a faster taper may also be possible, depending on clinician discretion/judgment.

For antipsychotic treatment duration >4 weeks, taper is recommended to avoid withdrawal symptoms (withdrawal dyskinesia, etc.) and to reduce potential for symptom worsening and destabilization. The taper schedule should be tailored depending on patient diagnosis and individual characteristics, as well as, the goal of medication switch vs. discontinuation. A faster taper may be possible under close monitoring during inpatient hospitalization.

Tapering to discontinue: Antipsychotic taper should occur in increments over at least 3-4 weeks [example taper schedule: 25%-50% dose reduction initially (from initial dose), then reduce by 25% bi-weekly or once a week]. A longer taper is recommended if withdrawal symptoms occur or if clinical presentation worsens during taper, or if the goal of taper is to discontinue after remission of symptoms has occurred for an adequate period depending on the condition being treated.

Switching between antipsychotics: If switching antipsychotics, it is generally advisable to cross-taper/titrate agents concurrently over approximately 2 weeks. Judicious dosing of the newly started agent is advised to reduce the potential for extrapyramidal adverse effects. Direct switch between antipsychotics has been studied in adult patients with mixed results. If direct antipsychotic switch is utilized in youth, close monitoring is recommended. Gradual discontinuation/cross-taper may be most appropriate for the majority of patients. In all cases, the period of overlapping antipsychotic administration should be minimized to no longer than 4 weeks.

Antipsychotic polypharmacy taper: In patients taking two antipsychotics concurrently for maintenance treatment, you may consider slowly tapering one antipsychotic agent over 6-8 weeks, with the goal of maintenance treatment with only one antipsychotic medication. Maintenance treatment with two antipsychotic medications (i.e., antipsychotic polypharmacy) is not advised due to a lack of evidence for efficacy as replicated in numerous studies, and evidence of significantly increased adverse effects.

In patients with neurodevelopmental disorders, slower antipsychotic taper (12-14 weeks) may be advised due to reported rebound symptomatology and agitation with more rapid taper (Baumeister, 1998; Kuijper, 2014).

# Levels of Evidence for Efficacy in Child & Adolescent Psychopharmacology

This tool provides summary information for health care providers in determining levels of evidence for psychopharmacological treatment. Information summarized here is not reviewed at a level of detail to allow detailed inferences about specific medications within medication classes. For example, although there might be support for one medication within a class (e.g., SSRIs), there might be minimal or no support for others within that same class. For more specific information, please seek detailed reviews of specific medications and their use. FDA approved medications for a given indication are marked with an asterisk*

| PROBLEM AREA | MEDICATION | SHORT-TERM EFFICACY | LONG-TERM EFFICACY |
|---|---|---|---|
| **Anxiety Disorders** | SSRIs<br>Benzodiazepines | A<br>C | B<br>C |
| **OCD** | SSRIs* | A | C |
| **ADHD** | Stimulants*<br>Atomoxetine* & TCAs<br>Central Adrenergic Agonists* | A<br>A<br>A | A<br>B<br>C |
| **Autism (for irritability and aggression)** | Atypical antipsychotics * | A | B |
| **Aggressive Conduct Problems with or without ADHD** | Lithium<br>Valproate<br>Carbamazepine<br>Atypical antipsychotics | B<br>A -<br>C<br>A | C<br>C<br>C<br>B |
| **Bipolar Disorder** | Lithium*<br>Valproate<br>Carbamazepine<br>Atypicals* | A<br>C<br>C<br>A | C<br>C<br>C<br>C |
| **Depression**<br><br>**Treatment Resistant MDD** | SSRIs*<br>TCAs<br>Switching: SSRIs = Venlafaxine | A<br>C<br>B | C<br>C<br>C |
| **Schizophrenia (psychotic disorders)** | Antipsychotics* | A | B |
| **Tourette's** | Antipsychotics*<br>Central Adrenergic Agonists | A<br>B | C<br>C |

SSRI = Selective Serotonin Reuptake Inhibitor TCA = Tricyclic Antidepressant

**A** = Adequate data to inform prescribing practices. For efficacy and safety: 2 $\geq$ randomized controlled trials (RCTs) in youth; long-term efficacy and safety are defined based on studies lasting 12 months or longer. Please note, for safety, "A" doesn't mean "safe", it merely indicates that the risks have been characterized in 2 or more carefully executed studies.

**B** = For short- and long-term efficacy and short-term safety: 1 RCT in youth or mixed results from $\geq$ 2 RCTs. For long-term safety, only 1 careful prospective study lasting 12 months or more, or mixed results from $\geq$ 2 longitudinal studies.

**C** = No controlled evidence or negative studies; case reports and FDA reports of adverse events only.

#=Safety category designations refer to whether sufficient data are available to determine the risks vs. benefits of treatment vis-à-vis the risks relatively common side effects. Very rare side effects cannot be anticipated and can sometimes be severe, so it cannot be assumed that the treatment benefits for a given child outweigh possible rare risks or side effects experienced by that child.

This table is provided for informational use, only by licensed health care providers, by The REACH Institute, www.TheReachInstitute.org. The table is not intended for use as a stand-alone guide but should only be used in conjunction with evidence- and consensus-based guidelines for specific disorders.

Adapted and used with permission from The Reach Institute Table last updated: December 20, 2018 -- Peter S. Jensen & M. Lynn Crismon

| Glossary |
| --- |
| **ANC =** absolute neutrophil count<br>**BMI** = Body Mass Index. A measure of body fat based upon height and weight.<br>**CBC** = Complete blood count. Lab test used to monitor for abnormalities in blood cells, e.g., for anemia.<br>**Cp** = Plasma concentration<br>**Serum creatinine** = A lab test used to calculate an estimate of kidney function.<br>**EKG =** Electrocardiogram<br>**EEG =** Electroencephalogram<br>**EPS =** Extrapyramidal side effects. These are adverse effects upon movement, including stiffness, tremor, and severe muscle spasm<br>**FDA =** U.S. Food and Drug Administration<br>**HbA1c =** Hemoglobin A1c is a laboratory measurement of the amount of glucose in the hemoglobin of the red blood cells. Provides a measure of average glucose over the previous 3 months<br>**LFTs =** Liver function tests<br>**MAOIs =** Monoamine Oxidase Inhibitors<br>**MRI =** Magnetic resonance imaging<br>**PRN =** as needed<br>**Prolactin =** A hormone produced by the pituitary gland<br>**TFTs =** Thyroid Function Tests |

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**Committee Members Disclosures**
Since January 1, 2013, the authors below disclose the following financial relationships:
- Dr. Blader has received funding as a consultant/researcher from Supernus Pharmaceuticals and research funding through his employer institution from Supernus.
- Dr. Crismon has nothing to declare.
- Dr. Lopez holds stock in Lilly, Merck, Proctor & Gamble, and Pfizer Pharmaceuticals.
- Dr. Pliszka has received funding as a consultant for Ironshore and Shire Pharmaceuticals. Through his employer institution he has served as an expert witness for Eli Lilly and Janssen Pharmaceuticals. He has received research grants through his employer institution from Ironshore, Purdue and Shire.
- The other members of the working group do not have any financial relationships to disclose.

# Disclaimer

The authors of this document have worked to ensure that all information in the parameters is accurate at the time of publication and consistent with general psychiatric and medical standards and consistent with FDA labeling and information in the biomedical literature. However, as medical research and practice continue to advance, therapeutic standards may change, and the clinician is encouraged to keep up with the current literature in psychiatry and clinical psychopharmacology. In addition, not all potential adverse drug reactions or complications are listed in the tables, and the clinician should consult the official FDA labeling and other authoritative reference sources for complete information. These parameters are not a substitute for clinical judgment, and specific situations may require a specific therapeutic intervention not included in these parameters.

# Acknowledgements

**Laura Roccograndi** (Pharm.D. Candidate, The University of Texas at Austin) assisted with the literature search and updating of the medication tables.

**Brad Fitzwater, MD (**Maternal & Child Health Medical Director, Texas Department of State Health Services) assisted with narrative regarding Medication Assisted Treatment.