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Disclaimer

The Kansas Psychotropic Medication Utilization Parameters for Children and Youth in Foster Care is intended to provide principles to guide prescriptive practices. Children in the child welfare system often present with complicated clinical pictures. The formation of treatment algorithms that clinicians must rigidly adhere to is unrealistic and is not in the best interest of the child. The Kansas PMUR is meant to inform the practice of pediatric psychopharmacology in this population and to provide a framework to promote the provision of quality psychiatric services to children in foster care in the state of Kansas. These guidelines are not meant to supersede the clinical judgment of providers working closely with foster children and their caregivers.

Committee:

Kansas Department for Children and Families

Psychotropic Medication Workshop

Psychotropic Medication Utilization Parameters for Children and Youth in Foster Care
State of Kansas

June 2023

***Psychotropic Medication Utilization Parameters***

***for Children and Youth in Foster Care***

***Introduction and General Principles***

The use of psychotropic medications by children and youth is an issue confronting parents, other caregivers, and health care professionals across the United States. Children and youth in foster care, in particular, have multiple needs, including those related to emotional or psychological stress. They typically have experienced abusive, neglectful, serial or chaotic caretaking environments. Birth family history is often not available. These children often present with a fluidity of different symptoms over time reflective of past traumatic events that may mimic many psychiatric disorders and result in difficulties with attachment, mood regulation, behavioral control, and other areas of functioning.

**Because of the complex issues involved in the lives of foster children, 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 actually 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 (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 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 indicates a need to address communication issues as well as differences in perspective 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 developmental 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. Additionally, 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.

**The role of non-pharmacological interventions should be considered before beginning a psychotropic medication, except in urgent situations such as suicidal ideation, psychosis, self-injurious behavior, physical aggression that is acutely dangerous to others, or severe impulsivity endangering the child or others; when there is marked disturbance or psychophysiological functioning (such as profound sleep disturbance), or when the child shows marked anxiety, isolation, or withdrawal.** Given the history of trauma, unusual stress and change in environmental circumstances associated with being a child in foster care, psychotherapy should generally begin before or concurrent with prescription of a psychotropic medication. Referral for trauma-informed, evidence-based psychotherapy should be considered when available and appropriate. Equally important, the role of the health care providers and the health care environment’s potential to exacerbate a child’s symptoms, given their respective trauma history, should be considered and minimized. 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 determine whether pharmaceutical company sponsored research indicates that medication is safe and effective for those indications that are listed in the approved product labeling. The FDA assures that information in the approved product labeling is accurate and limits the manufacturer’s marketing to the information contained in the approved labeling. The FDA does not regulate physician and other health provider practice. In fact, the FDA has stated that it does “not limit the manner in which a practitioner may prescribe an approved drug.” Studies and expert clinical experience often support the use of a medication for an “off-label” use. Physicians should utilize 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 all children’s mental health needs. Primary care clinicians are in an excellent position to perform screenings of children for potential mental disorders, and they should be able to diagnosis and treat relatively straightforward situations such as uncomplicated ADHD, anxiety, or depression. Primary care providers should provide advice to youth in foster care and their caregivers about handling feelings and behaviors, recognizing the need for help, making decisions regarding healthy lifestyles, 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. “The management of common presentations of ADHD, depression and anxiety, psychotherapy referral, psychopharmacology and appropriate child psychiatry referral are within the scope of general pediatric practice” (Southammakosane 2015). In addition, the American Academy of Pediatrics has recently provided a policy statement (“Health Care Issues for Children and Adolescents in Foster Care and Kinship Care”) which can be found at:

<http://pediatrics.aapublications.org/content/136/4/e1131>

***General principles regarding the use of psychotropic medications in children include:***

* A DSM-5 psychiatric diagnosis should be made before the prescribing of psychotropic medications.
* A comprehensive physical exam such as the annual well child exam should be considered prior to starting psychotropic medications to identify medical problems or issues that may impact treatment.
* 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 with a psychotropic medication. 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 making a decision regarding 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 care of an emergency, informed consent should be obtained from the appropriate party(s) 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.
* 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. 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.
* 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.
* 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 combined psychotropic medication regimens are needed, addition of each medication should occur in a systematic orderly process, accompanied by on-going monitoring, evaluation, and documentation. The goal remains to minimize the number of drugs while maximizing therapeutic outcomes. There is a lack of evidence for prescribing multiple medications within the same class, but, the practice has some support in specific clinical situations such as: Temporary use of two drugs when cross-tapering from one drug to another, combining a short-acting and long-acting stimulant, and the addition of trazodone to an SSRI to target insomnia.

* 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 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 initiating antidepressants, those having a history of suicidal behavior or deliberate self-harm and those with a history of anxiety or substance abuse disorders.
* 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 treatment 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.
* If a medication is being used in a child for a primary target symptom of severe aggression associated with a DSM-5 non-psychotic diagnosis (e.g., disruptive mood dysregulation disorder, 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 pharmacogenetic tests in prescribing psychotropic medications***

The Kansas PMUR committee would like to emphasize and encourage the use of to the American Academy of Child and Adolescent Psychiatry policy below:

**Clinical Use of Pharmacogenetic Tests in Prescribing Psychotropic Medications for Children and Adolescents**

**Background**

Several commercially available combinatorial pharmacogenomic tests are being marketed for psychiatric clinical practice. Commercial entities claim that the testing measures drug metabolism to guide medication choice and dosing to impact therapeutic response and side effects.

In October 2018, the Food and Drug Administration (FDA) issued a safety communication warning against the use of genetic tests with unapproved claims to predict medication response. The FDA stated that changing a patient’s medication regimen based on the results of a pharmacogenomic test leads to “inappropriate treatment decisions and potentially serious health consequences for the patient.”

Only a small fraction of the available commercial products have undergone randomized controlled trials in adults only.

Current studies are limited by:

* Potential conflicts of interest
* Small sample sizes
* Short duration of follow-up
* Lack of blinding
* Lack of appropriate control groups

Additionally, numerous factors affect medication response unaccounted for by genetic variation. Genetic variations are managed clinically with slow and thoughtful medication management.

Furthermore, pharmacogenomic testing provides little meaningful information when two or more medications are used concurrently.

**The American Academy of Child and Adolescent Psychiatry recommends:**

* **Clinicians avoid using pharmacogenetic testing to select psychotropic medications in children and adolescents.**
* **Future high-quality prospective studies to assess the clinical significance of pharmacodynamic and combinatorial pharmacogenomic testing in children and adolescents.**

Approved by Council March 2020

The link to this policy can be found at the top of page 5. *https://www.aacap.org/aacap/Policy\_Statements/2020/Clinical-Use-Pharmacogenetic-Tests-Prescribing-Psychotropic-Medications-for-Children-Adolescents.aspx*

***Use of PRN Medication***

* The use of “PRN” or as needed medication is generally discouraged. However, when deemed appropriate, such as a prn dose of antihistamine for anxiety or medication adverse effect, it is important to clearly document the medication that is used, the situation indicating need for the administration of a prn medication, as well as the maximum dosage in a 24-hour period and in a week. The frequency of administration should be monitored over time to assure that these do not become regularly scheduled medications unless clinically indicated.
* Psychotropic medications are not to be used in place of psychosocial and behavioral interventions for Kansas youth in DCF custody. A standing order for the use of pro re nata (PRN) medications for behavioral dysregulation outside of a treatment facility or without appropriate supervision by medical staff is strongly discouraged.

***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.

The publication includes specific guidelines and algorithms schematics developed by the PPWG to help guide treatment decisions for a number of 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 similar to 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-psychopharmacological interventions (for up to 12 weeks) before starting psychopharmacological treatment, in an effort 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.

***Distinguishing between Levels of Warning Associated with Medication Adverse Effects***

Psychotropic medications have the potential for adverse effects, some that are treatment limiting. 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.

***Black Box Warnings***

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. One example is the black box warning about the increased risk of suicidal thoughts and behavior for children, adolescents and young adults taking antidepressants. This includes multiple classes of medications taken for any indication and necessitates close monitoring and communication with the prescriber. It is important for clinicians to be familiar with all medication adverse effects, including boxed warnings, in order to appropriately monitor patients and minimize the risk of their occurrence. The medication tables include two columns that outline this important information – one for “Black Box Warning” and the other for “Warnings and Precautions.” 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 precautions 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>

***Usual Recommended Doses of Common Psychotropic Medications***

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 Kansas 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 does recommendation.

**See Psychotropic Medication Tables.**

**Antipsychotics: Second Generation (Atypical)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Drug (Brand)** | **Initial Dosage** | **Literature Based Maximum** | **FDA Approved Maximum Dosage for Children & Adolescents** | **Maximum Medicaid Dose (per day)** | **Schedule** |
| **Aripiprazole\*** | **Abilify®****Abilify Discmelt®** (oral disintegrating tab)**Abilify®** (oral solution) | Age ≥ 4 yrs.: 2 mg/day | Age 4-11 yrs.: 15 mg/dayAge ≥ 12 yrs.: 30 mg/day | Approved for treatment for Bipolar Mania or Mixed Episodes (age 10-17 yrs.) and Schizophrenia (13-17 yrs.): 30 mg/dayApproved for treatment of irritability associated with Autistic Disorder (age 6-17 yrs.): 15 mg/dayApproved for treatment of Tourette Syndrome, Age 6-18 yrs.: < 50 kg is 10 mg/day≥ 50 kg is 20 mg/day  | Age < 6 yrs: 15 mg Age 6-9 yrs: 20 mgAge 10-15yrs: 30 mgAge ≥ 16yrs: 45 mg  | Once daily |
| **Abilify Maintena®** |   | Not FDA approved in adolescents | Age ≥ 16yrs: 400 mg per 28 days  |
| **Aristada®** |   | Not FDA approved in adolescents | Age ≥ 16yrs: 882 mg per 28 days or 1064mg every 2 months  |
| **Aristada Initio ™** |   | Not FDA approved in adolescents | Age ≥ 16yrs: 675 mg single dose  |
| **Quetiapine\*** | **Seroquel®****Seroquel®XR**  (brand only) | Age 5-9 yrs.: 12.5-25 mg/day Age 10-17 yrs.: 50 mg/day | Age 5-9 yrs.: 400 mg/day Age 10-17 yrs.: 800 mg/day | Approved for treatment of Bipolar Mania Age 10-17 yrs.: 600 mg/dayApproved for treatment of Schizophrenia Age 13-17 yrs.: 800 mg/day | Age 6-9 yrs: 400 mgAge 10-15 yrs: 800 mgAge ≥ 16 yrs: 1200 mg | IR: One to three times dailyXR: 1x daily |
| **Olanzapine\*** | **Zyprexa®****Zyprexa Zydis®** | Age 4-5 yrs.: 1.25 mg/day Age 6-12 yrs.: 2.5 mg/day Age ≥ 13 yrs.: 2.5-5 mg/day | Age 4-5 yrs.: 12.5 mg/day Age 6-17 yrs.: 20 mg/day | Approved for treatment of Bipolar Mania or Mixed Episodes and Schizophrenia Age 13-17 yrs.: 20 mg/day Approved for treatment of depressive episodes associated with Bipolar I Disorders 12 mg/day in combination with 50 mg/day fluoxetine | Age 6-9 yrs: 12.5 mgAge 10-15 yrs: 20 mgAge ≥ 16 yrs: 40 mg  | Once daily |
| **Zyprexa Relprevv ®** |  |  Not FDA approved in adolescents | Age ≥ 16yrs: 300 mg per 14 days or 405 mg/28 days |
| **Risperidone\*** | **Risperdal®****Risperdal M-Tab®**(oral disintegrating tab)**Risperdal®**(oral solution) | Age 4-5 yrs.: < 20 kg: 0.25 mg/dayAge ≥ 6 yrs.: 0.5 mg/day | Age 4-11 yrs.: 3 mg/dayAge ≥ 12 yrs.: 6 mg/day | Approved for treatment **of** Schizophrenia Age 13-17 yrs. and Bipolar Mania or Mixed Episodes, Age 10-17 yrs.:6 mg/dayApproved for treatment of irritability associated with Autistic Disorder, Age 5-16 yrs.: 3 mg/day | Age < 6 yrs: 1.5 mgAge 6-9 yrs: 4 mgAge 10-15 yrs: 6 mgAge ≥ 16 yrs: 6 mg | Once or twice daily |
| **Risperdal Consta®** |  | Not FDA approved in adolescents | Age ≥ 16 yrs: 50 mg per 14 days  |
| **Perseris™** |  | Not FDA approved in adolescents | Age ≥ 16 yrs: 120 mg per 28 days  |
| **Clozapine** | **Clozaril®****Fazaclo®**(oral disintegrating tab)**Versacloz®**(oral suspension) | Age 8-11 yrs.: 6.25-12.5 mg/dayAge ≥ 12 yrs.: 6.25-25 mg/day | Age 8-11 yrs.: 150-300 mg/dayAge ≥ 12 yrs.: 600 mg/dayTarget serum Clozapine level of 350 ng/mL for optimal efficacy | Not approved for children and adolescents | Age 6-9 yrs.: 300 mgAge 10-15 yrs.: 600 mgAge > 16 yrs.: 900mg | Once or twice daily |
| **Asenapine** | **Saphris®** | Age > 10 yrs.: 2.5 mg twice daily (20 mg) | Age > 10 yrs.: 10 mg twice daily (20 mg) | Approved for acute treatment of Bipolar Mania and Mixed Episodes (age 10-17 yrs.): 10 mg twice daily | Age 6-9 yrs.: 10 mgAge > 10 yrs: 20 mg | Twice daily. Avoid eating or drinking for 10 minutes after sublingual administration |
| **Iloperidone\*\*** | **Fanapt®** | Insufficient Evidence | Insufficient Evidence | Not approved for children and adolescents | Age 6-9 yrs:12 mgAge ≥ 10 yrs: 24 mg | Insufficient Evidence |
| **Paliperidone\*** | **Invega®** | Children: Insufficient EvidenceAdolescents: (age ≥ 12 yrs.): 3 mg/day | Children: Insufficient EvidenceAdolescents (age ≥ 12 yrs.), Schizophrenia:Weight < 51 kg: 6mg/day Weight ≥ 51 kg: 12 mg/day | Approved for treatment of Schizophrenia (age 12-17 yrs.):Weight < 51 kg: 6 mg/dayWeight ≥ 51 kg: 12 mg/day | Age 6-9 yrs: 6 mgAge ≥ 10 yrs: 12 mg  | Once daily |
| **Invega Sustenna®** |  | Not FDA approved in adolescents | Age > 16 yrs: 234mg per 21 days |
| **Invega Trinza®** |  | Not FDA approved in adolescents | Age > 16 yrs: 819 per 84 days |
| **Ziprasidone\*** | **Geodon®** | Bipolar Disorder (age 10-17 yrs.): 20 mg/day Tourette’s Disorder: 5 mg/day | Bipolar Disorder (age 10-17 yrs.) Weight ≤ 45 kg: 80 mg/dayWeight > 45 kg: 160 mg/day Tourette’s Disorder: 40 mg/day | Not approved for children and adolescents | Age 6-9 yrs: 80 mgAge 10-15yrs: 160 mgAge ≥ 16 yrs: 240 mg | Twice daily: take with ³ 500 calorie meal |
| **Lurasidone**  | **Latuda®** | Children > 10 yrs: 20 mg | Insufficient Evidence  | Approved for treatment of Schizophrenia (age 13-17 yrs.) 80 mg/dayApproved for treatment of bipolar depression (age 10-17 yrs): 80 mg | Age 6-9 yrs: 80 mgAge 10-15 yrs: 120 mgAge ≥ 16 yrs: 160 mg | Once daily taken with >350 calorie meal  |
| **Brexpiprazole** | **Rexulti®** | Days 1-4: 0.5mg, Days 5-7: 1mg, Day 8: 2mgTarget Dose: 2-4mgMax Dose: 4mg/day | Insufficient Evidence | Approved for treatment of Schizophrenia (age 13-17 yrs.):Days 1-4: 0.5mg, Days 5-7: 1mg, Day 8: 2mgTarget Dose: 2-4mg, Max Dose: 4mg/day | Age ≥ 16 yrs: 4 mg | Once daily |
| **Cariprazine** | **Vraylar®** | Insufficient Evidence | Insufficient Evidence | Not approved for children and adolescents | Age > 16 yrs: 6mg | Insufficient Evidence |

\*\*See the FDA approved product labeling for each medication for full black box warnings

**Patient Monitoring Parameters- Second Generation (Atypical):**

* EPS evaluation (examination for rigidity, tremor, akathisia)
	+ Before initiation of any antipsychotic medication, then weekly for first two weeks after initiating treatment with a new antipsychotic, or until the dose has been stabilized, and weekly for two weeks after a dose increase.
* Screen for abnormal involuntary movements—annually.
* Monitor for changes in vision - Ask about blurry vision yearly.
* EKG and/or Cardiology consultation as clinically indicated
* Fasting plasma glucose level or hemoglobin A1c – at baseline, at 3 months, then annually
* Lipid screening—at baseline, at 3 months, then annually
* CBC as clinically indicated.
* Pregnancy test—as clinically indicated.
* Blood pressure, pulse, height, weight, and BMI measurement— at every visit
* A BMI exceeding the 90th percentile for age on the growth charts at: <https://www.cdc.gov/growthcharts/> 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.
* Endocrine/genitourinary function—inquire for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males (Priapism has been reported with iloperidone, Risperidone and Ziprasidone). This inquiry should be done at least every six months and more frequently during the first year of treatment or if clinically indicated.
* Monitor for EPS symptoms (rigidity, tremor, akathisia).

**Clozapine-Specific Monitoring Parameter**: Clozapine is associated with severe neutropenia (absolute neutrophil count (ANC) less than 500/mL). The requirements to prescribe, dispense, and receive clozapine are incorporated into a single, shared program called the Clozapine Risk Evaluation and Mitigation Strategy (REMS). Prescribers must follow requirements for CBC monitoring per REMS. Prescribers and pharmacies must certify the use of Clozapine at [www.clozapinerems.com](http://www.clozapinerems.com).

**Boxed Warning- Second Generation (Atypical):**

* Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies.
* 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

**Clozapine-Specific Black Box Warning:**

* Risk of life-threatening agranulocytosis
* Seizures
* Myocarditis
* Other adverse cardiovascular and respiratory effects

**Olanzapine Pamoate (Zyprexa Relprevv®)-Specific Black Box Warning:**

* Post-injection delirium/sedation syndrome
	+ Patients are at risk for severe sedation (including coma) and/or delirium after each injection and must be observed for at least three hours at a registered facility with ready access to emergency response services
* Because of this risk, Olanzapine Pamoate is only available through a restricted distribution program which requires prescriber, healthcare facility, patient, and pharmacy enrollment.

**Warnings and Precautions- Second Generation (Atypical):**

* Prolactinoma and gynecomastia (most common with risperidone and paliperidone)
* Metabolic effects (i.e. Weight gain, dyslipidemia)
* Orthostatic Hypotension
* Leukopenia, neutropenia, and agranulocytosis
* Lowers seizure threshold
* Cognitive and motor impairment potential
* Hyperthermia
* Dysphagia
* EPS
* Olanzapine can cause a rare but serious skin reaction known as DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms). Presence of a fever with rash and swollen lymph glands or swelling to the face requires immediate medical attention

**Antipsychotics: First Generation (Typical)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Drug (Brand)** | **Initial Dosage** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** | **Maximum Medicaid Dose (Per day)** | **Schedule** |
| **Chlorpromazine\*** | **ThorazineÒ** | Age >6 months: 0.25 mg/lb every 4-6 hours, as neededAdolescents: 10-25 mg/dose every 4-6 hours | Age < 5 yrs.: 40 mg/day Age 5-12 yrs.: 75 mg/day Age > 12 yrs.: 800 mg/day | Approved for treatment of severe behavioral problems (age 6 months -12 yrs.)Outpatient Children: 0.55 mg/kg every 4-6 hours, as neededInpatient Children: 500mg/dayApproved for the management of manifestations of Psychotic Disorders (age > 12 yrs.): 1000 mg/day | Age < 6 yrs: 40mg Age 6-9 yrs: 200mgAge 10-15yrs: 800mgAge ≥ 16yrs: 1500mg | One to six times daily |
| **Haloperidol\*** | **HaldolÒ** | Age 3-12 yrs. Weighing 15-40 kg: 0.025-0.05 mg/kg/day ≥ 40 kg: 1 mg/day Age > 12: 1 mg/day | Age 3-12 yrs: 0.15 mg/kg/day or 6 mg/day, whichever is lessAge > 12 yrs:Acute agitation: 10mg/dose Psychosis: 15 mg.day Tourette’s Disorder: 15mg/day | Approved for treatment of Psychotic Disorders, Tourette’s Disorder, and severe behavioral problems (age ³ 3 yrs.):Psychosis: 0.15 mg/kg/day Tourette’s Disorder and severe behavioral problems: 0.075 mg/kg/daySeverely disturbed children: 6 mg/day  | Age < 6 yrs: 6mg or 0.15mg/kg/day (whichever is less)Age 6-9 yrs: 6mgAge 10-15yrs: 15mg Age ≥ 16yrs: 60mg  | One to three times daily |
| **Perphenazine\*** | **TrilafonÒ** | Age 6-12 yrs.: Insufficient EvidenceAge > 12 yrs.: 4-16 mg two to four times daily | Age 6-12 yrs.: Insufficient EvidenceAge > 12 yrs.: 64 mg/day | Approved for treatment of psychotic disorders (age ³ 12 yrs.): Outpatient: 24 mg/day, Inpatient: 64 mg/day | Age < 6 yrs: Not ApprovedAge 6-9 yrs: 12mgAge 10-15 yrs: 22mgAge ≥ 16 yrs: 64mg | Two to four times daily |
| **Pimozide** | **OrapÒ** | Age ³ 7 yrs.: 0.05 mg/kgAt doses > 0.05 mg/kg/day CYP2D6 genotyping should be performed. In poor 2D6 metabolizers, dosage should not exceed 0.5 mg/kg/day. | Age 7-12 yrs.: 6 mg/day or 0.2 mg/kg/day, whichever is lessAge ≥ 12 yrs.: 10 mg/day or 0.2 mg/kg/day, whichever is less | Approved for treatment of Tourette’s Disorder (age ≥ 12 yrs.): 10 mg/day or 0.2 mg/kg/day, whichever is less | Age < 6 yrs: Not ApprovedAge 6-9 yrs: 6mg or 0.2mg/kg/day, whichever is lessAge 10-15 yrs: 10mg or 0.2mg/kg/day, whichever is lessAge ≥ 16 yrs: 20mg | Once or twice daily |

\*\*See the FDA approved product labeling for each medication for full black box warnings

**KS Medicaid Criteria (dosing not included in PMUR document)**

Fluphenazine (oral) - 6-10 yo: 5 mg; 10-<16 yo: 10 mg; >16 yo: 60 mg

Fluphenazine (injection) - >16 yo: 100 mg

Haloperidol (Haldol Deconate) - >16 yo: 500 mg/21 days

Loxapine (Adasuve, Loxitane) - 6-10 yo: 30 mg; 10-<16 yo: 60 mg; >16 yo: 250 mg

Thioridazine - >16 yo: 800 mg

Thiothixene - 10-<16 yo: 15 mg; >16 yo: 60 mg

Trifluoperazine - 6-10 yo: 15 mg; 10-<16 yo: 40 mg; >16 yo: 40 mg

**Patient Monitoring Parameters- First Generation (Typical):**

* Blood pressure, pulse, height, weight, and BMI measurement— at every visit
* A BMI exceeding the 90th percentile for age on the growth charts at: <https://www.cdc.gov/growthcharts/> 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.
* Endocrine/genitourinary function—inquire for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males (Priapism has been reported with iloperidone, Risperidone and Ziprasidone). This inquiry should be done at each visit for the first 12 months and every 6 months thereafter.
* Monitor for EPS symptoms (rigidity, tremor, akathisia).
* EPS evaluation (examination for rigidity, tremor, akathisia)
	+ Before initiation of any antipsychotic medication, then weekly for first two weeks after initiating treatment with a new antipsychotic, or until the dose has been stabilized, and weekly for two weeks after a dose increase.
* Screen for abnormal involuntary movements—annually.
* Monitor for changes in vision - Ask about blurry vision yearly.
* EKG requirement at baseline for pimozide; EKG and/or Cardiology consultation as clinically indicated

**Warnings and Precautions- First Generation (Typical):**

* Leukopenia, neutropenia, and agranulocytosis
* Drowsiness
* Orthostatic hypotension
* EKG changes
* Extrapyramidal symptoms
* Ocular changes
* Hyperprolactinemia
* Anticholinergic effects (constipation, dry mouth, blurred vision, urinary retention)
* Risk of prolonged QTc interval and torsades de pointes (particularly with pimozide)

**ADHD Stimulants: Amphetamine & Derivatives**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Drug (Brand)** | **Initial Dosage** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** | **Maximum Medicaid Dose (Per day)** | **Schedule** |
| **Amphetamine sulfate** | **Adzenys®XR-ODT** **(oral disintegrating tablets)****Adzenys® ER** **(oral suspension)****Dyanavel®** **(oral suspension)****Evekeo®** | Age ≥ 6 yrs.: 6.3 mg/day(3.1 mg = 5 mg Adderall®XR)Age ≥ 6 yrs.: 2.5 mg-5 mg/day (2.5 mg = 4 mg Adderall®XR)Age 3-5 yrs.: 2.5 mg once or twice dailyAge ≥ 6 yrs.: 5 mg once or twice daily | Age 6–12 yrs.:18.5 mg/dayAge 13-17 yrs.:12.5 mg/dayAge ≥ 6 yrs.: 20mg/dayApproved for children 3 yrs. and older: 40mg/day | Approved for children 6 yrs. and older:6-12 yrs.: 18.8 mg/day13-17 yrs.: 12.5 mg/dayApproved for children6 yrs. and older: 20 mg/dayApproved for children 3 yrs. and older: 40mg/day | 18.8mg 18.8mg20mg40mg  | Once dailyOnce dailyOnce dailyOne to three times a day |
| **Amphetamine mixed salts** | **Adderall®** **Adderall® XR****Mydayis®** | Age 3-5 yrs.: 2.5 mg once or twice dailyAge ≥ 6 yrs.: 5 mg once or twice dailyAge 3-5 yrs.: 2.5 mg/day Age 6-12 yrs.: 5 mg/day Age ≥ 13 yrs.: 10 mg/dayAge ≥ 13 yrs.: 12.5 mg/day | Age 3-5 yrs.: 30 mg/day(Max dose)Age ≥ 6 yrs.: ≥50 kg: 60 mg/day | Approved for children 3 yrs. and older: 40 mg/dayApproved for children 6 yrs. and older: 30 mg/dayApproved for youth 13 yrs. and older: 25 mg/day | 60mg60mg50mg | One to three times a dayOnce dailyOnce daily |
| **Dextroamphetamine** | **Dexedrine®****Zenzedi®****Procentra® (oral suspension)****Dexedrine Spansules®** | Age 3-5 yrs.: 2.5 mg/dayAge ≥ 6 yrs.: 5 mg once or twice dailyAge 3-5 yrs.: 2.5 mg/dayAge ≥ 6 yrs.: 5 mg once or twice dailyAge 3-5 yrs.: 2.5 mg/dayAge ≥ 6 yrs.: 5 mg once or twice dailyAge 3-5 yrs.: 5 mg/dayAge > 6 yrs.: 5 mg/day | Age ≥ 6 yrs. and weight: <50 kg: 40/day >50kg: 60 mg/day | Age > 6 yrs.: 40 mg/day |  |  |
| **Lisdexamfetamine** | **Vyvanse** | Age 3-5 yrs.: no dataAge ≥ 6 yrs.: 30 mg/day | Age 3-5 yrs.: no dataAge ≥ 6 yrs.: 70 mg/day | Approved for children: 6 yrs. and older: 70 mg/day | 70mg | Once daily |

**ADHD Stimulants: Methylphenidate & Derivatives**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Drug (Brand)** | **Initial Dosage** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** | **Maximum Medicaid Dose (Per day)** | **Schedule** |
| **Methylphenidate** | **Ritalin®****Methylin® (chewable and oral suspension)****Ritalin® SR****Methylin® ER****Metadate® ER****Ritalin® LA****Metadate® CD****Quillivant® XR (oral suspension)****Quillichew® ER (chewable)****Aptensio® XR****Adhansia® XR****Concerta®****JornayPM Extended Release****Daytrana® TD patch+****Cotempla® XR ODT** | Age 3-5 yrs.: 2.5 mg twice daily Age ≥ 6 yrs.: 5 mg twice dailyAge 3-5 yrs.: 2.5 mg twice daily Age ≥ 6 yrs.: 5 mg twice dailyAge ≥ 3 yrs.: 10 mg/dayAge ≥ 3 yrs.: 10 mg/dayAge ≥ 3 yrs.: 10 mg/dayAge 3-5 yrs.: 10 mg/day Age ≥ 6 yrs.: 10-20 mg/dayAge 3-5 yrs.: 10 mg/day Age ≥ 6 yrs.: 10-20 mg/dayAge 3-5 yrs.: 10 mg/day Age ≥ 6 yrs.: 10-20 mg/dayAge 3-5 yrs.: 10 mg/day Age ≥ 6 yrs.: 10-20 mg/dayAge 3-5 yrs.: 10 mg/day Age ≥ 6 yrs.: 10-20 mg/dayAge ≥ 6 yrs.: 25 mg/dayAge ≥ 3 yrs.: 18 mg/dayAge ≥ 6 yrs.: 20 mg/day at 8 pmAge ≥ 3 yrs.: 10 mg/dayAge 6-17 yrs.: 17.3 mg/day | Age 3-5 yrs.: 20 mg/dayAge ≥ 6 yrs. and weight: <50 kg: 60 mg/day >50 kg: 100 mg/dayDoses of Methylphenidate exceeding 60 mg/day should be used with caution and with attentive monitoring.No information availableAge 3-5 yrs.: 36 mg/day Age ≥ 6 yrs.: 72 mg/dayAge ≥ 6 yrs.: 100 mg/day at PM (6:30- 9:30 pm)Age 3-5 yrs.: 20 mg/dayAge ≥ 6 yrs.: 30 mg/day | Approved for children 6 yrs. and older: 60 mg/day70 mg/day Approved for children 6 yrs. and older: Age 6-12 yrs.: 54 mg/day Age 13-17 yrs.: lesser of 72 mg/day or 2 mg/kg/day, whichever is lessApproved for children 6 yrs. and older: The max dose per the manufacturer is 100 mg/dayApproved for children 6 yrs. and older: 30mg/dayApproved for children 6 yrs. and older: 51.8mg/day | 100mg100mg108mg100mg30mg/ 9hr /day51.8mg | One to three times a dayOnce dailyOnce daily |
| **Dexmethylphenidate** | **Focalin®****Focalin® XR** | Age 3-5 yrs.: 2.5 mg/dayAge ≥ 6 yrs.: 2.5 mg twice dailyAge 3-5 yrs.: 5 mg/dayAge ≥ 6 yrs.: 5-10 mg/day | Age 3-5 yrs.: 10 mg/dayAge ≥ 6 yrs.: 50 mg/dayAge 3-5 yrs.: 10 mg/dayAge ≥ 6 yrs.: 50 mg/day | Approved for children 6 yrs. and older: 20mg/dayApproved for children 6 yrs. and older: 30 mg/day | 20mg50mg  | Twice dailyOnce daily |
| **Serdexmethylpenidate-Dexmethylphenidate** | **Azstarys**  | Age 6-12 yrs: 39.2 mg/7.8 mgAge 13-17yrs: 39.2 mg/7.8 mg | No information available | Age 6-12 yrs: 52.3 mg/10.4 mgAge 13-17 yrs: s 52.3 mg/10.4 mg |  | Once daily |

**Patient Monitoring Parameters- ADHD Stimulants:**

* Baseline and ongoing: height, weight, blood pressure, and pulse
* Baseline: assessment using a targeted cardiac history of the child and family and a physical examination of the child. Order an EKG and/or a pediatric cardiology consult as indicated.

**Boxed Warning- ADHD Stimulants:**

* Abuse potential.
* Mixed amphetamine salts: Misuse of amphetamines may cause sudden death and serious cardiovascular adverse reactions

**Warnings and Precautions- ADHD Stimulants:**

* Hypertension
* Sudden death in those with pre-existing structural cardiac abnormalities or other serious heart problems
* Psychiatric adverse event such as psychotic or manic symptoms
* Long-term use of stimulants has been associated with suppression of growth that may be reversible upon discontinuation of the stimulant
* Decreased appetite/weight
* Possible sleep disturbance
* Tics
* Peripheral vasculopathy including Raynaud’s Phenomenon
* May lower the seizure threshold
* Priapism
* Risk of Serotonin Syndrome when combined with other drugs that increase serotonin
* Daytrana TD Patch: post-marketing reports of acquired skin depigmentation or hypopigmentation of the skin

**ADHD Non-Stimulants**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Drug (Brand)** | **Initial Dosage** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** | **Maximum Medicaid Dose (Per day)** | **Schedule** |
| **Atomoxetine** | **Strattera®** | Age ≥ 6 yrs.: <70 kg: 0.5 mg/kg/day> 70 kg: 40.5 mg/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 | 100mg | Once or twice daily |
| **Viloxazine** | **Qelbree®** | Age 6-11 yrs.: 100mg/dayAge 12-17 yrs.: 200mg/day  | 400mg/day  | Approved for treatment of ADHD (6-17 years): 400mg/day | 400mg | Once daily |
| **Clonidine** | **Catapres®****Kapvay® (ER)** | Age ≥ 6 yrs.: < 45 kg: 0.05 mg/day> 45 kg: 0.1 mg/dayAge ≥ 6 yrs.: 0.1 mg/day | Age ≥ 6 years AND Weight 27-40.5 kg: 0.2 mg/day Weight 40.5-45kg: 0.3mg/day Weight >45kg: 0.4 mg/dayAge ≥ 6 yrs.: 0.4 mg/day | Not approved for the treatment of ADHD in children and adolescentsApproved for monotherapy and adjunctive therapy to stimulants for treatment of ADHD (age 6-17 yrs.) 0.4 mg/day | 0.4mg/day0.4mg/day | One to four times dailyOnce or twice daily |
| **Guanfacine** | **Tenex® (IR)****Intuniv® (ER)** | Age ≥ 6 yrs.: weight < 45 kg: 0.5 mg/day weight > 45 kg: 1 mg/dayAge ≥ 6 yrs.:1 mg/day | Age > 6 yrs:-weight 27- 40.5 kg: 2mg/day -weight 40.5-45 kg: 3mg/day -weight >45 kg: 4 mg/day Age 6-12 yrs.: 4 mg/dayAge 13-17 years: 7 mg/day  | Not approved for children and adolescentsApproved for monotherapy and adjunctive therapy to stimulants for treatment of ADHDAge 6-12 yrs.: 4 mg/day Age 13-17 yrs.: 7 mg/dayDoses > 4mg/day have not been studied in adjunctive trials | 4mg/day7mg/day | One to four times dailyOnce daily |
| **Bupropion** | **Wellbutrin®****Wellbutrin® SR****Wellbutrin® XL** | Age ≥ 6 yrs.: 3 mg/kg/day or 150mg/day, whichever is less | Age ≥ 6 yrs.: 6 mg/kg/day or 300 mg/day, with no single dose > 150 kg., whichever is less Age ≥ 6 yrs.: 400 mg/dayAge ≥ 6 yrs.: 450 mg/day | Not approved for children and adolescents | 300mg/day400mg/day450mg/day | Once or twice dailyOnce or twice dailyOnce daily  |
| **Tricyclic Antidepressants** | **Multiple Individual Medications** | Reviewed but not included / recommended for psychiatric indications |

**Patient Monitoring Parameters- ADHD Non-Stimulants:**

* Baseline and ongoing: Height, weight, blood pressure, and pulse
* Baseline: Personal and family cardiovascular history
* Atomoxetine: Onset of therapeutic effect typically delayed three weeks
* Bupropion: Mental status exam and suicide assessment

**Boxed Warning- ADHD Non-Stimulants:**

* Atomoxetine & Viloxazine: suicidal ideation in children and adolescents being treated for ADHD
* Bupropion: increase risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major depressive disorder and other psychiatric disorders

**Warnings and Precautions- ADHD Non-Stimulants:**

* Atomoxetine & Viloxazine:
	+ Rare severe liver injury (atomoxetine only) – Patient education, monitoring signs and symptoms and lab as clinically indicated
	+ Contraindicated to use within 14 days of an MAOI
	+ Increased blood pressure and pulse
	+ Psychiatric adverse events
	+ Priapism (rare)
* Clonidine & Guanfacine:
	+ Hypotension, bradycardia, and syncope
		- Caution if used with antipsychotics or other drugs that may lower BP or pulse
	+ Sedation/somnolence
	+ Abrupt discontinuation may cause nervousness, anxiety, or cardiovascular symptoms such as rebound hypertension and increases in heart rate, in some cases leading to hypertensive encephalopathy. Taper, do not discontinue abruptly: The manufacturer recommends tapering the total daily dose in “decrements of not more than 1 mg every 3 to 7 days” for Guanfacine and 0.1 mg every 3 to 7 days for Clonidine.
	+ Do not administer with high fat meals (Guanfacine ER only)
* Bupropion:
	+ Lowers seizure threshold (use with caution with comorbid Bulimia or Seizure Disorder or with other agents that may lower seizure threshold-e.g. antipsychotics, TCA’s, excessive alcohol)
	+ Discontinuation syndrome
	+ Activation of mania/hypomania
	+ Suicidal ideation
	+ Contraindicated within 14 days of an MAOI
* Tricyclic Antidepressants:
	+ Caution with cardiac disease—cardiac conduction abnormalities and orthostatic hypotension
	+ Activation of mania/hypomania
	+ Anticholinergic and cognitive adverse effects
	+ Lowers seizure threshold
	+ Discontinuation syndrome
	+ Contraindicated within 14 days of an MAOI
	+ Use caution in those with history of suicide attempts; may be cardiotoxic in overdose

**SSRI Antidepressants**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Drug (Brand)** | **Initial Dosage** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** | **Maximum Medicaid Dose (Per day)** | **Schedule** |
| **Citalopram** | **Celexa®** | Age 6-11 yrs: 10 mg/dayAge ≥ 12 yrs: 20 mg/day | Age ≥ 6 yrs: 40 mg/day | Not approved for children and adolescents | 40mg/day | Once daily |
| **Escitalopram** | **Lexapro®** | Age 6-11 yrs.: 5 mg/dayAge ≥ 12 yrs.(MDD): 10 mg/day | Age 6-11 yrs: 20 mg/dayAge ≥ 12 yrs: 30 mg/day | Not approved for childrenApproved for treatment of MDD in adolescents (age 12-17 yrs.) 20 mg/day | Ages 6-11 yrs: 20 mg/dayAges 12 -17 yrs: 30 mg/day | Once daily |
| **Fluoxetine** | **Prozac®** | Age 6-11 yrs: 5-10 mg/day Age ≥12 yrs. 10 mg/day  | Approved for treatment of MDD (age 8-18 yrs.) 20 mg/dayApproved for treatment of OCD (age 7-17 yrs.) 60 mg/day | Approved for treatment of MDD (age 8-18 yrs.) 20 mg/dayApproved for treatment of OCD (age 7-17 yrs.) 60 mg/day | 60mg/day | Once daily |
| **Paroxetine** | **Paxil® (oral tablet and oral suspension)****Paxil® CR** | Reviewed but not included or recommended - evidence of possible harm | Once daily |
| **Fluvoxamine** | **Luvox®****Luvox® CR** | Age ≥ 8 yrs: 25 mg/dayThe CR formulation is not approved in children and adolescents\* | Age 8-11 yrs.: 200 mg/day Age 12-17 yrs.: 300 mg/day | Approved for treatment of OCD (age 8-17 yrs.): Ages 8-11 yrs: 200 mg/day Ages 12-17 yrs.: 300 mg/dayThe CR formulation is not approved in children and adolescents+ | Ages 8 -11 yrs: 200 mg/day Ages 12 -17 yrs: 300 mg/day | Daily doses > 50 mg. should be divided Once daily  |
| **Sertraline** | **Zoloft®** | Age 6-12 yrs.: 12.5-25 mg/dayAge 13-17 yrs.: 25-50 mg/day  | Age >6 yrs.: 200 mg/day | Approved for treatment of OCD (age 6-17 yrs.) 200 mg/day | 200mg/day  | Once daily |
| **Vilazodone**  | **Viibryd®** | Age 12-17 yrs.: 5 mg/day on days 1-3, then 10mg/day on days 4-7  | Age 12-17 yrs.: 30 mg/day | Not approved for children and adolescents | 30mg/day | Once daily |

**SNRI Antidepressants**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Drug (Brand)** | **Initial Dosage** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** | **Maximum Medicaid Dose (Per day)** | **Schedule** |
| **Venlafaxine** | **Effexor®** **Effexor® XR** | Reviewed but not included or recommended - evidence of possible harm |
| **Duloxetine** | **Cymbalta®** | Age 7-17 yrs.: 30 mg/day  | Age 7-17 yrs.: 120 mg/day | Approved for treatment of Generalized Anxiety Disorder Age 7-17 yrs.: 120 mg/day | 120mg/day | Once or twice daily |
| **Desvenlafaxine** | **Pristiq®** | Reviewed but not included or recommended |
| **Levomilnacipram** | **Fetzima®** | Reviewed but not included or recommended - evidence of possible harm |
| **Clomipramine** | **Anafranil®** | Age 10-17 yrs.: 25 mg/day  | Age 10-17 yrs.: 3 mg/day or 200 mg/day, whichever is less | Approved for treatment of OCD: Age 10-17 yrs.: 3 mg/day or 200 mg/day, whichever is less | 200mg/day | Once daily  |

**Other Antidepressants**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Drug (Brand)** | **Initial Dosage** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** | **Maximum Medicaid Dose (Per day)** | **Schedule** |
| **Mirtazapine**  | **Remeron®** | Age ≥ 3 yrs.: 7.5 mg/day  | Age ≥ 3 yrs.: 45mg/day  | Not approved for children and adolescents |  | Once daily  |
| **Vortioxetine** | **Trintellix®** | Reviewed but not included / recommended - insufficient evidence |
| **Monoamine Oxidase Inhibitors (MAOIs)** | Reviewed but not included / recommended - increased risk of adverse events and risk of safety issues in youth, based on drug-food interactions and drug-drug interactions |
| **St. John’s Wort** | Reviewed but not included / recommended - insufficient evidence |

**Patient Monitoring Parameters- Antidepressants:**

* Pregnancy test—as clinically indicated
* Monitor for emergence of suicidal ideation or behavior
* Monitor weight and growth
* Obtain serum sodium if symptoms of hyponatremia occur (e.g. headaches, confusion, etc.)
* CBC at baseline and periodically
* SNRI Antidepressants:
	+ Blood pressure during dosage titration and as clinically indicated
	+ Hepatic function testing—baseline and as clinically indicated
	+ EKG at baseline and as clinically indicated for Clomipramine

**Boxed Warning- Antidepressants:**

* Increased risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies or major depressive disorder (MDD) and other psychiatric disorders

**Warnings and Precautions- Antidepressants:**

* Suicidal ideation
* Activation of mania/hypomania
* Discontinuation syndrome
* Abnormal bleeding
* Contraindicated to use within 14 days of an MAOI; for fluoxetine, do not start MAOI for 5 weeks after fluoxetine discontinuation
* Serotonin syndrome
* Hyponatremia risk
* SSRI Antidepressants:
	+ QTc prolongation potential (citalopram, fluoxetine, possibly escitalopram)
* SNRI Antidepressants:
	+ Severe skin reactions
	+ Hepatoxicity
	+ Elevated blood pressure and pulse
	+ Seizures
	+ Rare cases of drug rash with eosinophilia and systemic symptoms (DRESS)
* Mirtazapine:
	+ Weight gain
	+ Orthostatic hypotension and syncope
	+ Hepatoxicity
	+ Seizures
	+ Neutropenia

**Mood Stabilizers**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Drug (Brand)** | **Formulations** | **Initial Dosage** | **Target Dose Range** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** |
| **Carbamazepine**(Epitol®, Tegretol®, Tegretol® XR, Carbatrol®, Equetro®) | TabletChewable tabletOral suspensionER tabletER capsule | Age 4-5 yrs.: 10-20 mg/kg/day (in 2-3 divided doses)Age 6-12 yrs.: 10 mg/kg/day or 100 mg BIDAge ≥ 13 yrs.: 200 mg BID**OR**Children: 100 mg BID Adolescents: 100 mg TID | Age 4-5 yrs.: 35 mg/kg/dayAges 6-12 yrs.: 400-800 mg/dayAge >13 yrs.: 800-1200 mg/day | Age 4-5 yrs.: 35 mg/kg/dayAges 6-12 yrs.: 400-800 mg/dayAge >13 yrs.: 800-1200 mg/day | Approved for treatment of seizure disorders in all agesAge < 6 yrs.: 35 mg/kg/dayAge 6-15 yrs.: 1000 mg/dayAge > 15 yrs.: 1200 mg/daySafety & efficacy not established for Equetro® for under age 18 |

**Patient Monitoring Parameters:**

* Pregnancy Test - baseline as appropriate, and as clinically indicated
* CBC with differential—baseline, 1 to 2 weeks after each dose increase, annually, and as clinically indicated
* Comprehensive Metabolic Panel (electrolytes, hepatic function, serum creatinine, BUN) – baseline, every 3 months for the first year of treatment, then annually and as clinically indicated
* Medication Levels: CBZ—obtain 1 week after initiation and 3-4 weeks after dose adjustment, then as clinically indicated (trough level 4-12mcg/mL)
* Monitor for emergence of suicidal ideation or behavior
* For patients with Asian descent, genetic test for HLA-B\*1502 at baseline (prior to 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.
	+ 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)

**Boxed Warnings:**

* Serious rashes including Stevens-Johnson syndrome
* Aplastic anemia/agranulocytosis

**Warnings and Precautions:**

* Suicidal ideation
* Teratogenicity
* Withdrawal seizures
* Hyponatremia
* Induces metabolism of itself and many other drugs through strong CYP 3A4 induction (decreased efficacy of oral contraceptives)
* Contraindicated to use within 14 days of an MAOI

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Drug (Brand)** | **Formulations** | **Initial Dosage** | **Target Dose Range** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** |
| **Valproic Acid or** **Divalproex Sodium**(Depakene® , Depakote® DR, Depakote® ER, Depakote® sprinkles) | IR capsuleIR solutionDR tabletER tabletDR sprinkle | Age ≥ 6 yrs.: 10-15 mg/kg/day in 2 or 3 divided doses | Age ≥ 6 yrs.: 30-60 mg/kg/day | Age ≥ 6 yrs.: Target serum level: 50-125 µg/mL or 60 mg/kg/day | Approved for treatment of seizure disorders (age ≥ 10 yrs.)Maximum dose based upon serum level: 50-100 µg/mL or 60 mg/kg/day |

**Patient Monitoring Parameters:**

* Pregnancy Test - baseline as appropriate, and as clinically indicated
* CBC with differential—baseline, 1 to 2 weeks after each dose increase, annually, and as clinically indicated
* Comprehensive Metabolic Panel (electrolytes, hepatic function, serum creatinine, BUN) – baseline, every 3 months for the first year of treatment, then annually and as clinically indicated
* Medication Levels: VPA—obtain 1-2 weeks after initiation and dosage change, then as clinically indicated (trough level 50-125mcg/mL)
	+ Consider using higher levels for acute mania (trough level 85-125mcg/mL)
	+ Timing of lab draw for trough level dependent on formulation used
* Monitor for emergence of suicidal ideation or behavior
* Weight—baseline and quarterly for the first year of treatment then annually and as clinically indicated

**Boxed Warning:**

* Hepatotoxicity
* Teratogenicity
* Pancreatitis

**Warnings and Precautions:**

* Suicidal ideation
* Teratogenicity
* Withdrawal seizures
* Urea cycle disorders
* Neutropenia and leukopenia- increased risk with concomitant quetiapine use
* Thrombocytopenia
* Hyperammonemia
* Multi-organ hypersensitivity reaction
* Polycystic ovarian syndrome
* Alopecia

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| **Drug (Brand)** | **Formulations** | **Initial Dosage** | **Target Dose Range** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** |
| **Lithium**(Eskalith®, Eskalith® CR, Lithobid®) | IR capsule carbonate)Solution (citrate)IR tablet (carbonate)ER tablet (carbonate) | Age 6-11 yrs.: Lesser of 15-20 mg/kg/day or 150 mg twice per dayAge ≥ 12 yrs.: Lesser of 15-20 mg/kg/day or 300 mg twice per day | Dose adjustment based upon serum-level 12-hour post dose serum level: 0.6-1.2 mEq/L | Age ≥ 6 yrs,: Serum level: 0.6-1.2 mEq/L | Approved for treatment of manic episodes (age ≥ 12 yrs.)Maximum dose based upon 12-hour post dose serum level: 1.2 mEq/L |

**Patient Monitoring Parameters:**

* Pregnancy Test - baseline as appropriate, and as clinically indicated
* CBC with differential—baseline, annually, and as clinically indicated
* Comprehensive Metabolic Panel (electrolytes, hepatic function, serum creatinine, BUN) – baseline, every 3 months for the first year of treatment, then annually and as clinically indicated
* Medication Levels: LI—obtain 1 week (5-7 days) after initiation or dosage change, 3 months after initiation, every 6 months for maintenance, and as clinically indicated (trough level 0.6-1.2 meq/L)
* Monitor for emergence of suicidal ideation or behavior
* Weight—baseline and quarterly for the first year of treatment then annually and as clinically indicated

**Boxed Warning:**

* Toxicity above therapeutic serum level

**Warnings and Precautions:**

* Suicidal ideation
* Teratogenicity
* Chronic renal function impairment
* Special risk patients: those with significant renal or cardiovascular disease, severe debilitation, dehydration, or sodium depletion
* Polyuria
* Tremor
* Diarrhea and nausea
* Hypothyroidism

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| **Drug (Brand)** | **Formulations** | **Initial Dosage** | **Target Dose Range** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** |
| **Lamotrigine**(Lamictal®, Lamictal XR®) | IR tabletER tabletIR chewable tabletOrally disintegrating tablet | Age 6-11 yrs.: 2-5 mg/dayAge ≥ 12 yrs.: 25 mg/day (increase by 25 mg every 2 weeks)ER formulation has no published data for mood stabilization in pediatrics | Age 6-11 yrs.Monotherapy: 4.5-7.5 mg/kg/day With Valproate: 1-3 mg/kg/dayWith Valproate and EIAEDs•: 1-5 mg/kg/dayWith EIAED’s: 5-15 mg/kg/day Age ≥ 12 yrs.: Monotherapy: 225-375 mg/dayWith Valproate: 100-200 mg/dayWith Valproate and EIAEDs•: 100-400 mg/dayWith EIAEDs•: 300-500 mg/day  | Age ≥ 6 yrs.: 15 mg/kg/day or 500 mg/day, whichever is less | Approved for adjunctive therapy for seizure disorders: Age 2-12: 400 mg/day Age > 12: 500 mg/day (use > 200 mg/day in adults for bipolar depression has not conferred additional efficacySafety and effectiveness for treatment of bipolar disorder in patients younger than 18 yrs. has not been established |

\*EIAEDs= enzyme-inducing antiepileptic drugs

**Patient Monitoring Parameters:**

* Pregnancy Test - baseline as appropriate, and as clinically indicated
* CBC with differential—baseline, 1 to 2 weeks after each dose increase, annually, and as clinically indicated
* Comprehensive Metabolic Panel (electrolytes, hepatic function, serum creatinine, BUN) – baseline, every 3 months for the first year of treatment, then annually and as clinically indicated
* Monitor for emergence of suicidal ideation or behavior
* Monitor for potentially lethal rash especially during the first two months of therapy

**Boxed Warning:**

* Serious rashes including Stevens-Johnson syndrome

**Warnings and Precautions:**

* Suicidal ideation
* Teratogenicity
* Withdrawal seizures
* Concomitant use with VPA increases serum LTG levels significantly (increased risk of rash/SJS without LTG dose adjustment)
* Concomitant use with EIAEDs (CBZ, Phenytoin, Phenobarbital, Primidone) reduces serum LTG levels significantly
* Concomitant use with oral contraceptives increases LTG clearance

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| **Drug (Brand)** | **Formulations** | **Initial Dosage** | **Target Dose Range** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** |
| **Oxcarbazepine**(Trileptal®, Oxtellar XR®) | IR tabletER tabletSuspension | 8-10 mg/kg/day | Monotherapy (based on weight):20-24.9 kg: 600-900 mg/day25-34.9 kg: 900-1200 mg/day35-44.9 kg: 900-1500 mg/day45-49.9 kg: 1200-1500 mg/day50-59.9 kg: 1200-1800 mg/day60-69.9 kg: 1200-2100 mg/day≥ 70 kg: 1500-2100 mg/day | Age 7-12 yrs.: 60 mg/kg/day or 1500 mg/dayAge 13-17 yrs.: 60 mg/kg/day or 2100 mg/day | Approved for treatment of seizure disorders as monotherapy (age ≥ 4 yrs.), or as adjunctive therapy in (age ≥ 2 yrs.): 60 mg/kg/day or 1800 mg/dayReviewed but not recommended due to lack of safety and effectiveness for treatment of bipolar disorder in patients younger than 18 yrs. |

**Patient Monitoring Parameters:**

* Pregnancy Test - baseline as appropriate, and as clinically indicated
* CBC with differential—baseline, 1 to 2 weeks after each dose increase, annually, and as clinically indicated
* Comprehensive Metabolic Panel (electrolytes, hepatic function, serum creatinine, BUN) – baseline, every 3 months for the first year of treatment, then annually and as clinically indicated
* Monitor for emergence of suicidal ideation or behavior
* Obtain serum sodium if symptoms of hyponatremia (headaches, confusion, etc.) occur

**Warnings and Precautions:**

* Suicidal ideation
* Teratogenicity
* Withdrawal seizures
* Hyponatremia (incidence may be as high as 24% in children)
* Anaphylactic reactions and angioedema
* Patients with a history of hypersensitivity reaction to carbamazepine
* Serious dermatological reactions
* Cognitive/neuropsychiatric adverse events
* Multi-organ hypersensitivity
* Hematologic events

Sedatives-Hypnotics

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|  | **Drug (Brand)** | **Initial Dosage** | **Literature Based Maximum Dosage** | **FDA Approved Maximum Dosage for Children and Adolescents** | **Schedule** |
| Diphenhydramine | Benadryl® | Age 3-5 yrs.: 6.25-12.5 mg (1mg/kg max)Age 5-11 yrs.: 12.5-25mgAge ≥ 12 yrs.: 25-50 mg | 11-16 kg.: 12.5 mg17-22 kg.: 19 mg23-45 kg.: 25 mgEvidence suggests that tolerance develops to the hypnotic effects within 5-7 nights of continuous use. | Approved for treatment of insomnia (age ≥12 yrs.): 50 mg at bedtime | Once at bedtime |
| Trazodone | Desyrel® | Children: Insufficient EvidenceAdolescents: 25 mg | Children: Insufficient EvidenceAdolescents: 100 mg | Not approved for children or Adolescents as a hypnotic | Once at bedtime |
| Eszopiclone | Lunesta® | Reviewed, but not included or recommended - insufficient evidence/increased rate of adverse events in pediatric patients |
| Melatonin |  | Age 3-5 yrs.: 0.5 mgAge ≥ 6 yrs.: 1 mg | Age 3-5 yrs.: 0.15 mg/kg or 3 mg, whichever is lessAge ≥ 6 yrs.: 0.15 mg/kg or 6 mg, 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) |
| Ramelteon | Rozerem® | Reviewed, but not included or recommended - insufficient evidence |
| Hydroxyzine  |  | Age 3-5 yrs.: 25 mgAge ≥ 6 yrs.: 50 mg | Age 3-5 yrs.: 25 mgAge 6-11 yrs.: 50 mgAge 12 yrs. and older: 100 mg | Age < 6 yrs.: 50 mg/day in divided dosesAge equal to or ≥ 6 years: 50-100 mg/day in divided dosesApproved as a sedative when used as a premedication and following general anesthesia | Once at bedtime |
| Suvorexant | Belsomra®  | Reviewed, but not included or recommended - insufficient evidence |
| Zolpidem | Ambien | Reviewed, but not included or recommended - evidence of possible harm |
| Benzodiazepines | Alprazolam/ Xanax® Clonazepam/ Klonopin® Diazepam/ Valium® Lorazepam/ Ativan® Oxazepam/ Serax® Temazepam/ Restoril® | Reviewed, but not included or recommended except in exceptional circumstances – evidence of possible harm/increased incidence of adverse effects and potential for abuse and/or addiction |

Behavioral intervention is first-line treatment for insomnia and should always be included. Psychopharmacological interventions are not to be the first-line intervention for insomnia.

**Boxed Warning- Sedative-Hypnotics:**

* Trazodone—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
* Benzodiazepines—risks from concomitant use with opioids

**Warnings and Precautions- Sedative-Hypnotics:**

* There is a lack of evidence for long-term usage for treatment of insomnia.
* Diphenhydramine & Hydroxyzine:
	+ Drowsiness and dizziness
	+ Dry mouth
	+ Blurred vision
	+ Nervousness
	+ Diminished mental alertness
	+ Paradoxical excitation
	+ May lower seizures threshold (avoid in epilepsy)
	+ Associated with a small but definite risk of QT interval prolongation and torsades de pointes (hydroxyzine only)
* Melatonin:
	+ Should be given directly before sleep onset due to short half-life
	+ May adversely affect gonadal development
* Ramelteon:
	+ Hypersensitivity reactions
	+ Abnormal thinking and behavioral changes
	+ CNS depression
	+ Decreased testosterone
	+ Hyperprolactinemia
* Trazodone:
	+ Serotonin syndrome
	+ Contraindicated for use within 14 days of an MAOI
	+ Suicidal ideation
	+ Activation of mania/hypomania
	+ Discontinuation syndrome
	+ Abnormal bleeding
	+ QT prolongation and risk of sudden death
	+ Orthostatic hypotension and syncope
	+ Priapism
	+ Hyponatremia
	+ Cognitive and motor impairment
* Zolpidem & Eszopiclone:
	+ Complex sleep behaviors possible
	+ Abnormal thinking and behavior changes
	+ Withdrawal effects
	+ Drug abuse and dependence
	+ Tolerance
	+ Hallucinations in children 6-17 years old have been reported (zolpidem only)
* Suvorexant:
	+ Sleep paralysis and somnolence
* Benzodiazepines:
	+ Withdrawal effects
	+ Drug abuse and dependence
	+ Sedation potential

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