NYC ADMINISTRATION FOR CHILDREN'S SERVICES

Psychiatric Medication Monitoring Guidelines

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These are general guidelines, intended to be used for reference by pediatric and mental health clinicians involved in the psychiatric treatment of children in foster care. These guidelines were developed by Suchet Rao, M.D., with assistance from Martin Irwin, M.D., with thanks to John DiLallo, M.D. for his work on previous drafts of these guidelines. General adherence to these guidelines is expected as a component of obtaining informed consent for treatment from any of our designated foster care agencies. It is recognized that new practice recommendations may develop before we have a chance to update these guidelines, or that exceptions to them may sometimes occur according to the clinical judgment of the prescriber. In any such situation, the prescriber is well advised to document in the patient's clinical record a clear rationale for diverting from any of the recommendations outlined here. Comments or suggestions may be directed to martin.irwin@acs.ny.gov or suchet.rao@acs.nyc.gov

USE OF PSYCHIATRIC MEDICATIONS

The following guidelines are intended to be used as a reference to those prescribing psychiatric medication to children in foster care.

GENERAL PRINCIPLES

With respect to the use of psychiatric medication in children, some general rules should be kept in mind:

Medication should ALWAYS be used sparingly and judiciously, that is:

- There should be a clear indication for use of a medication based on a recent comprehensive psychiatric examination and documented in an evaluation or current progress note.
- Other (non-pharmacologic) treatment options should always be considered, and should be employed where appropriate, either instead of, or in addition to, treatment with medication. If at all possible, other home and community based interventions should be attempted first especially in younger children and when the target symptoms are primarily behavioral.
- Except in extreme circumstances as determined by clinical judgement (and should be clearly documented), no more than one medication should be started at any one time.
- Medications with less risk, as determined by the clinical judgement of the prescriber, should be considered first especially when used off label targeting mood dysregulation and/or behavioral symptoms. Anti-psychotic medication should rarely be the medication of first choice when used “off-label.”
- Medication that is FDA approved for the indicated use in the specific age group is highly preferred over an “off-label” alternative.
- Symptoms and impairment should be monitored on a regular basis, and medication should be adjusted in accordance with this, such that the minimum effective dose of medication is used at all times.
- When significant weight gain secondary to medication is present, strong consideration should be given to switching to a weight-neutral alternative, along with appropriate dietary changes/recommendations.
- Whenever symptoms persist despite use of medication, it must be ensured that the dosage of the current medication has been optimized (within limits of tolerability) before an additional medication is started.
- A second medication should not be added when the original medication is only partially effective if there is an alternative medication that might be sufficient if used alone.

- A second medication should not be added to address side effects if there is an alternative medication that might not cause such side effects if used alone.
- For any child prescribed two or more psychiatric medications, re-evaluation of the treatment plan should occur frequently to ensure that there is diagnostic clarity and that target symptoms are being appropriately addressed.
- Consideration should be given to the context in which the medication is being prescribed (that is, caution should be exercised, particularly with medication which requires extensive monitoring or which could be harmful if not taken consistently).
- At some point, usually within a year or two after initiation of a new medication, a good faith effort should be made to try to taper and/or discontinue the medicine.

THE FOLLOWING SHOULD BE DONE FOR ALL PSYCHIATRIC MEDICATIONS

Before any medication is prescribed, it must be ensured that the patient's legal guardian has provided **INFORMED** consent for the specific medication being prescribed.

Before any medication is prescribed, and at each follow up visit, a history should be obtained about use of other prescribed/non-prescribed substances which may interact with any psychiatric medication being prescribed. This includes medications prescribed elsewhere, tobacco, alcohol, illicit substances, complementary treatments and dietary supplements.

Routine Premedication Screening:

- Physical Exam (within past 6 months) including Vital Signs (HR, BP, RR, Temp)
- Height and Weight (for BMI)

Routine Follow Up:

- At each visit:
    - Monitor for side effects/interactions specific to the medication
- Every three months:
    - BP/HR,
    - Height, Weight, BMI

The following pages summarize **additional** steps and precautions that should be taken with respect to **specific** medications.

Medication-Specific Recommendations

Routine premedication and follow up steps, as described above, should be taken in all cases. The following pages summarize **additional** steps and precautions that should be taken with respect to **specific** medications.

ADHD Medications
Stimulants

Amphetamine salts (Adderall XR, Adderall)*
Dextroamphetamine (Dexedrine, Dextrostat, ProCentra)*
Methylphenidate (Concerta, Ritalin (SR/LA/XR); Metadate (CD/ER); Methylin; Focalin (XR); Daytrana)*
Lisdexamfetamine (Vyvanse)*

*See Appendix for additional information regarding FDA approval.

Prior to starting treatment:

- Take a thorough medical history and family medical history, and perform a physical examination to evaluate patients for cardiac disease.

An EKG should be performed prior to starting treatment with a stimulant IF:
There is any history of:

1. The patient having experienced cardiac symptoms,
2. The patient having a diagnosed cardiac condition,
3. Non-ischemic heart disease in the first- or second-degree relatives of the patient.

Or:

4. If such history is not available (for example, because of a lack of a reliable source of information).

Follow up:

- Promptly conduct cardiac evaluation in patients who develop chest pain, unexplained syncope, or any other symptom of cardiac disease during treatment.
- CBC with differential and platelet count once a year.

ADHD Medications

Alpha-2 Agonists (Non-Stimulant ADHD Medications)

Guanfacine (Tenex, Intuniv)*
Clonidine (Catapres, Kapvay)*

*See Appendix for additional information regarding FDA approval. Note: Only extended release preparations (Intuniv and Kapvay) are FDA-approved for treatment of ADHD in children.

Prior to starting treatment:

- Take a thorough medical history and family medical history, and perform a physical examination to evaluate patients for cardiac disease.

An EKG should be performed prior to starting treatment with an alpha-2 agonist (non-stimulant medication) IF:

There is any history of:

1. The patient having experienced cardiac symptoms,
2. The patient having a diagnosed cardiac condition,
3. Non-ischemic heart disease in the first- or second-degree relatives of the patient.

Or:

4. If such history is not available (for example, because of a lack of a reliable source of information).

Baseline BP measurement.

Advise regarding risk of drowsiness, dizziness/syncope and risk of rebound hypertension if medication is abruptly discontinued.

Follow up:

- BP measurement at each appointment.
- Promptly conduct cardiac evaluation in patients who develop chest pain, unexplained syncope, or any other symptom of cardiac disease during treatment.

Other Non-Stimulant ADHD Medications

Atomoxetine (Strattera)*

*FDA-approved for treating ADHD in children ≥ 6 years old.

Prior to starting treatment:

- Provide information when obtaining informed consent regarding the "BLACK BOX" warning for suicidal ideation.
- Take a thorough medical history and family medical history, and perform a physical examination to evaluate patients for cardiac disease.
- Baseline LFTs (because of risk of hepatotoxicity).

An EKG should be performed prior to starting treatment with atomoxetine IF:

There is any history of:

1. The patient having experienced cardiac symptoms,
2. The patient having a diagnosed cardiac condition,
3. Non-ischemic heart disease in the first- or second-degree relatives of the patient.

Or:

4. If such history is not available (for example, because of a lack of a reliable source of information).

Hepatotoxicity Risk:

- Use may be associated with rare but severe hepatotoxicity, including hepatic failure.
- DISCONTINUE and do not restart if signs or symptoms of hepatotoxic reaction (eg: jaundice, pruritus, flu-like symptoms, dark urine, and/or right upper quadrant tenderness) or laboratory evidence of liver injury are noted.
- The majority of reported cases occurred within 120 days of initiation of therapy.[1]

Follow up:

- Promptly conduct cardiac evaluation in patients who develop chest pain, unexplained syncope, or any other symptom of cardiac disease during treatment.
- LFTs every 6 months to monitor for evidence of hepatotoxicity.

"Off-Label" ADHD Medications

Bupropion (Wellbutrin (XL/SR))

- Bupropion is FDA-approved for use in ADULTS with certain depressive disorders and for smoking cessation.
- It is not FDA-approved for ADHD treatment in any age group.
- It is not FDA-approved for any use in children.

Prior to starting treatment:

- Provide information when obtaining informed consent regarding the "BLACK BOX" warning for suicidal ideation.
- Documentation of a negative history for seizures and severe head trauma - Consider EEG if indicated.
- Assess history of anorexia/bulimia.

Modafinil (Provigil, Nuvigil)

- Reports of serious dermatologic adverse effects and psychiatric events has resulted in the FDA's Pediatric Advisory Committee unanimously recommending that a specific warning against the use of modafinil in children be added to the manufacturer's labeling.[13]
- Use only if first- and second-line treatments have failed and the benefits outweigh the risks.
- Modafinil is FDA-approved for use in ADULTS with certain sleep-related disorders.
- It is not FDA-approved for ADHD treatment in any age group.
- It is not FDA-approved for any use in children.

Antidepressants
Selective Serotonin Reuptake Inhibitors (SSRIs)

Fluoxetine (Prozac, Sarafem)*
Fluvoxamine (Luvox)*
Sertraline (Zoloft)*
Citalopram (Celexa)
Escitalopram (Lexapro)**

*See Appendix for additional information regarding FDA approval.

- Provide information when obtaining informed consent regarding the "BLACK BOX" warning for suicidal ideation.

Follow up:

- Monitor for suicidal ideation.
- Monitor for induction of mania.

Paroxetine (Paxil)

- Not FDA-approved for use in children.
- The FDA recommends that paroxetine not be used in pediatric patients for the treatment of depression. Three well-controlled trials in pediatric patients with depression have failed to show therapeutic superiority over placebo.[14]
- In addition, an increased risk for suicidal behavior was observed in patients receiving paroxetine when compared to other SSRIs.
- Therefore, the risks of use in children very likely outweigh any potential benefits.

"Off-Label" Antidepressant Medications

Bupropion (Wellbutrin (XL/SR))

- Bupropion is FDA-approved for use in ADULTS with certain depressive disorders and for smoking cessation.
- It is not FDA-approved for ADHD treatment in any age group.
- It is not FDA-approved for any use in children.

Prior to starting treatment:

- Provide information when obtaining informed consent regarding the "BLACK BOX" warning for suicidal ideation.
- Documentation of a negative history for seizures and severe head trauma - Consider EEG if indicated.
- Assess history of anorexia/bulimia.

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

Venlafaxine (Effexor (XR))/**Desvenlafaxine** (Pristiq)

Duloxetine (Cymbalta)

Milnacipran (Savella)/**Levomilnacipran** (Fetzima)

- None are FDA-approved for use in children, though there is some limited evidence to suggest that they may be helpful in treating depression in children that has not responded to adequate trials of an initial and an alternate SSRI.

Prior to starting treatment:

- Baseline BP.

Follow up:

- Check BP every one to two weeks for the first month, then every month for the next six months, then every three to six months.[2]

Trazodone (Desyrel)

- Not recommended for first- or second-line treatment of depression (AACAP 2007).[15]

Prior to starting treatment:

- Advise regarding risk of priapism in male patients.

Mirtazapine (Remeron)

- Generally avoided in children as a result of evidence suggesting lack of efficacy.[16]

"Off-Label" Antidepressant Medications (continued)
Tricyclic Antidepressants

Amitriptyline (Elavil)
Clomipramine (Anafranil)*
Desipramine (Norpramin)
Doxepin (Sinequan)
Imipramine (Tofranil)*
Nortriptyline (Aventyl, Pamelor)

*See Appendix for additional information regarding FDA approval. None of the tricyclic antidepressants are FDA-approved for treatment of depressive disorders in children.

- Tricyclics are rarely indicated for treatment of depression in children because of a frequent (especially in younger children) lack of efficacy, an unfavorable side effect profile, high lethality in overdose, and the availability of preferred medications.[17]
- However, it is reasonable to administer tricyclics to patients who do not respond to multiple trials of SSRIs, SNRIs and other medications.[17]

Prior to starting treatment:

- Take a thorough medical history and family medical history, and perform a physical examination to evaluate patients for cardiac disease.
- Electrolytes, particularly serum potassium, to rule out hypokalemia.

An EKG should be performed prior to starting treatment with a tricyclic IF:
There is any history of:

1. The patient having experienced cardiac symptoms,
2. The patient having a diagnosed cardiac condition,
3. Non-ischemic heart disease in the first- or second-degree relatives of the patient

Or:

4. If such history is not available (for example, because of a lack of a reliable source of information)

(Although tricyclic antidepressants have been rarely associated with bone marrow and liver toxicity, it is not recommended that CBC or LFTs be checked either at baseline or as part of routine monitoring in the absence of specific concerns based on history or symptoms).[10]

Follow up:

- Promptly conduct cardiac evaluation in patients who develop chest pain, unexplained syncope, or any other symptom of cardiac disease during treatment.
- Serum levels are used to help establish the proper dose and can also help assess adherence.
- Levels should be drawn at least five days after a dose change (allows for steady state).
- The level should be drawn approximately 12 hours after the last dose.[18]

Mood-Stabilizing Medications

Lithium*[6]

(Eskalith (CR), Lithobid, Carbolith, Cibalith-S, Duralith, Lithane, Lithizine, Lithonate, Lithotabs)

*Lithium is FDA-approved for management of acute manic episodes, and for maintenance treatment of mania in children ≥ 12 years old.

Prior to starting treatment:

- CBC (with differential).
- Thyroid function tests.
- BUN/creatinine.
- Electrolytes, particularly serum calcium.
- Urinalysis.
- Pregnancy test. Advise female patients regarding risk of birth defects, even if this test is negative.
- Advise regarding need to maintain adequate hydration (especially during GI illness, fever, exercise or hot weather).
- EKG if indicated (see below).

AVOID use in patients with/suspected of having Brugada syndrome[7] (Brugada syndrome is an inherited condition which can result in sudden death. It is associated with characteristic EKG findings and symptoms include syncope and palpitations, though it is often asymptomatic).

Generally avoid use in patients with other significant cardiovascular disease due to an increased risk of lithium toxicity; if use is unavoidable, use with extreme caution and monitor serum lithium levels closely.

An EKG should be performed prior to starting treatment with lithium IF:

There is any history of:

1. The patient having experienced cardiac symptoms,
2. The patient having a diagnosed cardiac condition,
3. Non-ischemic heart disease in the first- or second-degree relatives of the patient.

Or:

4. If such history is not available (for example, because of a lack of a reliable source of information).

After starting treatment:

- Check lithium level after 5-6 days, then at each dose change.
- Because of increased risk of renal toxicity, dose may need to be adjusted (or treatment temporarily suspended) if there is fluid loss, sodium depletion or fever.

Once a stable lithium dose has been obtained, follow up every 3 to 6 months:

- Lithium level.
- Thyroid function tests.
- BUN/creatinine.
- Electrolytes, particularly serum calcium.
- Urinalysis.
- Advise female patients periodically regarding risk of birth defects (repeat pregnancy test if indicated).

"Off-Label" Mood-Stabilizing Medications

Valproic Acid[6,19] (Depakote, Depakene)

- Various formulations of valproic acid are FDA-approved for use in children and adults with certain seizure disorders and for treatment of manic episodes in ADULTS.
- Valproic acid is not FDA-approved for treatment of any psychiatric illness in children.

Prior to starting treatment:

- CBC.
- LFTs.
- Pregnancy test.

"BLACK BOX" warnings:

- **Severe teratogenic risks** and pregnancy prevention strategies must be discussed and documented if prescribing to a female patient of childbearing age.
- There must be a specific discussion about what the patient would do if she did become pregnant while taking valproic acid. If she would not be willing to consider termination of the pregnancy, then valproic acid **MUST NOT** be prescribed.
- Advise regarding the potentially fatal risks of heptatotoxicity and pancreatitis.
- Should not be used in patients with known or suspected mitochondrial disease.

Follow up every 3 to 6 months:

- Serum valproic acid level.
- CBC.
- LFTs.
- Repeat pregnancy test if indicated.

Additional warning:

- Hyperammonemia and/or encephalopathy, sometimes FATAL, has been reported following the initiation of valproate therapy and may be present with normal transaminase levels.
- Ammonia levels should be measured in patients who develop unexplained lethargy, vomiting, or changes in mental status, and in patients who present with hypothermia.
- Discontinue therapy if ammonia levels are increased and evaluate for a possible urea cycle disorder.
- Hyperammonemia and/or encephalopathy may also occur with concomitant topiramate therapy in patients who previously tolerated monotherapy with either medication.

"Off-Label" Mood-Stabilizing Medications

Carbamazepine (Tegretol)

- Various formulations of carbamazepine are FDA-approved for use in children and adults with certain seizure disorders and for treatment of certain neuralgic disorders and acute manic and mixed episodes in ADULTS.
- Carbamazepine is not FDA-approved for treatment of any psychiatric illness in children.

Prior to starting treatment:

- Provide information when obtaining informed consent regarding the "BLACK BOX" warning for potentially fatal skin reactions and aplastic anemia/agranulocytosis.
- LFTs.
- CBC with differential and platelets.
- BUN/creatinine.
- Electrolytes.
- Thyroid function tests.[9]
- Pregnancy test.
- Teratogenic risks and pregnancy prevention strategies must be discussed and documented if prescribing to a female patient of childbearing age
- HLA-B*1502 allele testing in Asian patients *(oxcarbazepine, carbamazepine, and phenytoin should be avoided in patients carrying the HLA-B*1502 allele unless the estimated benefits clearly outweigh the risks.)*[8]

Follow up:

- Monitor for symptoms (recurrent infections, bleeding, anemia) that may suggest aplastic anemia.
- CBC after 1 month:
    - If the white blood count (WBC) is significantly decreased, it is repeated every 3 to 4 weeks until the counts stabilize.
    - **If ANC falls below 1000/mcL, carbamazepine should be stopped.**[9]
- Carbamazepine level after 3 weeks, 6 weeks and 9 weeks (because of auto-induction), then every 2 months until stable, then every 6 months.[9]

"Off-Label" Mood-Stabilizing Medications

Oxcarbazepine (Trileptal)

- Oxcarbazepine is FDA-approved for treatment of certain seizure disorders in children and adults, but it is not FDA-approved for treatment of any psychiatric illness in children or adults.
- No specific additional monitoring required.
- Hyponatremia has been reported with the use of oxcarbazepine, but this is very rare in children.[11]

Lamotrigine (Lamictal)[20]

- Lamotrigine is FDA-approved for use in children and adults with certain seizure disorders and for maintenance treatment of bipolar I disorder in ADULTS.
- Lamotrigine is not FDA-approved for treatment of any psychiatric illness in children.

Prior to starting treatment:

- Provide information when obtaining informed consent regarding the "BLACK BOX" warning for potentially fatal skin reactions.
- Rash is more likely in children than adults.
- Medication must be **IMMEDIATELY DISCONTINUED** if rash occurs. However, discontinuation may not prevent a rash from becoming life-threatening or permanently disfiguring/disabling.
- Must advise regarding extreme importance of taking medication exactly as prescribed, and warn of the high risks, including DEATH, associated with restarting medication after even a brief period of non-adherence.

Topiramate (Topamax)

- Various formulations of topiramate are FDA-approved for use in children and adults with certain seizure disorders and for prophylaxis of migraines.
- Topiramate is not FDA-approved for treatment of any psychiatric illness in children or adults.

Prior to starting treatment:

- Serum bicarbonate.

Follow up every 3 to 6 months:

- Serum bicarbonate.
- Dose reduction or drug discontinuation should be considered in patients with persistent or severe metabolic acidosis.[11]
- Hyperammonemia and/or encephalopathy may also occur with concomitant valproic acid therapy in patients who previously tolerated monotherapy with either medication.

Atypical Antipsychotics

Aripiprazole (Abilify)*
Asenapine (Saphris)*
Iloperidone (Fanapt)
Lurasidone (Latuda)*
Olanzapine (Zyprexa, Zydis)*
Paliperidone (Invega)*
Quetiapine (Seroquel)*
Risperidone (Risperdal, Consta)*
Ziprasidone (Geodon)[21]

*****See Appendix for additional information regarding FDA approval.

Prior to starting medication:

- AIMS evaluation.
- Fasting serum glucose and fasting lipid panel.
- CBC.
- LFTs.
- Prolactin level.
- EKG for ziprasidone or iloperidone.

Follow up:

- AIMS evaluation every 3 months.
- Repeat labs in 3 months, then every 6 months.
- Annual EKG for ziprasidone.
- Ask about changes in sexual function and abnormal lactation at each visit for 12 weeks and annually thereafter.
    - Prolactin elevation can occur with any antipsychotic medication, but is most likely with typical antipsychotics, risperidone and paliperidone.[25]
    - A serum prolactin level is indicated if the patient develops signs of sexual dysfunction, galactorrhea, or (in boys) breast enlargement.[4]
    - In most cases, elevated prolactin can be managed by switching to an antipsychotic with a lower likelihood of causing prolactin elevation.
    - As examples, quetiapine and aripiprazole have a low likelihood of increasing prolactin levels, and aripiprazole may lower prolactin levels.[22]
    - If prolactin level is significantly elevated or if there is any clinical abnormality, discontinue the offending agent and replace with an alternative medication. If switching medication would be unsafe, consult with ACS.
    - If prolactin level is only mildly elevated and there is no clinical abnormality, the same medication can be continued as long as prolactin level is checked at least

once per month. If the level remains high for greater than 3 months, discontinue the offending agent and replace with an alternative medication. If switching medication would be unsafe, consult with ACS.

- Weight should be monitored in accordance with general guidelines. If patient develops BMI > 30 or gains 10% of baseline weight, should consider discontinuing or changing medication, otherwise consult with ACS.
- Reports of leukocytosis and neutropenia occur in up to 4% of patients receiving risperidone, 2% of those on paliperidone or quetiapine, and ≤ 1% of patients taking other (non-clozapine) atypical antipsychotics.[24] If a patient has previously experienced a drug-induced leukocytopenia or has a pre-existing low WBC count or low ANC, monitoring is recommended as follows:
    - ANC at baseline.
    - Repeat ANC after 1 to 2 weeks.
    - Repeat ANC again after 3 to 6 months.

Additional Notes:

- Due to its greater capacity to prolong the QT interval, ziprasidone is generally not considered to be a first-line agent. In June 2009, an FDA advisory panel advised that ziprasidone is effective in patients 10-17 years of age for the treatment of mixed and manic episodes of bipolar disorder, but did not conclude that it was safe due to large number of subjects lost to follow-up and ambiguity within QT_c prolongation data.
- In cases where an antipsychotic medication is indicated but weight (gain) is an issue, lurasidone should be considered as it is relatively weight-neutral.

Typical Antipsychotics

Chlorpromazine (Thorazine)*
Fluphenazine (Prolixin)
Haloperidol (Haldol)*
Loxapine (Loxitane)
Perphenazine (Trilafon)*
Pimozide (Orap)*
Thioridazine (Mellaril)
Thiothixene (Navane)*
Trifluoperazine (Stelazine)*

*****See Appendix for additional information regarding FDA approval.

Prior to starting medication:

- AIMS evaluation.
- Fasting serum glucose and fasting lipid panel.
- CBC.
- LFTs.
- Prolactin level.

ADDITIONALLY

When compared with other typical antipsychotics, higher rates of QT prolongation and cardiac arrhythmia are seen with:

- Intravenous haloperidol.
- Oral thioridazine.
- Oral pimozide.

Patients should have an EKG and serum potassium level prior to the first dose of these agents.[3]

Follow up:

- AIMS evaluation every 3 months.
- Repeat labs every 6 months.
- Ask about changes in sexual function and abnormal lactation at each visit for 12 weeks and annually thereafter.
    - Prolactin elevation is most likely with typical antipsychotics, risperidone and paliperidone.[25]
    - A serum prolactin level is indicated if the patient develops signs of sexual dysfunction or galactorrhea.[4]

- In most cases, elevated prolactin can be managed by switching to an antipsychotic with a lower likelihood of causing prolactin elevation.
- As examples, quetiapine and aripiprazole have a low likelihood of increasing prolactin levels, and aripiprazole can lower prolactin levels.[22]
- If prolactin level is significantly elevated or if there is any clinical abnormality, discontinue the offending agent and replace with an alternative medication. If switching medication would be unsafe, consult with ACS.
- If prolactin level is only mildly elevated and there is no clinical abnormality, the same medication can be continued as long as prolactin level is checked at least once per month. If the level remains high for greater than 3 months, discontinue the offending agent and replace with an alternative medication. If switching medication would be unsafe, consult with ACS.

Clozapine (Clozaril)[23]

- Clozapine is not FDA-approved for use in children.
- The prescriber must register with the FDA's Clozapine Risk Evaluation and Mitigation Strategy (REMS) program at **http://www.clozapinerems.com**.
- *Patients must also be enrolled in the program and comply with ANC testing and monitoring requirements in order to receive clozapine[5].*
- Provide information when obtaining informed consent regarding the various "BLACK BOX" warnings that have been issued by the FDA with respect to clozapine:
    - Severe neutropenia, defined as an absolute neutrophil count (ANC) less than 500/mcL. Severe neutropenia can lead to serious infection and death.
    - Orthostatic hypotension, bradycardia, syncope, and cardiac arrest.
    - Fatalities due to myocarditis and cardiomyopathy have been reported.
    - Seizures have been associated with clozapine use in a dose-dependent manner.

NOTE: If dosing is interrupted for ≥48 hours, therapy must be reinitiated at 12.5 mg once or twice daily to minimize the risk of hypotension, bradycardia, and syncope[5].

Prior to starting medication:

- AIMS evaluation.
- Fasting serum glucose and fasting lipid panel.
- CBC.
- LFTs.
- Thyroid function tests.
- EKG.

Follow up:

- CBC (according to REMS guidelines).

After 3 months then every 6 months:

- Fasting serum glucose and fasting lipid panel.
- LFTs.

Every 6 months:

- AIMS evaluation.
- Thyroid function tests.
- EKG.

NOTE: If neutropenia develops during treatment:

- Mild neutropenia (ANC: 1000 to 1499/microL): Continue treatment but increase monitoring frequency to three times per week.

- Moderate neutropenia (ANC: 500 to 999/microL): Interrupt clozapine treatment, increase monitoring to daily until ANC is 1000/microL at which point clozapine can be reinstituted.
- Severe neutropenia/agranulocytosis (ANC: <500/microL): Discontinue clozapine. Rechallenge should only occur if the benefits outweigh the risks, in consultation with hematology.

Other Medications

Beta-blockers

Propranolol (Inderal)
Nadolol (Corgard)
Atenolol (Tenormin)
Metoprolol (Lopressor, Toprol XL)

Use only in consultation with primary care provider in patients with asthma or diabetes.

Prior to starting medication and at follow up:

- Advise regarding risk of rebound hypertension if abruptly discontinued.
- EKG if clinically indicated.

Benzodiazepines

Lorazepam (Ativan)*
Clonazepam (Klonopin)
Diazepam (Valium)
Oxazepam (Serax)
Alprazolam (Xanax)
Chlordiazepoxide (Librium)

Should generally be avoided because of paradoxical effect in younger children and risk of dependence. *Lorazepam is FDA-approved for treatment of anxiety in children ≥ 12 years old.

"Z" drugs

Zolpidem (Ambien)
Zaleplon (Sonata)
Eszopiclone (Lunesta)

Should generally be avoided. CBT for insomnia should be utilized instead.

Medications to counteract extrapyramidal side effects

Benztropine (Cogentin)
Amantadine (Symmetrel)
Trihexyphenidyl (Artane)

Use these medications only if needed.

Opioid Antagonist

Naltrexone (Revia)

Prior to starting medication:

- Liver Function Test (LFTs)

APPENDIX

Medications with FDA Approval for Psychiatric Use in Children

Listed Alphabetically by Generic Name[12]

Generic Name	Trade Name	Indication	Age
Amphetamine salts	Adderall	ADHD	≥ 3
		Narcolepsy	≥ 6
Amphetamine salts	Adderall XR	ADHD	≥ 6
Aripiprazole	Abilify	Schizophrenia	≥ 13
		Acute mania or mixed episodes	≥ 10
		Autism-associated Irritability	6 - 17
		Tourette's disorder	6 - 18
Asenapine	Saphris	Mania or mixed episodes	≥ 10
Atomoxetine	Strattera	ADHD	≥ 6
Chlorpromazine	Thorazine	Severe behavioral problems and short-term treatment of hyperactivity	1 - 12
Clomipramine	Anafranil	Obsessive-Compulsive Disorder	≥ 10
Clonidine (Extended Release)	Kapvay	ADHD	6 - 17
Dextroamphetamine	ProCentra	ADHD	3 - 16
		Narcolepsy	≥ 6
Dextroamphetamine	Dexedrine Spansule	ADHD	6 - 16
		Narcolepsy	≥ 6
Escitalopram	Lexapro	Major Depressive Disorder	≥ 12
Fluoxetine	Prozac	Major Depressive Disorder	≥ 8
		Obsessive-Compulsive Disorder	≥ 7
Fluvoxamine	Luvox	Obsessive-Compulsive Disorder	≥ 8
Guanfacine (Extended Release)	Intuniv	ADHD	6 - 17
Haloperidol	Haldol	Psychotic disorders	≥ 3
		Tourette's disorder	≥ 3

		Severe behavioral problems and short-term treatment of hyperactivity	3 - 12
Imipramine	Tofranil	Childhood enuresis	≥ 6
Lisdexamfetamine	Vyvanse	ADHD	≥ 6
Lithium	Lithobid Lithotabs	Acute mania and bipolar maintenance	≥ 12
Lorazepam	Ativan	Anxiety	≥ 12
		Insomnia	≥ 12
Lurasidone	Latuda	Schizophrenia	≥ 13
Methylphenidate	Concerta	ADHD	≥ 6
Methylphenidate	Ritalin LA Qullivant XR	ADHD	6 - 12
Methylphenidate	Metadate CD	ADHD	6 - 15
Methylphenidate	Metadate ER Methylin Ritalin Ritalin SR	ADHD	≥ 6
		Narcolepsy	≥ 6
Methylphenidate	Daytrana	ADHD	≥ 6
Olanzapine	Zyprexa	Schizophrenia	≥ 13
		Acute and maintenance treatment of mania or mixed episodes	≥ 13
Paliperidone	Invega	Schizophrenia	≥ 12
Perphenazine	Trilafon	Schizophrenia	≥ 12
Pimozide	Orap	Severe/Non-responsive Tourette's disorder	≥ 2
Quetiapine	Seroquel	Schizophrenia	≥ 13
		Acute mania	≥ 10
Risperidone	Risperdal	Schizophrenia	≥ 13
		Acute mania or mixed episodes	≥ 10
		Autism-associated Irritability	5 - 16
Sertraline	Zoloft	Obsessive-Compulsive Disorder	≥ 6
Thiothixene	Navane	Schizophrenia	≥ 12
Trifluoperazine	Stelazine	Schizophrenia	≥ 6

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