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Florida Best Practice Guidelines for Children and Adolescents

Expert Panel Meeting

**Conducted June 9 -11, 2006
Tampa, Florida**

Disclaimer

The Florida Best Practices Medication Guidelines for the use of psychotropic medication in children and adolescents reflect the state of knowledge, current at the time of publication, on effective and appropriate care, as well as clinical consensus judgments when research is lacking. The inevitable changes in the state of scientific information and technology mandate that periodic review, updating, and revisions will be needed. These guidelines do not apply to all patients and each must be adapted and tailored to each individual patient. Proper use, adaptation, modifications, or decisions to disregard these or other guidelines, in whole or in part, are entirely the responsibility of the clinician who uses the guidelines. The authors bear no responsibility for the use of these guidelines by third parties.

Table of Contents

Click on the links below to read that section.

1

Meeting Deliberations	3
The Expert Panel Process	3
Summary of Guideline Development Process	3
Principles of Practice	3
Principles of Practice for the Use of Psychotropic Agents in Children Under the Age of Six	4
Level Framework for Best Practice Guidelines	4
Dosing Recommendations (Off-label) and Principles of Practice Statements	4
Florida Best Practice Guidelines for ADHD in Children and Adolescents	5
Florida Best Practice Guidelines for Depression in Children Under Age Six	6
Florida Best Practice Guidelines for Depression in Children From Age Six to Adolescence	6
Florida Best Practice Guidelines for Depression in Adolescence	7
Florida Best Practice Guidelines for Bipolar Disorder in Children and Adolescents	8
Florida Best Practice Guidelines for Severe Tic Disorders and Tourette’s Syndrome	9
Best Practice Guidelines for Chronic Impulsive Aggression in Children and Adolescents	10
Principles of Practice for the Use of Antipsychotics in Children and Adolescents	11
Table 1: Anticonvulsants & Mood Stabilizers - SAFETY	12
Table 2: Antidepressant - SAFETY	13
Table 3: Antidepressant - SAFETY (SSRI)	14
Table 4: Antidepressant - SAFETY (Tricyclics)	15
Table 5: Antidepressant - SAFETY (Heterocyclic)	16
Table 6: Antidepressant - SAFETY (MAOI)	16
Table 7: Safety and Tolerability of TCAs versus SSRIs	17
Table 8: Adverse Events for Each SSRI that Occured 1% More Often than with Other SSRIs	17
Table 9: Atypical Antipsychotics Class - SAFETY	18
Table 10: Typical Antipsychotics Class - SAFETY	19
Table 11: Stimulant & Non-stimulant - SAFETY	20
The Expert Panel	21
Expert Panel Disclosure Information	25
Bibliography	27

Meeting Deliberations

From June 9-11, 2006, a group of child psychiatrists, adult psychiatrists and pharmacists met in Tampa, Florida to discuss and debate the use of psychotropic medications for children and adolescents and to formulate the Florida Best Practice Medication Guidelines in the context of an overall program for the Agency for Healthcare Administration.

The Expert Panel Process

On June 9, 2006, the experts were presented information from Rajiv Tandon, MD, the chief psychiatrist for the Department of Children and Families; Robert Constantine, PhD, the primary investigator for the project; John March, MD, an outside consultant and expert in child and adolescent psychiatry from Duke University; and Wayne Goodman, MD, the current chair of the FDA advisory panel on psychotropic medication and current chairman for the department of psychiatry at the University of Florida. The experts were provided information regarding current prescribing patterns with respect to multiple classes of medications, including stimulants, antipsychotics, mood stabilizers, and antidepressants across different age groups in the state of Florida. They were also provided the legislative and policy context and the purpose for the expert panel. In addition, they were provided information on current guidelines in the field and an overview of the mission and principles of evidence-based medicine. For instance, Sackett's definition of evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of the individual and a guideline systematically developed to assist practitioner and patient in making decisions about appropriate healthcare for specific clinical circumstances. In addition to presentations, the panel was provided a number of documents. One document was an evidence-based table derived from the drug monographs that are published by Gold Standard, Inc. The evidence-based tables provided information on stimulants, mood stabilizers, antipsychotic drugs, and antidepressants then categorized the information about these agents into Level A Evidence – randomized control trial data that supported their use, Level B Evidence – either one randomized controlled trial or open-label study or a small control study, and Level C Evidence – evidence which comprised systemic reviews, guideline statements, or small, uncontrolled trials and case studies. In addition to that, the expert panel was provided summaries of articles submitted to the Center for Mental Health Care Improvement by the Department of Children and Families. The expert panel members were provided draft reviews of the new guidelines and practice parameters produced by the American Academy of Child and Adolescent Psychiatry across multiple conditions. Furthermore, the expert panel was provided the Fall 2004 Edition of *The Journal of Lifelong Learning in Psychiatry*, which covers the TRAAAY recommendations and a comprehensive review of other issues in child and adolescent psychiatry. Supplemental articles reviewing the use of antipsychotics in youth was also provided. Finally, an overview of the Texas Children's Medication Algorithm Program Algorithms for Attention Deficient Disorder and Hyperactivity were provided.

Summary of Guideline Development Process

These experts were facilitated through an interactive presentation of the above mentioned scientific information and existing guidelines and debated the best possible options for the use of psychotropic medications in the treatment of children. In the context of experts presenting information and guideline recommendations, expert panel members were able to review particular articles if necessary, using immediate online access to PubMed and online access to monographs, while concurrently looking at evidence-based tables and articles and reviews by the American Academy of Child and Adolescent Psychiatry. The evidence-based discussions included studies in the Level A Evidence – randomized control trials, Level B Evidence – small randomized control trials and open-label studies, and Level C Evidence – retrospective studies and expert consensus data. Patient safety issues and drug monitoring were also discussed.

Principles of Practice

The expert panel agreed on a series of principles of practice statements that are consistent with other guidelines produced by national bodies in the field of child and adolescent psychiatry.

1. The use of medications should be part of a comprehensive plan that includes non-biological intervention and addresses the developmental, psychological, social, and medical needs of the patient.
2. Monotherapy should be initiated before complex therapy based on the clinical condition.
3. There should be an attempt to minimize multiple medications in the same class.
4. Monitoring of target symptoms can be supported by the use of rating scales.
5. Adverse event and adherence monitoring are important aspects of addressing safety and effectiveness issues in clinical practice.

Principles of Practice for the Use of Psychotropic Agents in Children Under the Age of Six

1. Given current scientific information and clinical experience, the expert panel agreed not to provide any recommendations for the use of antidepressants in children under the age of six.
2. Given current science and clinical experience, the use of antipsychotics in children under the age of six is generally not recommended and should only be considered under the most extraordinary circumstances. Disruptive aggression in Autism is one such circumstance.
3. Given current science and clinical experience, the use of stimulant medications for children under age four should be rare and only after a failed behavioral intervention such as parent training.

Level Framework for Best Practice Guidelines

The panel decided to use the existing format of the Adult Florida Best Practice Guidelines, where the panel opinions are categorized in different levels rather than create an algorithm where specific options were mandatory, had to be used in a specific order, or diagrammatically appeared that they had to be used in a specific order. These levels were based upon strength of science and expert consensus regarding a particular agent or treatment option. The panel weighed both safety and efficacy issues when assigning a particular treatment options to a level. Level 1 options were considered to have stronger evidence and consensus than level 2 and below. The panel chose this approach with an understanding that using a particular option in any level would depend upon clinical judgment and patient or family needs or preferences. Level 0 refers to an assessment level prior to any decisions regarding treatment options.

Dosing Recommendations (Off-label) and Principles of Practice Statements

The dosing guidelines are based on expert opinion and therefore are Level C Evidence. Multiple large sample, adequately powered studies have not been conducted in children and adolescents for a number of psychiatric disorders. Therefore the use of these medications is largely off-label.

The Dosing Guidelines for the use of Psychotropic Medications in ADHD developed by the American Academy for Child and Adolescent Psychiatry will be available in October 2006.

Unlike other medications, stimulant dosages are not weight-dependent. Clinicians should begin with a low dose of medication and titrate upward because of marked individual variability in the dose response relationship. With respect to the use of antipsychotics and antidepressants, target dose ranges are primarily based on Level B and Level C Evidence.

Antipsychotics:

Haloperidol: 0.25 – 10 mg/day
Fluphenazine: 0.5 – 10 mg/day
Perphenazine: 2 – 40 mg/day
Risperidone: 0.25 – 6 mg/day
Olanzapine: 1.25 – 20 mg/day
Quetiapine: 25 – 800 mg/day
Ziprasidone: 20 – 160 mg/day
Aripiprazole: 2 – 30 mg/day

Antidepressants:

Fluoxetine: 5 – 40 mg/day
Sertraline: 25 – 200 mg/day
Citalopram: 10 – 40 mg/day
Escitalopram: 5 – 30 mg/day
Venlafaxine: 37.5 – 300 mg/day
Paroxetine: 10 – 40 mg/day
Bupropion: 50 – 300 mg/day

Florida Best Practice Guidelines for ADHD in Children and Adolescents

The panel discussed the use of stimulants and other agents for the treatment of ADHD.

Level 0: Appropriate assessment and non-medication interventions as a critical part of care. This approach is consistent with the recommendations of the American Academy of Child and Adolescent Psychiatry and the Texas Children's Medication Algorithm Program.

With regards to pharmacotherapy options for ADHD, the panel was provided with information regarding the Texas algorithms, the Expert Consensus Guidelines, and the American Academy of Child and Adolescence Psychiatry's work on ADHD. There was general agreement with the options for ADHD without co-occurring anxiety, psychotic, tic, or mood disorders.

Level I: The panel felt that there was substantial evidence to support the use of monotherapy with stimulants using either methylphenidate or amphetamine preparations. The expert panel agreed that the practice of using agents within the same class with different half-lives was appropriate.

Level II: Options included the stimulant class not tried at Level I. If failure occurred with a methylphenidate agent then amphetamine agents could be used. The experts did not recommend combining classes. The panel discussed the use of skin patches and decided not to recommend them as first-line agents due to the fact that hypersensitivity reactions to methylphenidate could occur if switched to oral preparations from a skin patch.

Level III: The expert panel supported the use of Atomoxetine, a non-stimulant that is approved by the FDA for ADHD. There was extensive discussion with regards to the use of Atomoxetine. The panel decided to place this option at a lower level due to a lower effect size than stimulants and safety warnings regarding suicidality. However it could be used as first-line in patients with severe anxiety disorders, or in cases where stimulants were unacceptable due to possible side effects, and patient or family preference. The panel agreed that there might be situations where adjunctive use of Atomoxetine in a patient with partial response to stimulants would be appropriate.

Level IV and V: Options included Bupropion or tricyclics with the exception of desipramine, which is shown to have some significant cardiac issues related to its use in children. Imipramine, Bupropion, and Nortryptiline have been evaluated in small sample size studies in children with ADHD. Once again, monotherapy should be attempted with these agents.

Level VI: Alpha-2 agonist such as Guanfacine and Clonidine were recommended and have shown some benefit as monotherapy and in combination with stimulants in children with ADHD with co-occurring tic disorders. These data are derived from single studies. The expert panel decided against placing Modafinil in the current guidelines due to safety issues raised by the FDA. A decision is still pending. In addition, the panel decided not to vote on the selegiline patch due to lack of data and clinical experience.

The issue of combination therapy was discussed for co-occurring disorders and the panel decided to place those recommendations regarding treatment options in the guidelines for depression, bipolar disorder, tic disorders, and aggression respectively.

Florida Best Practice Guidelines for Depression in Children Under Age Six

In the area of depression, the panel recommended the following for children under the age of six:

Level 0: An appropriate diagnostic assessment, including a caregiver and family assessment, should be the first step. Second, the development of a psychosocial intervention and treatment strategy of the family and/or caregiver, if necessary, should be considered. This was recommended due to recent published articles that examined the correlation between depressed parents and children and the findings that the mental health of children improved when parents were treated for depression.

Level I: The panel agreed to support the use of emerging best practices in the use of psychosocial therapies from behavior therapy to family behavior therapy and other current practices in psychosocial therapy. The panel was informed that a separate group would be assembled to develop the specifics of the different therapies available for children and adolescents that are non-biological.

The expert panel decided not to support any pharmacological recommendations in the treatment for depression for children under six years of age due to the fact that there is not a large body of science to support this and the potential safety issues involved in the use of antidepressants in children.

Florida Best Practice Guidelines for Depression in Children From Age Six to Adolescence

With regards to children from ages six to adolescence:

Level 0: Diagnostic assessment, caregiver and family assessment, and, if possible, collateral information from the school setting and psychosocial intervention and treatment strategy of family and/or caregiver if necessary.

Level I: The expert panel decided to make psychotherapy (i.e., cognitive behavioral therapy and family therapy) appropriate options for treatment in the Level I category. Other emerging best practices in psychotherapy can also be utilized and these will be fully delineated by a later expert panel.

Level II: SSRI monotherapy for two iterations were recommended.

Level III: Reassessment of the diagnosis in the environment to ensure that non-biological issues are addressed and to determine whether the diagnosis of depression is appropriate.

Level IV: If there has been a failure of two separate trials of SSRI monotherapy, alternative antidepressants can be utilized if there is no contributing comorbidity or occurring disorder.

Level V: Augmentation with lithium or buspirone can be done sequentially. Agents other than those mentioned above can be used but multiple antidepressants should be avoided. The expert panel did discuss options for psychosis, tics, and other conditions in upcoming recommendations.

Florida Best Practice Guidelines for Depression in Adolescence

Level 0: A diagnostic assessment, caregiver and family assessment, and, if possible, collateral information from the school setting and psychosocial intervention and treatment strategy of family and/or caregiver if necessary.

Level I: Only one pharmacotherapy agent, fluoxetine, is recommended as it is the only agent with proven efficacy in a well-controlled, randomized control trial.

Level II: Medications including sertraline and citalopram have some evidence to support their use. The results from small, randomized control trials do not support the use of mirtazapine, paroxetine, or venlafaxine in this population. Other SSRI have some limited evidence from small open studies and randomized control trials. Bupropion may also be considered at this level.

Level III: Re-evaluation and consideration of empirically supported psychotherapy, if not already part of the clinical treatment approach, either in combination or alone as part of the treatment. Although this panel was meant to develop guidelines for the use of medications at this level, the panel thought that it was important to support the use of cognitive behavioral therapy if it had not already been implemented in this age group, as emerging evidence indicates that psychotherapy can be very beneficial in this population.

Level IV: Augmentation with two agents with targeting symptoms, for instance the use of alternative agents, stimulants for comorbid ADHD, atomoxetine or antipsychotics for psychotic features, buspirone, and/or lithium are all considered options but there is no necessity for using two antidepressants at the same time, unless one was attempting a crossover strategy.

Level V: The use of three agents but primary using symptom targeting as the basis for co-occurring psychotic symptoms, anxiety symptoms, and/or ADHD symptoms.

Level VI: The expert panel recommends that the AACAP parameters for ECT should be followed.

Florida Best Practice Guidelines for Bipolar Disorder in Children and Adolescents

The panel took up the discussion of bipolar disorder. There was significant debate regarding the phenomenology, longitudinal course, the difference between bipolar disorder in children, adolescents, and adults, and, after substantial and significant discussion, the expert panel decided to make recommendations for the use of medications in the treatment of bipolar disorder in children using only the narrow phenotype.

Level 0: Careful assessment to ensure that ADHD, oppositional defiant disorder, and conduct disorder are ruled out without classical bipolar. The panel chose the narrow phenotype of classical bipolar, meaning grandiosity, elevated mood, decreased need for sleep, rapid cycling, flight of ideas, and hypersexuality and agreed to use the framework of frequency, intensity, number, and duration similar to the existing published guidelines on bipolar disorder to monitor symptoms. Monitoring the frequency of symptoms, the severity of symptoms, the quantity of symptoms, and the duration of symptoms in different domains would have to be considered prior to selecting an agent and prior to determining that a child had a disorder consistent with mania.

An emphasis was made during this discussion that, as part of treatment, mood monitoring and the concept of measurement-based care would be critical in this population.

Level I: Monotherapy could be attempted with either a mood stabilizer, like lithium, valproic, carbamazepine, olanzapine, quetiapine, risperidone, aripiprazole, or ziprasidone. The panel also agreed that, similar to the adult best practice guidelines, two antipsychotics should not be used or could not be supported in the treatment of bipolar symptoms in this age group.

Level II: Monotherapy, up to two iterations of any of these agents listed above.

Level III: Combination treatment. Two mood stabilizers could be used or a mood stabilizer and an atypical antipsychotic, but not two atypical antipsychotics.

Level IV: Up to three agents, including agents like lamotrigine, a typical antipsychotic, or oxcarbazepine could be introduced as a third agent if previous treatments have failed.

Level V: Clozapine and ECT were selected for the most complex and refractory cases. Clinicians should refer to the AACAP guidelines for ECT as noted above.

The panel agreed that data for the treatment for bipolar disorder in children are scant. The panel used the existing data on bipolar guidelines to inform their discussion. Finally, psychotherapy approaches such as behavioral family therapy and social rhythm therapy warrant consideration in addition to medication options.

Florida Best Practice Guidelines for Severe Tic Disorders and Tourette's Syndrome

Severe and chronic tic disorders, in particular Tourette's Syndrome, was the focus of this expert panel.

Level 0: In addition to previous Level 0s about careful assessment, it is important to note symptom duration greater than six weeks. Issues of social, educational, or physical impairment as well as contributing comorbidities need to be evaluated.

Level I: Habit reversal therapy was recommended with the greatest amount of expert opinion support and safety. If severe symptoms and severe impairment were part of the picture, however, the expert panel thought that providers could use Level II options.

Level II: Haloperidol, risperidone, and also aripiprazole, once emerging data is available on this agent, however, many experts felt that these two agents, risperidone and aripiprazole, would be appropriate options in patients with severe tic disorders.

Level III: Options including quetiapine, olanzapine, ziprasidone, and also pimozide were included, however, the expert panel noted that safety issues related to pimozide should be considered prior to use.

Level IV: Antipsychotics could be used in combination with SSRIs, clonazepam, alpha-2 agonist, and anticonvulsants, primarily based on targeting symptoms.

The experts agreed that severity of the illness should drive the use of one or two agents in this condition and that habit-reversal therapy should be a mainstay in severe tic disorders. Furthermore, caregivers and patients should be aware of the expected outcomes, and that their participation in tracking and monitoring and being a part of measurement-based care would be critical in the optimal resolution or treatment of these conditions and symptoms.

Best Practice Guidelines for Chronic Impulsive Aggression in Children and Adolescents

The expert panel did also take up the issue of aggression and treatment of aggression based on earlier work by Jensen and colleagues to create the treatment of aggressive youth. The expert panel did agree to support four of the initial TRAAAY recommendations:

1. For all new cases, clinicians should conduct or review the results of comprehensive, psychiatric, diagnostic interviews with the patients and parents or guardians before prescribing, changing, or discontinuing medication.
2. Standardized symptom and behavior rating scales with proven reliability and validity should be used to measure the severity and frequency of target symptoms before treatments are initiated at regular intervals throughout treatment during acute episodes, and when treatments are changed or discontinued.
3. Structured psychosocial and educational intervention should be the first-line of treatment and should be continued, even if subsequent medications are initiated to manage aggression.
4. Symptoms of aggression are common in a wide range of psychiatric conditions. Aggressive patients who also present with persistent and clinically significant symptoms of hyperactivity, anxiety, depression, or mania should receive at least one adequate trial of a first-line agent for these primary disorders.

The expert panel agreed that there are different types of aggression that have been described in literature and have been discussed in expert panel meetings. The panel noted that aggression is a complex phenomenon and that the chronicity of the aggression needs to be taken into account. There are also many subtypes of aggression, including affective and impulsive subtypes, and also instrumental and predatory aggression. There are many individuals who may have both. The group most apt to benefit from treatment with medications will most likely have affective impulsive aggression, whereas predatory aggression is much more difficult to treat. The expert panel recommended that it is important for clinicians to differentiate affective impulsive aggression from instrumental and/or predatory aggression as part of their diagnostic assessment or evaluation, and then, from that point, select interventions based on the type of aggressive syndrome.

Level I: The panel thought an atypical antipsychotic could be used with multiple iterations of monotherapy consistent with the recommendations in the TRAAAY guidelines.

Level II: Lithium, valproic, carbamazepine, and typical antipsychotics could be used as an adjunctive medication, however the panel noted that mood stabilizers have not been shown to be successful in pervasive developmental disorders and, therefore, clinicians should be aware of these data.

Level III: Mood stabilizer combination could be attempted with antipsychotics if not attempted in the past

Principles of Practice for the Use of Antipsychotics in Children and Adolescents

The panel also made a general statement about the use of antipsychotics in children. The panel agreed that the use of antipsychotics should be restricted to, as mentioned before, the diagnosis of schizophrenia, which is extremely rare in children, psychotic depression and bipolar disorder, psychotic disorders not otherwise specified, drug-induced psychosis, Tourette's and tic disorders, and, to some extent, bipolar disorder, aggression as a target symptom, and on rare occasions in OCD and only after treatment resistance or failure of two SSRI trials and extensive CBT. There may be instances as well where antipsychotics are used for parasuicidal behaviors and severe self-injurious behaviors. The panel agreed that antipsychotics should not be used primarily to target attention deficit and hyperactivity symptoms, should not be used to promote weight gain, and should not be used as sedatives for children. Adjustments could be made in existing therapies in these disorders, for example, in ADHD to not use agents in the evenings that would stimulate patients to use alternative behavioral means to help patients gain weight or to eat.

Table 1: Anticonvulsants & Mood Stabilizers - SAFETY

	Special Considerations, P450, & Drug Interactions	Contraindications and High Risk Patients	Monitoring	ADRs - most frequent, higher incidence, and/or significant effect
Carbamazepine Oral dosage (regular-release tablets)	Numerous Drug-interxns (see ref.) Metabolized by CYP3A4 & Induces CYP1A2 and CYP3A4. Carbamazepine induces its own metabolism. Several weeks of therapy may be required before the maintenance dose and therapeutic serum concentrations are achieved. Carbamazepine induces hepatic microsomal enzymes, which, in turn, accelerates carbamazepine metabolism or the metabolism of other drugs. Interactions between carbamazepine and other anticonvulsants are complex. Anticonvulsants that can be potentially affected by carbamazepine enzyme induction include barbiturates, clonazepam, ethosuximide, lamotrigine , phensuximide, phenytoin , or fosphenytoin (and possibly ethotoin), tiagabine, topiramate, valproic acid, and zonisamide. Others: contraceptives, warfarin.	“Contraindicated in : Agranulocytosis, AV block, Bone marrow suppression, Bundle-branch block MAOI therapy, TCA hypersensitivity. Caution in patients with preexisting hypercholesterolemia. Clinically significant hyponatremia (serum sodium <125 mmol/L) may develop during treatment with carbamazepine. Caution in any patient with cardiac disease & hepatic disease. Concomitant use of nefazodone & carbamazepine to be contraindicated.”	“• CBC • LFTs • serum carbamazepine concentrations • urinalysis Therapeutic serum concentrations usually range 4—12 mcg/ml. Monitoring of sodium levels should be considered. Pretreatment & periodic baseline hematologic counts should be obtained. “	“Anticholinergic, central antidiuretic (syndrome of inappropriate antidiuretic hormone, SIADH), cardiac effects, antiarrhythmic, muscle relaxant, antidepressant (possibly through blockade of norepinephrine release), sedative, and neuromuscular-blocking properties. “
Lamotrigine	Hepatic glucuronidation. Concurrent administration of hepatic enzyme inducing antiepileptic drugs (EIADs) with lamotrigine results in changes in lamotrigine half-life in both adult and pediatric patient populations. Valproic acid more than doubles the elimination half-life and steady-state concentration of lamotrigine in both pediatric and adult patients.	Black Box Warning: Stevens-Johnson syndrome. Initiate at a low-dose, with gradual increase to minimize occurrence of skin rash. Do not abruptly d/c due to withdrawal seizures. Caution in hepatic & renal disease	Rash & CBC	ADRs difficult to assess due to trials conducted in patients receiving other anticonvulsants concomitantly. Most frequent ADRs assoc. with lamotrigine in combination with other AED: dizziness, diplopia, ataxia, drowsiness, headache, blurred vision, nausea/vomiting, and asthenia. Dose-related side effects include dizziness, diplopia, ataxia, blurred vision, and nausea/vomiting. Other: tremor, depression, anxiety and insomnia.
	*NOTE - Lamotrigine - Due to life-threatening rashes (including Stevens-Johnson syndrome and toxic epidermal necrolysis), lamotrigine carries a Black-Box warning stating the drug should be discontinued if a rash appears at any time during treatment. Factors to predict a serious rash are not available; however, children appear to be at greater risk. Post-marketing surveillance and controlled clinical studies have revealed that as many as 8 in 1000 pediatric patients develop a potentially life-threatening rash compared with 3 in 1000 adults.			
Lithium	“Eliminated renally. Lithium competes at cellular sites with sodium, potassium, calcium, and magnesium ions. Lithium administration increases renal sodium and potassium clearance. Caution w/ : ACE inhibitors (ACEIs) or angiotensin II receptor antagonists, Alkalinizing agent,Caffeine, Carbamazepine, calcium-channel blockers, TCAs, SSRIs, Diuretics. “	“Contraindicated in hepatic disease,renal disease, brain trauma, & severe cardiac disease. Caution in dehydration, diarrhea,hyponatremia, hypothyroidism & infection. “	“• CBC • serum electrolytes • serum lithium concentrations • thyroid function tests (TFTs) Data confirm that serum concentrations of 0.8—1.0 mEq/L are more effective in preventing relapse in bipolar disorder. Patients more sensitive to lithium may exhibit toxic signs at serum levels of 1—1.5 mEq/L.”	“Sodium restriction, renal impairment, dehydration, vomiting/diarrhea, or other factors that may alter sodium levels or renal function may cause lithium toxicity. Many adverse reactions are dose- and concentration-related. fine hand tremor, xerostomia, dysgeusia, weight gain, polydipsia, polyuria, mild nausea/vomiting, impotence, libido decrease, nephrotic syndrome, and diarrhea. “
Oxcarbazepine	Oxcarbazepine undergoes rapid reduction in the liver to MHD. Oxcarbazepine and MHD produce a dose-related inhibition of CYP2C19 and induction of CYP3A4/5. Renally excreted. Coadministration with meds metabolized through the hepatic CYP2C19 isoenzyme may produce significant drug interxns. Oxcarbazepine and its active metabolite, MHD, are dose-dependent inducers of the hepatic CYP3A4/5 isoenzymes thereby having the potential to lower the plasma levels of medications metabolized through these pathways.	“Caution with :abrupt discontinuation, children ,ethanol intoxication, females, hyponatremia, & renal impairment “	Monitoring of sodium levels should be considered if oxcarbazepine is used with other medications known to decrease sodium levels, in those with baseline hyponatremia, or if symptoms possibly indicating hyponatremia develop. Otherwise - laboratory monitoring not necessary	Cognitive effects more frequent in pediatric pts - headache, sedation, dizziness, ataxia, & impaired concentration. Other: gastrointestinal complaints (common) & allergic skin reactions such as rash (uncommon). Serious dermatological reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in both children and adults in association with oxcarbazepine use
Valproic Acid (Divalproex)	Valproic acid is metabolized by the hepatic CYP450 microsomal enzymes CYP2C19 and CYP2C9, and also is metabolized by UGT (UDP-glucurono syltransferase). Valproic acid inhibits the activity of CYP2C9 and UGT. Co-administration of high doses with drugs metabolized by CYP2C9 may result in significant drug interxns.	“Contraindicated in Encephalopathy, Hepatic disease, Hepatitis, Pancreatitis & Urea cycle disorders. “	“• CBC • LFTs • serum ammonia • serum valproic acid concentrations Therapeutic valproic acid serum concentrations are generally considered to be between 50-100 mcg/ml. Platelet counts and coagulation tests recc. before tx. and at periodic intervals.	Thrombocytopenia,unusual bleeding, bruising, abnormal coagulation parameters, nausea/vomiting, indigestion, abdominal pain, constipation or diarrhea. Both anorexia with weight loss and appetite stimulation with weight gain have been reported. Dermatologic reactions & Hyperglycemia reported.

Table 2: Antidepressant - SAFETY

SSRI Class Effect - Safety Considerations
Black Box Warning: On October 15, 2004 the FDA directed manufacturers of all antidepressants to include a Black Box warning, expanded warning statements, and clinical trial results detailing the increased risk of suicidality in children and adolescents. A Patient Medication Guide (MedGuide) will also accompany all prescriptions for antidepressants. The FDA is currently assessing the risk of suicidality in adults taking antidepressants and a final report is expected by mid- to late 2006.
Monitoring: Pediatric patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior, particularly within the first few months of starting therapy or at the time of dose increases or decreases.
Exacerbation of Mania Hypomania: May precipitate hypomania or mania in predisposed patients.
Drug Interaction Class Effect: The available data indicate that the SSRIs as a group are remarkably similar in all of these ways with the exception of pharmacokinetically mediated drug-drug interactions. Any drug that increases serotonin concentrations, including: MAOIs, tramadol (Ultram), sibutramine (Meridia), meperidine (Demerol), sumatriptan (Imitrex), lithium, St. John's wort, ginkgo biloba, and atypical antipsychotic agents. Serotonin syndrome: mental status changes, agitation, myoclonus, hyperreflexia, diaphoresis, shivering, tremor, diarrhea, incoordination, and fever. May be life-threatening.
MAOI Caution: All SSRIs as a class produce adverse effects that are the result of interaction with MAOI
Serotonin Syndrome: All SSRIs are capable of causing serotonin syndrome when administered with other drugs that have serotonergic properties such as certain amphetamines, buspirone, cocaine, dextromethorphan, lithium, MAO inhibitors, meperidine, nefazodone, sibutramine, St. John's wort, and tryptophan.
Side Effects Class Effect: Commonly observed side effects of SSRIs including anorexia, headache, nausea, and sexual dysfunction
TCA Class Effect - Safety Considerations
Cardiac Effects: such as orthostatic hypotension, generally occur more frequently with tertiary amines because as a group they possess more potent alpha-blocking properties.
Monitoring: TCAs, baseline electrocardiogram, resting blood pressure and pulse (supine or sitting, standing), and weight should be monitored regularly.
Overdose: The higher incidence of morbidity and mortality in TCA overdose compared to most other antidepressants limits their practicality and should be taken into consideration when choosing the appropriate course of treatment.
MAOI Interxn: Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs.
Contraindicated: In selected cardiac conditions: , QT prolongation. bundle-branch block, cardiac arrhythmias, the recovery phase of myocardial infarctions Also in glaucoma, ileus, increased intraocular pressure, MAOI therapy, tricyclic antidepressant hypersensitivity, urinary retention, seizure disorders, and prostatic hypertrophy.
Anticholinergic Effects: The tertiary-amine tricyclic antidepressants tend to be more sedating and have greater anticholinergic effects than the secondary amines.
Abrupt Discontinuation: Should be avoided because it could precipitate symptoms of cholinergic rebound such as nausea, vomiting, or diarrhea.

Table 3: Antidepressant - SAFETY (SSRI)

	Special Considerations, P450, & Drug Interactions	Contraindications and High Risk Patients	Monitoring	ADRs - most frequent, higher incidence, and/or significant effect
Fluoxetine	Fluoxetine is a potent inhibitor of CYP2D6 interxn w/ meds metabolized through CYP2D6 such as phenothiazines, tricyclic antidepressants and Type IC antiarrhythmics. Fluoxetine and its metabolite, norfluoxetine, inhibit CYP3A4 and may interact with astemizole, carbamazepine, cisapride, cyclosporine, and terfenadine, as well as others that use this pathway. Can increase plasma levels of macrolides, atomoxetine, amphetamine, bupropion, phenytoin, antipsychotics, zolpidem, and eszopiclone. Fluoxetine & Warfarin - possible increase in risk of bleeding. TCAs, carbamazepine, phenytoin - Increase in levels, with possible toxicity.	May precipitate hypomania or mania. Concurrent MAOI tx. Long half-life - caution w/ renal or hepatic impairment. Caution in Diabetics - hypoglycemia. SIADH (See SSRI class effect)	"• LFTs: baseline • thyroid function tests (TFTs): baseline "	"Weight loss, Insomnia, fast or irregular heart rate, palpitations, anxiety, agitation, panic attacks, inability to sleep, irritability, hostility or extreme anger, aggressiveness, restlessness or inability to sit still, skin rash, seizures. "
Sertraline	Pharmacokinetic drug interactions occurring with sertraline is more difficult to predict since it is generally considered mild inhibitors of the hepatic CYP450 system (see Monographs). Sertraline - TCAs Increase in levels, with possible toxicity (high doses only) Paroxetine (Paxil) Warfarin (Coumadin) Possible increase in risk of bleeding, TCAs Increase in levels, with possible toxicity. can increase plasma levels of macrolides, atomoxetine, amphetamine, bupropion, phenytoin, antipsychotics, zolpidem, and eszopiclone	(See SSRI class effect)	"• LFTs: baseline • thyroid function tests (TFTs): baseline "	Diarrhea, abnormal bleeding (mostly ecchymosis and purpura), impaired platelet aggregation.
Citalopram	Pharmacokinetic drug interactions occurring with citalopram is more difficult to predict since it is generally considered mild inhibitor of the hepatic CYP450 system (see Monographs). No clinically significant drug interactions have been documented. Associated with low rates of insomnia, anxiety, and other activating side effects. Lower risk of drug interactions but drug interactions still possible.	(See SSRI class effect)	"• LFTs: baseline • thyroid function tests (TFTs): baseline "	"Common: agitation, anxiety, or restlessness, especially in the first week of treatment or when doses are changed. Blurred vision, increased or decreased appetite, sexual difficulties & taste alterations "
Paroxetine	Paroxetine is a potent inhibitor of CYP2D6 resulting in interactions with medications metabolized through this pathway such as phenothiazines, tricyclic antidepressants and Type IC antiarrhythmics. Paroxetine tends to be more sedating and constipating. The potential for weight gain, drug interactions, and sexual dysfunction tends to be slightly higher with paroxetine.	(See SSRI class effect)	"• LFTs: baseline • serum creatinine/BUN: baseline • thyroid function tests (TFTs): baseline "	Weight Gain, Sedation, Constipation. Paroxetine exhibit a higher affinity for cholinergic receptors than other SSRIs, therefore, > anticholinergic effects: dry mouth, constipation, & tachycardia.
Venlafaxine	Drugs that inhibit CYP2D6 may result in elevated venlafaxine plasma concentrations. Additionally, the use of venlafaxine with a drug that is a potent inhibitor of both CYP2D6 and CYP1A2 may increase the risk for venlafaxine toxicity. Venlafaxine is a weak inhibitor CYP2D6 Venlafaxine is more difficult to predict since it is generally considered mild inhibitor of the hepatic CYP450 system (see drug interaction table).	Venlafaxine should be used with caution in patients with preexisting hypertension, seizure disorders, hyperthyroidism, recent myocardial infarction, or heart failure. Hepatic and renal impaired - require dosage adjustments.	• Serum cholesterol regularly Monitor height and weight changes in pediatric patients.	"More common: agitation, anxiety, or restlessness, changes in vision, sexual difficulties, vomiting. Possible height & weight changes in pediatric pts. Other: Hypercholesterolemia, Hyponatremia, abnormal bleeding,"
Bupropion	Bupropion inhibits CYP2D6 and can reduce the clearance of TCAs. Either ethanol abuse or abrupt discontinuation of ETOH has been associated with seizures and fatalities, and may increase the risk of seizures and/or neuropsychiatric events with bupropion treatment. Other drugs which may lower the seizure threshold should be used with great caution or avoided in patients taking bupropion include: some antidepressants; antipsychotics, cocaine; psychostimulants; theophylline; tramadol; and systemic corticosteroids. Bupropion can increase levels of atomoxetine, amphetamine, and risperidone.	"Exhibits a greater potential for causing seizures than other antidepressants. Warning of using any TCAs with bupropion due to the potential for increased risk of seizures from the lowering of seizure threshold. Not be used in patients with a preexisting seizure disorder. The incidence of seizures occurring with bupropion is dose-dependent. Use with caution in the following : abrupt discontinuation, anorexia nervosa, bulimia, MAOI tx., seizure disorder May precipitate motor or phonetic tics in those with Tourette's syndrome"	"• laboratory monitoring not necessary • weight "	"Tremor, Weight loss Other: constipation, difficulty sleeping, dizziness, dry mouth, headache, increased sweating, nausea "
Buspirone	"Hepatically metabolized via cytochrome P450 3A4. Substances that are potent inducers of hepatic cytochrome P450 isoenzyme CYP3A4 may increase the rate of buspirone metabolism. Use cautiously in patients with impaired hepatic/renal functioning. Increased ALT when combined with trazodone. Do not use with MAOIs. "	Contraindicated for concomitant use in patients receiving MAOI therapy. Caution in hepatic and renal disease	"• laboratory monitoring not necessary "	"Safe and effective use in children < 18 years old has not been established. No long-term safety data in children. Most common are CNS effects such as dizziness, drowsiness, headache, nausea/vomiting, restlessness with nervousness and excitement."

Table 4: Antidepressant - SAFETY (Tricyclics)

	Special Considerations, P450, & Drug Interactions	Contraindications and High Risk Patients	Monitoring	ADRs - most frequent, higher incidence, and/or significant effect
Amitriptyline	“Amitriptyline and its metabolites are metabolized via multiple pathways, however amitriptyline is metabolized by the liver via cytochrome P450 2C9/19, with a half-life 10–50 hours. It does not alter hepatic metabolism. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. MAOI interaction: Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs. ”	“Contraindicated in the recovery phase of myocardial infarctions, seizure disorders and prostatic hypertrophy. Varying degrees of sedation can be produced, and the seizure threshold can be lowered. “	• ECG: baseline • LFTs: baseline • serum amitriptyline concentrations • thyroid function tests (TFTs): baseline ”	Anticholinergic, Antihistaminic, Anti- Alpha-1 adrenergic adverse effects. Changes in sex hormone concentrations and blood glucose can result from amitriptyline’s effect on the endocrine system. Cardiac dysrhythmias can result from the direct quinidine-like effect on cardiac function combined with anticholinergic activity and norepinephrine potentiation.
Clomipramine	“Hepatically metabolized via cytochrome P450 2C9/19 isoenzymes but does not alter hepatic metabolism. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. MAOI interaction: Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs. ”	“Contraindicated in cardiac conditions (see class effect), of acute myocardial infarction, QT prolongation, AV block, & bundle-branch block, Ileus, MAOI therapy, convulsive disorders, and prostatic hypertrophy.”	“ECG: baseline • LFTs: baseline • thyroid function tests (TFTs): baseline”	Anticholinergic, Antihistaminic, Anti- Alpha-1 adrenergic adverse effects. (See TCA class effect)
Desipramine	“Hepatically metabolized via cytochrome P450 2D6, with a half-life of 11-46 hours. It does not alter hepatic metabolism, however. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. MAOI interaction: Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs. ”	Tricyclic antidepressants should be used with caution in patients with any cardiac disease (e.g., heart failure, history of myocardial infarction), because of the alterations in ECG. Do not administer tricyclic antidepressants to patients with QT prolongation or familial histories of long-QT syndromes or in those patients with cardiac conduction defects (e.g., cardiac arrhythmias, AV block, bundle-branch block). Contraindicated in cardiac conditions (see class effect), convulsive disorders and prostatic hypertrophy.	• ECG: baseline • LFTs: baseline • serum desipramine concentrations • thyroid function tests (TFTs): baseline ”	Desipramine may cause significant sedation & orthostasis, during initial dosing. Anticholinergic, Antihistaminic, Anti- Alpha-1 adrenergic adverse effects. Cardiac, Seizure. Changes in sex hormone concentrations and blood glucose may result from desipramine’s effect on the endocrine system. Mydriasis, disturbance of accommodation, and dry eyes may contribute to blurred vision and lens intolerance. (See TCA class effect)
Imipramine	“Metabolized via cytochrome P450 1A2, with a half-life of 6-34 hours. Imipramine does not alter hepatic metabolism. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. MAOI interaction: Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs. Do not break, crush or chew imipramine film-coated tablets. ”	Do not administer tricyclic antidepressants to patients with QT prolongation or familial histories of long-QT syndromes or in those patients with cardiac conduction defects (e.g., cardiac arrhythmias, AV block, bundle-branch block). Contraindicated in selected cardiac conditions (see class effect), convulsive disorders and prostatic hypertrophy.	• ECG: baseline • LFTs: baseline • serum imipramine concentrations • thyroid function tests (TFTs): baseline ”	Anticholinergic, Antihistaminic, Anti- Alpha-1 adrenergic adverse effects. (See TCA class effect)
Trimipramine	Tricyclics are metabolized via CYP2D6; therefore, slow metabolizers of this isozyme are expected to have higher plasma levels of the drugs.	Contraindicated in selected cardiac conditions (see class effect), convulsive disorders and prostatic hypertrophy.	• ECG • LFTs • thyroid function tests (TFTs) ”	Anticholinergic, Antihistaminic, Anti-Alpha-1 adrenergic adverse effects. sexual dysfunction including libido decrease, impotence, testicular swelling, ejaculation dysfunction, breast enlargement, and galactorrhea in females, and gynecomastia in males. (SIADH) has also been reported. Glucose metabolism can be altered and should be monitored in patients with diabetes mellitus.
Nortriptyline	“Metabolized by primarily cytochrome P450 2D6, with a half-life of 16-88 hours. It does not alter hepatic metabolism. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. MAOI interaction: Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs. ”	Contraindicated in selected cardiac conditions (see class effect), convulsive disorders and prostatic hypertrophy.	Baseline electrocardiogram, resting blood pressure and pulse (supine or sitting, standing), and weight should be monitored regularly.	Anticholinergic, Antihistaminic, Anti- Alpha-1 adrenergic adverse effects. (See TCA class effect)
Protriptyline	Metabolized via (CYP2D6) pathway. Can increase the sedative effects of other drugs.	Contraindicated in selected cardiac conditions (see class effect), convulsive disorders and prostatic hypertrophy.	Baseline electrocardiogram, resting blood pressure and pulse (supine or sitting, standing), and weight should be monitored regularly.	Instead of sedation, protriptyline can have a stimulant effect. Anticholinergic - moderate, Antihistaminic, Anti- Alpha-1 adrenergic adverse effects. (See TCA class effect)
Doxepin	“Plasma levels of both doxepin and desmethyldoxepin are highly variable and are poorly correlated with dosage. Doxepin is metabolized in the liver by cytochrome P450 (CYP) 2D6 to the active metabolite desmethyldoxepin. ”	Contraindicated in selected cardiac conditions (see class effect), convulsive disorders and prostatic hypertrophy.	The suggested therapeutic range for doxepin plus the demethylated metabolite is 110—250 ng/ml. Plasma concentration monitoring should be considered in patients who have an inadequate response or excessive adverse effects	Anticholinergic, Antihistaminic, Anti- Alpha-1 adrenergic adverse effects. (See TCA class effect)

Table 5: Antidepressant - SAFETY (Heterocyclic)

	Special Considerations, P450, & Drug Interactions	Contraindications and High Risk Patients	Monitoring	ADRs - most frequent, higher incidence, and/or significant effect
Amoxapine	“ It is metabolized by the liver, with a half-life of 8-30 hours, and does not alter hepatic metabolism. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. MAOI interxn: Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs. “	“Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders, prostatic hypertrophy. Do not administer amoxapine to patients with QT prolongation or familial histories of long-QT syndromes or in those patients with cardiac conduction defects (e.g., cardiac arrhythmias, AV block, bundle-branch block). Use with extreme caution in patients with a preexisting seizure “	“• ECG: baseline • LFTs: baseline • serum amoxapine concentrations • thyroid function tests (TFTs): baseline “	Significant sedation, anticholinergic effects, Mydriasis, disturbance of accommodation, and dry eyes may contribute to blurred vision and lens intolerance.
Maprotiline	Maprotiline does not inhibit monoamine oxidase or interfere with dopamine reuptake. .	“Contraindicated for concomitant use in patients receiving MAOI therapy and in the following: acute myocardial infarction • agranulocytosis • AV block • MAOI therapy • QT prolongation • tricyclic antidepressant hypersensitivity “	“• ECG: baseline • LFTs: baseline • thyroid function tests (TFTs): baseline “	“Maprotiline appears to produce sedation in depressed patients. The seizure threshold can be lowered, and anticholinergic activity is present. Cardiac dysrhythmias can result from the direct quinidine-like effect on cardiac function in combination with anticholinergic activity and the potentiation of norepinephrine “
Trazodone	Metabolized by cyt P450 2D6 is a substrate of CYP2D6 and CYP3A4. Coadministration with inhibitors of these enzymes may lead to substantial increases in trazodone plasma concentrations. If used with a potent CYP3A4 inhibitor, a lower dose of trazodone should be considered.	“ Caution in patients with cardiac disease and cardiac arrhythmias. Not be used following acute myocardial infarction. Caution in patients with hepatic disease because the drug could accumulate and adverse reactions could increase “	“• ECG: baseline • LFTs: baseline • serum creatinine/BUN: baseline • thyroid function tests (TFTs): baseline “	“Primary adverse effects are sedation, orthostatic hypotension, tachycardia, dry mouth, constipation, and blurred vision. Anticholinergic activity is lower with trazodone than with the tricyclic antidepressants. It has a sedative effect“

Table 6: Antidepressant - SAFETY (MAOI)

	Special Considerations, P450, & Drug Interactions	Contraindications and High Risk Patients	Monitoring	ADRs - most frequent, higher incidence, and/or significant effect
Isocarboxazid	Food and drug interactions with isocarboxazid can be serious. Consider patient’s intake of foods/beverages containing large amounts of tyramine, tryptophan, and/or caffeine. Should not be used concurrently with other MAOI therapy or other drugs that possess MAOI-like activity	“Contraindicated in hypertension, elderly, CHF, severe hepatic disease, pheochromocytoma, severe renal disease and severe cardiac disease. Should be reserved for patients who are refractory to other antidepressants. Potential food and drug interactions should be identified to prevent serious cardiovascular or neurological sequelae. In patients receiving contraindicated drugs known to interact with MAOIs. Hepatic impairment patients “	“LFTs: baseline, serum creatinine/ BUN: baseline and Hypertension sx. “	“Sexual dysfunction Appetite stimulation and weight gain may occur during therapy Shaking or tremor. Large amounts of tyramine from food, can result in severe hypertension. Anticholinergic Effects - dizziness, orthostatic hypotension, syncope, and xerostomia. “
Phenelzine	Potential food and drug interactions should be identified to prevent serious cardiovascular or neurological sequelae. Should not be used concurrently with other MAOI therapy or other drugs that possess MAOI-like activity	“Contraindicated in hypertension, elderly, CHF, severe hepatic disease, pheochromocytoma, severe renal disease and severe cardiac disease. Phenelzine can cause serious side effects; it should be reserved for patients who are refractory to other antidepressants. In patients receiving contraindicated drugs known to interact with MAOIs. Hepatic impairment patients “	“LFTs: baseline, serum creatinine/ BUN: baseline and Hypertension sx. “	Large amounts of tyramine from food, which can result in severe hypertension. Foods containing tyramine or high concentrations of sympathetic amines (e.g., dopamine) should be avoided; beverages containing caffeine or ethanol may also cause problems
Tranlycypromine	Potential food and drug interactions should be identified to prevent serious cardiovascular or neurological sequelae. Should not be used concurrently with other MAOI therapy or other drugs that possess MAOI-like activity	“Contraindicated in hypertension, elderly, CHF, severe hepatic disease, pheochromocytoma, severe renal disease and severe cardiac disease. In patients receiving contraindicated drugs known to interact with MAOIs. Hepatic impairment patients. “	“LFTs: baseline, serum creatinine/ BUN: baseline and Hypertension sx. “	Large amounts of tyramine from food, which can result in severe hypertension. Foods containing tyramine or high concentrations of sympathetic amines (e.g., dopamine) should be avoided; beverages containing caffeine or ethanol may also cause problems

Table 7: Safety and Tolerability of TCAs versus

Consideration	TCAs	SSRIs
Safety		
Overdose lethality risk	high	low
Alcohol potentiation	high	low
Tolerability		
Anticholinergic adverse events	high	low
Antihistamine adverse events	high	low
Anti- α_1 adrenergic adverse events	high	low
Serotonin adverse events	low	high

Table 8: Adverse Events for Each SSRI that Occured 1% More Often Than With Other SSRIs

Fluvoxamine	Paroxetine	Sertraline	Fluoxetine
Nausea	Anorexia [†]	Loose stools	Nervousness/agitation/anxiety [†]
Drowsiness	Frequent micturition	Tremors	Respiratory complaints
Constipation	Asthenia/fatigue [†]	Dry mouth	Headache
Anorexia [†]	Dizziness		
	Sweating		

Table 9: Atypical Antipsychotics Class - SAFETY

FDA Warning: Required atypical antipsychotics to include product label warnings about the potential for an increased risk of hyperglycemia and diabetes with the use of atypical antipsychotics.

Warnings: The atypical antipsychotics (aripiprazole, clozapine, olanzapine, quetiapine, risperidone, and ziprasidone) have been associated with causing hyperglycemia, even diabetic ketoacidosis, hyperosmolar, hyperglycemic states, and diabetic coma.

Side Effects: Atypicals less likely than the typical antipsychotics to cause extrapyramidal side effects.

	Special Considerations, P450, & Drug Interactions	Contraindications and High Risk Patients	Monitoring	ADRs - most frequent, higher incidence, and/or significant effect
Clozapine	Metabolism of clozapine is extensive and occurs primarily via the CYP1A2, CYP2D6 and CYP3A4 hepatic microsomal isoenzymes.	Warning: potential for life-threatening agranulocytosis, the label contains a Black Box warning stating that clozapine should be reserved for schizophrenic patients who have failed treatment with two or more trials of typical schizophrenia drugs or who are at risk for recurrent suicidal behavior. Myeloproliferative disorders.	“White blood cell (WBC) count monitoring schedule for agranulocytosis. AIMS assessment q 3-6 months • blood glucose • LFTs • neurologic function • serum cholesterol profile • weight cardiovascular monitoring.”	“Anticholinergic effects, paradoxically, it can cause hypersalivation. Seizure threshold is lowered more by clozapine than other antipsychotics, causing seizures in ~10% of patients exposed to higher doses Little to no hyperprolactinemia. “
Olanzapine	“Metabolized via cyt P450 1A2 and 2D6. Inducers of these enzymes may increase olanzapine clearance. Co-administration of carbamazepine(CBZ) (200 mg PO bid) results in a 50% increase in systemic olanzapine clearance via the induction of CYP1A2 by CBZ. Monitor for reduced olanzapine effectiveness if any inducers are used concurrently. D/C of these drugs may produce an increase in olanzapine concentrations. The combined effects of age, smoking, and gender could lead to sig. pharmacokinetic differences. “	“Safety and efficacy of olanzapine use in children and adolescents have not been established. Use cautiously in patients with hypertension, hepatic disease, and cardiac disease “	“AIMS assessment q 3-6 months • blood glucose • LFTs • neurologic function • serum cholesterol profile • weight Routine cardiovascular monitoring suggested for children receiving psychotropic medications If pre-existing hepatic disease, periodic assessment of liver function is recommended”	Weight gain, glucose intolerance, anticholinergic effects, and hyperlipidemia. Most common adr in trials is drowsiness. Other common side effects include agitation (23%), akathisia (5%), constipation (9%), dizziness (10.9%), non-aggressive objectionable behavior with emotional lability (8%), postural hypotension (5.5%), and weight gain (6%, averaging 2.8 kg). Clinically important differences in EPS reactions with olanzapine treatment versus placebo were not evident in trials, with the exception of akathisia (5%, defined as hyperkinesia)
Quetiapine	“Hepatically metabolized by cyt P450 3A4 and possibly 2D6. Quetiapine is not a known inducer or inhibitor of the cytochrome P450 system. Use with caution in patients taking antihypertensives and CNS depressants. “	Adolescents and children: Safe and effective use has not been established. Caution in patients with pre-existing hypotension, cerebrovascular disease, & cardiac disease. Also caution in patients with dysphagia, risk of aspiration pneumonia, seizure disorder, .	“ Baseline liver function tests and thyroid panel for hypothyroidism. Lens examination of eye to detect cataract formation is recommended upon initiation and at six month intervals. AIMS assessment q 3-6 months • blood glucose • LFTs • neurologic function • serum cholesterol profile • weight cardiovascular monitoring.”	Somnolence - most common. Orthostatic hypotension, mild weight gain, drowsiness, dizziness, constipation, orthostatic hypotension, xerostomia, and dyspepsia. Highest rate of anticholinergic adverse effects compared to other atypical antipsychotics.
Risperidone	“Metabolized by cyt P450 2D6 to an active metabolite, 9-hydroxyrisperidone. Both are equally effective. Drugs that inhibit or induce CYP2D6 may affect the incidence of side effects and the efficacy of risperidone. Drugs that are inhibitors or inducers of CYP2D6 could lead to elevated or lowered serum concentrations of the parent drug risperidone, respectively. “	“Adolescents and children 7—14 years: Safety and efficacy have not been established. Contraindicated in breast-feeding, torsade de pointes, and QT prolongation. Patients should avoid exposure to extremes of cold (to prevent hypothermia) or heat (ambient temperature increase) to prevent heat stroke “	“• AIMS assessment • blood glucose • ECG • LFTs • neurologic function • serum cholesterol profile • weight Orthostatic vital signs in patients for whom hypotension is of concern. Cardiovascular monitoring.”	In children, drowsiness and weight gain were significant adrs. Hyperprolactinemia, Weight gain, Menstrual irregularity, Photosensitivity, & Orthostatic hypotension
Ziprasidone	“Oxidation through hepatic cytochrome P450 isoenzyme CYP3A4; Does not appear to affect metabolism of other drugs cleared via hepatic CYP450 isoenzymes. QTc interval prolongation and should not be combined with other medications that may produce this effect. A decrease in ziprasidone plasma levels could potentially occur if the drug is used concurrently with other inducers of CYP3A4 “	“Avoid use of this drug in children who have known cardiac conduction defects or congenital heart disease (i.e. congenital long QT syndrome). Risk of QT prolongation is increased in the presence of hypokalemia or hypomagnesemia. Patients should avoid exposure to extremes of cold (to prevent hypothermia) or heat (ambient temperature increase) to prevent heat stroke “	“Monitor ECGs in children, Periodic monitoring of potassium and magnesium levels should be performed when loop diuretics or thiazide diuretics are used. AIMS assessment q 3-6 months • blood glucose • LFTs • neurologic function • serum cholesterol profile • weight cardiovascular monitoring.”	Orthostatic hypotension, more favorable effect on weight gain than clozapine, olanzapine, and risperidone. Endocrine effects. Asthenia, constipation, diarrhea, dizziness, somnolence/drowsiness, and dry mouth most common.

Table 10: Typical Antipsychotics Class - SAFETY

	Special Considerations, P450, & Drug Interactions	Contraindications and High Risk Patients	Monitoring	ADRs - most frequent, higher incidence, and/or significant effect
Butyrophenone				
Haloperidol	"Metabolized via cyt P4501A2 and 3A4, with a half-life of 15-30 hours. Can potentiate the actions of other CNS depressants. Fluoxetine, paroxetine and sertraline may all inhibit the hepatic metabolism of haloperidol via inhibition of the CYP2D6 isozyme."	"Haloperidol is associated with an established risk of QT prolongation and torsades de pointes. Contraindicated in alcohol and barbiturate withdrawal states, Parkinson's disease, angina, epilepsy, and urinary retention. "	"• CBC • ophthalmologic exam • serum prolactin • urinalysis • AIMS for EPS Routine cardiovascular monitoring "	"NMS Extrapyramidal symptoms, Anticholinergic effects, Hypothermia and hyperthermia, Cardiovascular reactions, Melanosis, Pigmentary retinopathy, Ocular changes including deposition of fine particles in the lens and cornea, Symptoms of blurred vision, Hematologic disturbances "
Phenothiazines				
Chlorpromazine	Hepatic microsomal CYP450 enzyme CYP2D6 is involved in phenothiazine metabolism. Numerous drug-drug interxns (see drug intrxn ref), tcas, SSRIs, stimulants, phenothiazines, neuroleptics. Increased metabolism of phenothiazines in smokers	Phenothiazines should not be administered to children or adolescents whose signs and symptoms are suggestive of Reye's syndrome. Contraindicated in patients who have experienced bone marrow suppression, blood dyscrasias, sig. CNS depression, or jaundice due to phenothiazine therapy. Caution in patients with preexisting hematological disease & in patients with significant pulmonary disease. Risk of phenothiazine-induced neurological disease. Agranulocytosis and other hematologic disorders - rare. May lower the seizure threshold. Risk of QT prolongation and/or torsades de pointes	"• CBC • ophthalmologic exam • serum prolactin • AIMS for EPS Routine cardiovascular monitoring has been suggested for children and adolescents receiving phenothiazines due to the potential to produce adverse cardiac effects."	"Children with acute illnesses (e.g., varicella-zoster infections, CNS infections, measles, gastroenteritis, or dehydration) may be more susceptible to developing adverse reactions, respiratory depression, and extrapyramidal symptoms from the phenothiazines. Children may also be more susceptible to the cardiac effects of the phenothiazines, particularly if there is a known history of familial QT prolongation. Children most often develop dystonic reactions. May cause various forms of ocular disease Extrapyramidal symptoms, Orthostatic Hypotension, Hematological disorders, and Anticholinergic effects. Skin hyperpigmentation, Hyperprolactinemia, Galactorrhea, Weight gain Photosensitivity, Priapism, Amenorrhea or other menstrual irregularity "
Fluphenazine	Phenothiazine class effect (see chlorpromazine)	Phenothiazine class effect (see chlorpromazine)	Phenothiazine class effect (see chlorpromazine)	Phenothiazine class effect (see chlorpromazine)
Mesoridazine	Phenothiazine class effect (see chlorpromazine)	The safety and efficacy of mesoridazine in children < 12 years of age has not been established. Phenothiazine class effect (see chlorpromazine)	"AIMS for EPS • CBC • ECG • ophthalmologic exam • serum prolactin A baseline ECG should be performed prior to mesoridazine initiation."	Changes in visual acuity and corneal deposits. High incidence of sedation and anticholinergic effects and a low incidence of extrapyramidal reactions. Cardiovascular effects, Dose-related effects on ventricular repolarization may lead to QTc interval prolongation. Phenothiazine class effect (see chlorpromazine)
	<i>*Note: Mesoridazine - Because of potential cardiovascular risks including torsade de pointes and sudden death, the manufacturer recommends that mesoridazine therapy be reserved for treating schizophrenic patients who have failed to respond to adequate courses of other antipsychotic drugs, either because of inadequate efficacy or intolerable side effects.</i>			
Perphenazine	Phenothiazine class effect (see chlorpromazine)	Children: Safe and effective use is not established. Phenothiazine class effect (see chlorpromazine)	Phenothiazine class effect (see chlorpromazine)	Phenothiazine class effect (see chlorpromazine)
Thioridazine	Phenothiazine class effect (see chlorpromazine)	The use of thioridazine concomitantly with cytochrome P450 (CYP) 2D6 inhibitors is contraindicated due to the theoretical risk of prolongation of QTc interval and subsequent arrhythmias due to elevated serum concentrations of thioridazine. Phenothiazine class effect (see chlorpromazine)	"• AIMS assessment • CBC • ECG • ophthalmologic exam • serum potassium (esp. if on thiazide diuretic) • serum prolactin Phenothiazine class effect (see chlorpromazine)"	Fewest extrapyramidal symptoms (EPS) of any typical phenothiazine antipsychotic. Electrolyte disturbances (e.g., hypokalemia, hypomagnesemia, hypercalcemia) may occur with administration of thiazide diuretics. Phenothiazine class effect (see chlorpromazine)
	<i>*Note: Thioridazine - Because of the potential cardiovascular risks, the manufacturer recommends that therapy with thioridazine be reserved for patients who have failed to respond to adequate courses of other anti-psychotic drugs</i>			
Trifluoperazine	Phenothiazine class effect (see chlorpromazine)	Phenothiazine class effect (see chlorpromazine)	Caution in patients with known sulfite hypersensitivity due to sulfites in oral conc. Trifluoperazine should be used with caution in prostatic hypertrophy, closed-angle glaucoma, paralytic ileus, or urinary retention because the drug exhibits anticholinergic activity that can exacerbate these conditions. Phenothiazine class effect (see chlorpromazine)	Trifluoperazine possesses weak anticholinergic and alpha-adrenergic receptor blocking effects. Phenothiazine class effect (see chlorpromazine)
Other				
Thiothixene	Numerous drug-interxns. Use with antipsychotic phenothiazines, is not generally recommended. Additive cardiac effects (e.g., prolonged QT interval), CNS effects, or antimuscarinic effects may occur. Inhibits CYP2D6 in vitro and serum concentrations of affected drugs, Cigarette smoking can induce hepatic metabolism and reduce plasma concentrations of thiothixene.	Caution in patients with thyroid disease such as thyrotoxicosis or hyperthyroidism. Caution in cardiac disease, history of seizures,	"• CBC • ophthalmologic exam • serum prolactin • thyroid function tests (TFTs) • urinalysis "	"Blockade of alpha1-adrenergic receptors produces sedation; muscle relaxation; and cardiovascular effects such as hypotension, reflex tachycardia, and minor changes in ECG patterns. Other similar to phenothiazine class)Extrapyramidal symptoms, orthostatic hypotension, and anticholinergic effects. Skin hyperpigmentation, hyperprolactinemia & galactorrhea. Weight gain, priapism amenorrhea or other menstrual irregularity "

Table 11: Stimulant & Non-stimulant - SAFETY

FDA : Requested that all manufacturers of stimulant medications include a class label change that sudden death has been reported in association with CNS stimulant treatment at usual doses in pediatric patients with structural cardiac abnormalities. On March 22, 2006 the Pediatric Advisory Committee suggested that potential episodes of psychosis, aggression, and cardiac events with ADHD drugs in children do not warrant a black box warning, but should be included as an important warning in the label.

“Contraindications: Arteriosclerosis, moderate/severe hypertension, hyperthyroidism, glaucoma, diabetes mellitus, agitated states, patients with a history of drug abuse/dependence and those on a monoamine oxidase inhibitor.”

	Special Considerations, P450, & Drug Interactions	Contraindications and High Risk Patients	Monitoring	ADRs - most frequent, higher incidence, and/or significant effect
Stimulants				
Amphetamine	“Drug interxns w/: Potential for additive increases in blood pressure and heart rate. Guanethidine: Amphetamines can decrease the antihypertensive effect of guanethidine. Monoamine oxidase inhibitors: Can increase the pressor response to amphetamines. Tricyclic antidepressants: Can decrease the effects of amphetamines.”	“Contraindicated in arteriosclerosis, moderate/severe hypertension, hyperthyroidism, glaucoma, diabetes mellitus, agitated states, patients with a history of drug abuse/dependence and those on a monoamine oxidase inhibitor.”	“Monitor: growth rate & weight. Require ongoing management and monitoring.”	Growth inhibition is a possible long-term side effect. Palpitations, sinus tachycardia, hypertension, overstimulation, restlessness, dizziness, insomnia, dyskinesia, euphoria, dysphoria, xerostomia, diarrhea, constipation, anorexia, weight loss, impotence.
Dextroamphetamine	Stimulant Class effect (See Amphetamine)			
Mixed Amphetamine/ Dextroamphetamine	Stimulant Class effect (See Amphetamine)			
Dexmethylphenidate	In vitro studies showed that dexmethylphenidate did not inhibit cytochrome P450 isoenzymes. Avoid MAOI therapy or agents with MAO inhibitor activity within the past 14 days.	“Caution in patients with hypertension, seizures or EEG abnormalities. It is contraindicated in glaucoma, Tourette’s Disorder, severe hypertension, hyperthyroidism, arteriosclerosis, patients with a history of drug abuse/dependence, persons with severe anxiety or agitation, and those on a monoamine oxidase inhibitor.”	“• CBC with differential • growth rate • LFTs: baseline • weight”	Nervousness and insomnia are the most common adverse reactions reported with other methylphenidate products. In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and sinus tachycardia may occur more frequently. Growth inhibition is a possible long-term side effect
Methylphenidate	Numerous possible drug interxns. Methylphenidate reduces the hypotensive effect of antihypertensive. may inhibit the metabolism of certain anticonvulsants. Carbamazepine may reduce methylphenidate blood concentrations. Methylphenidate may decrease the metabolism of warfarin and other coumarin anticoagulants. Can increase TCA conc.	“Caution in patients with hypertension, seizures or EEG abnormalities. It is contraindicated in glaucoma, Tourette’s Disorder, severe hypertension, hyperthyroidism, arteriosclerosis, patients with a history of drug abuse/dependence, persons with severe anxiety or agitation, and those on a monoamine oxidase inhibitor.”	“• CBC with differential: baseline • growth rate • LFTs: baseline • platelet count • weight”	“Adverse effects include nervousness, insomnia, anorexia, tachycardia, and changes in blood pressure. Most adverse effects can be resolved by lowering the dose.”
Pemoline	In October, 2005 the FDA concluded that the overall risk of liver toxicity from Cylert® and generic pemoline products outweighed the benefits of this drug. In May 2005, Abbott chose to stop sales and marketing of Cylert® in the U.S.			
Non-stimulants				
Atomoxetine	“A dosage adjustment of atomoxetine is recommended in extensive metabolizers when atomoxetine is administered with strong inhibitors of the CYP2D6 enzyme. Use with monoamine oxidase inhibitors (MAOIs) is contraindicated. Use cautiously with vasopressors, & sympathomimetics.”	“ Any patient who exhibits jaundice or laboratory evidence of liver injury while taking atomoxetine should discontinue the drug. Contraindicated in the following: closed-angle glaucoma • jaundice • MAOI therapy • angioedema There have been reports of suicidal ideation in pediatric patients being treated for ADHD with atomoxetine.”	“• Growth rate • Weight Consider monitoring the patient’s blood pressure and heart rate at baseline and regularly if sympathomimetics or vasopressors are coadministered”	ADRs that occurred commonly in both pediatric patients and adults included: nausea/vomiting, anorexia or a decrease in appetite, and dizziness. In pediatrics, additional common ADRs were: dyspepsia, fatigue, and emotional lability. Potential for growth inhibition w/ long term use.
	<i>* NOTE* On December 17, 2004, the FDA issued a new bolded warning in the U.S. drug label for atomoxetine following reports of markedly elevated hepatic enzymes and bilirubin in two patients, both of whom recovered. Any patient who exhibits jaundice or laboratory evidence of liver injury while taking atomoxetine should discontinue the drug. Currently, routine liver function tests are not recommended for those who take atomoxetine.</i>			
Clonidine	Concurrent use of clonidine with phenothiazines & TCAs should be avoided	Caution in patients with cerebrovascular disease, myocardial infarction, or severe heart failure. In patients with a history of major depression, can induce depressive episodes.	AHA rec. that children and adolescents be monitored for changes in BP at tx. initiation, periodically during treatment, and when tapering the drug, even when used for psychotropic indications. Laboratory monitoring not necessary	In the use of clonidine for attention deficit hyperactivity disorder (ADHD), sedation and hypotension have been reported. Cardiovascular effects of clonidine therapy include hypotension, orthostatic hypotension, palpitations, sinus tachycardia, and sinus bradycardia. Severe rebound hypertension can occur during withdrawal from clonidine. weight gain during the first few days of oral clonidine therapy.
	<i>***Note* - Safe and effective use of clonidine in children has not been adequately established; there are no clear guidelines for clonidine use in pediatric patients. Reports of sudden death and hypotension in children receiving oral clonidine in combination with other therapies for ADHD have been published. Such cases have also been reported with the use of clonidine alone. This may indicate that children and infants are more sensitive to the effects of clonidine and should be treated with extreme caution.</i>			
Guanfacine	Tricyclic antidepressants can inhibit the hypotensive effects of guanfacine, causing an increase in blood pressure if given concomitantly. Guanfacine has been associated with sedative effects and can potentiate the actions of other CNS depressants	Safe and effective use of guanfacine in children aged < 12 years has not been established; caution should be used in administering guanfacine to patients with severe coronary artery disease, acute myocardial infarction, cerebrovascular disease, severe hepatic disease (hepatic failure), or renal disease associated with renal impairment or renal failure.	Children and adolescents receiving guanfacine should be monitored for changes in blood pressure at treatment initiation, periodically during treatment, and when tapering the drug, even when the drug is used for psychotropic indications. laboratory monitoring not necessary	Most common: dry mouth, weakness, drowsiness, constipation, fatigue, headache, insomnia, and impotence. Patients should be warned of hazards assoc. with abrupt cessation of therapy and cautioned not to miss a dose or to stop taking the drug abruptly.
	<i>*Note- Safe and effective use of guanfacine in children aged < 12 years has not been established; there are no clear guidelines for guanfacine use in pediatric patients. In the use of guanfacine for (ADHD) and other behavior disorders in children, clinicians should be alert for sedation, hypotension and other potential side effects. Mania and aggressive behavioral changes have been reported in some children who received guanfacine for ADHD.</i>			

The Expert Panel

Leigh Ann Anderson, PharmD, has been an Editor for Gold Standard, Inc. since February 2001. After acquiring her BS in Pharmacy (University of Georgia, 1987) and PharmD (Summa Cum Laude, Campbell University, 1992), Dr. Anderson completed a Drug Information Specialty Residency at Shands Hospital at the University of Florida. In 1993, Dr. Anderson relocated to Denver, Colorado where she served as coordinator and clinical pharmacy specialist for the Drug Information Service at Kaiser Permanente, Rocky Mountain Region. In 1995, Dr. Anderson accepted a position with Multum Information Services, also in Denver, and worked to develop the patient-specific health information database, MediSource. In 1998, Dr. Anderson accepted a position as Regional Medical Scientist with GlaxoSmithKline, in Research Triangle Park, North Carolina. In this position, Dr. Anderson worked with national thought leaders in the gastrointestinal area, specifically focusing on Irritable Bowel Syndrome and the drug treatment alosetron (Lotronex®). Dr. Anderson has authored several peer-reviewed articles and is a full member of the American College of Clinical Pharmacy (ACCP). She has also practiced in the areas of hospital and retail pharmacy. Dr. Anderson currently focuses on the Gastrointestinal, Neurological, and Psychotropic therapeutic areas for Clinical Pharmacology® and has a special interest in drug interaction pharmacology. Dr. Anderson also coordinates the Drug Information rotation at Gold Standard for University of Florida PharmD students.

Louis Bernard Antione, MD, graduated from The Faculte de Medicine et Pharmacie Universite d'Etat d' Haiti and completed post-graduate training in Pediatrics and Psychiatry and a fellowship in Child and Adolescent Psychiatry in Brooklyn, New York. He then joined the faculty of the University of Miami School of Medicine where he is currently an Associate Professor of Clinical Psychiatry. He has co-authored multiple articles and has published several books including non-fiction essays, fiction novels, and poetry collections. Dr. Antoine has held various directorships at the Jackson Memorial Hospital / University of Miami and is currently the Medical Director of the Juvenile Assessment Receiving Facility for Adolescents, the Partial Hospitalization Program for Adolescents, and the Statewide Inpatient Program for Adolescents at Jackson Mental Health Medical Center.

Jorge L. Armenteros, MD, is a voting member of the Psychopharmacologic Drugs Advisory Committee of the Food and Drug Administration. In this capacity, he reviews and evaluates data concerning the safety and effectiveness of marketed and investigational human drug products for the use in the treatment of psychiatric disorders and makes appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Armernteros is a member of the American Academy of Child and Adolescent Psychiatry and has a special interest in the pharmacological treatment of schizophrenia, impulsive aggression, autism, and behavioral disorders. He has published numerous scientific articles and book chapters dealing with the efficacy of specific drugs, as well as the diagnosis and biological factors in mental illness. He is a reviewer for the Journal of the American Academy of Child & Adolescent Psychiatry. His honors and awards include the New Clinical Drug Evaluation Program / National Institute of Mental Health's New Investigator Award, and the American College of Neuropsychopharmacology / National Institute of Mental Health's Minority Travel Award.

Dr. Armenteros received his MD degree from the University of Puerto Rico School of Medicine in 1988. He completed his residency training in Psychiatry and his fellowship in Child and Adolescent Psychiatry at New York University School of Medicine in New York City. Dr. Armenteros undertook a research fellowship in Child Psychopharmacology under a NIMH-funded Institutional Training Grant at New York University and, upon completion in 1995, was made an Assistant Professor in Clinical Psychiatry at Columbia University College of Physicians and Surgeons where he started his research work in Child and Adolescent Psychopharmacology at the University of Miami Miller School of Medicine until 2005. Dr. Armenteros now devotes his efforts to the private practice of Psychiatry in Coral Gables, Florida.

R. Scott Benson, MD, is a native of Gainesville, Florida. He has practiced child and adolescent psychiatry in Pensacola since 1976. His interest in pediatric consult liaison psychiatry developed out of his experience as a pediatrician at Camp Lejeune, North Carolina. His practice in Pensacola evolved from a solo practice to a multi-disciplinary group at Creekside. Dr. Benson's center has a unique consultation service at Sacred Heart Hospital where he treats child victims of sexual abuse and recently completed a project in juvenile court. Dr. Benson has been a member of the AACAP Workgroup for Quality Issues (Practice Parameters) for 10 years. He represents the FPS in the APA Assembly and serves on the Public Affairs Committee and the Patient Safety Committee.

His recent reads were *The Wisdom of Crowds*, *The Swamp*, and *Escape Fire*. Dr. Benson lives in Pensacola with his wife, former State Representative Lois Benson. His daughter, State Representative Holly Benson, is chair of the Health Council. His daughter, Megan Pratt, has her PhD in Neurobiology from Harvard. She and her husband practice at the Institute for Human and Machine Cognition in Pensacola.

Daniel Castellanos, MD, is a Voluntary Associate Professor of Psychiatry & Pediatrics at the University of Miami School Of Medicine. He is the Director of the Children's Crisis Service and the Child and Adolescent Psychiatry Inpatient Unit at the University of Miami / Jackson Memorial Medical Center. His private practice in Coral Gables specializes in the psychiatric treatment of children, adolescents and young adults.

Naakesh A. Dewan, MD, president of the Center for Mental Healthcare Improvement, is in private practice at Advanced Psychiatry, P.A. in Clearwater. In addition to providing medical consultation, care management, and psychotherapy services, he provides mental skills coaching to amateur and world-class golfers and tennis players. Dr. Dewan has been a practicing psychiatrist and physician leader in a multi-national medical and psychiatric hospital corporation, a non-profit managed behavioral healthcare company, and in two major academic medical and psychiatric systems of care. He is board certified in psychiatry and has been practicing emergency and outpatient psychiatry for the past decade.

He graduated from the Medical College of Ohio in 1987 and was in residency training in psychiatry at the Los Angeles County-University of Southern California Medical Center and the University of California San Diego School of Medicine. He also completed a National Institute of Mental Health (NIMH) fellowship in Psychiatric Epidemiology Research at the University of California at San Diego. He is a nationally known speaker and has numerous publications including a book on Behavioral Healthcare Informatics.

Wayne Goodman, MD, is Professor and Chairman of the Department of Psychiatry at the University of Florida College of Medicine in Gainesville, Florida. Dr. Goodman was raised in New York City where he attended the Bronx High School of Science. He graduated from Columbia University with a degree in Electrical Engineering and received his Medical Degree from Boston University. He completed his internship, residency, and a research fellowship at Yale University School of Medicine where he rose to the rank of Associate Professor of Psychiatry. He founded and served as chief of the Obsessive Compulsive Disorders Clinic at Yale's Clinical Neuroscience Research Unit. While on faculty at Yale, he conducted research on the phenomenology, neurobiology, and treatment of obsessive-compulsive disorder (OCD), Tourette's Syndrome, and Anxiety Disorders. He is the principal developer of the Y-BOCS, the gold standard for rating OCD. He conducted some of the first controlled trials of selective serotonin reuptake inhibitors in OCD. He was co-founder of the Obsessive Compulsive Foundation, today's major consumer advocacy organization for this disorder, and served as Chair of its Scientific Advisory Board from 1987-1995.

Dr. Goodman joined the University of Florida College of Medicine as Professor of Psychiatry in 1993 and was appointed Department Chairman in July 1998. Dr. Goodman has over 150 publications, is listed among the 20 Mostly Highly Cited researchers in Psychiatry / Psychology, was named one of the "Best Doctors" in 2005-2006, and holds several grants from NIMH including a study of Deep Brain Stimulation in refractory OCD and another on PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Strep). At the state level, he is a member of the Governor's Task Force on Suicide Prevention. At the national level, Dr. Goodman chairs the FDA's Psychopharmacology Drugs Advisory Committee. In his role on the FDA Panel, Dr. Goodman chaired the hearings on the association between antidepressants and suicidality in children. Dr. Goodman is a member of the ACNP (American College of Neuropsychopharmacology), the Alpha-Omega-Alfa medical honor society, NIMH Interventions Study Section and a Distinguished Fellow of the American Psychiatric Association.

Martin Lazoritz, MD, is board certified in both General Psychiatry and Child / Adolescent Psychiatry and in Forensic Psychiatry. After completing his training, Dr. Lazoritz joined the faculty at the University of Florida Department of Psychiatry and transformed the general inpatient unit into three programs (evaluation, adult, and adolescent). On October 1, 2001, Dr. Lazoritz was appointed by the Dean of the College of Medicine as Associate Dean for Managed Care and Faculty Practice.

His clinical interests include the diagnosis and treatment of addictive disorders, eating disorders, anxiety disorders, ADHD, and forensic psychiatry. He has a great deal of experience in evaluating and treating those who have been abused and neglected. He is interested in developing effective clinical programs and systems of clinical care that traverse the clinical continuum. As Medical Director of Shands at Vista, Dr. Lazoritz has reviewed policies and procedures, supervised and mentored faculty, developed clinical programs, provided 24/7 supervision of the inpatient intake and call system, and developed a QI/Peer review process.

John March, MD, is Professor of Psychiatry and Chief of Child and Adolescent Psychiatry at Duke University Medical Center. Though based formally in the Department of Psychiatry and Behavioral Sciences, Dr. March also holds faculty appointments at the Duke Clinical Research Institute and in the Department of Psychology: Social and Health Sciences. Dr. March received a BA from the University of California at Riverside and an MS in Molecular Biology from the University of California at Berkeley. He obtained an MD-MPH (epidemiology) from the UCLA School of Medicine and later completed a residency in Family Practice at that institution. Following several years as a family practitioner in rural Montana, Dr. March trained in General and Child and Adolescent Psychiatry in the Department of Psychiatry, University of Wisconsin, Madison. Dr. March has extensive experience developing and testing the efficacy of cognitive-behavioral and pharmacological treatments for pediatric mental disorders. He holds a K24 career development award from the NIMH devoted to clinical trials methods, is a member of the Steering Committee of the Multimodal Treatment of ADHD Study, and PI of several NIMH funded treatment outcome studies including the Pediatric OCD Treatment Study (POTS I and POTS II), Research Units on Pediatric Psychopharmacology / Psychosocial Interventions, the Child Anxiety Management Study (CAMS), and the Coordinating Center for the Treatment of Adolescent Depression Study (TADS). Dr. March is the Principal Investigator of the first NIMH-funded practical clinical trials network in pediatric psychiatry, the Child and Adolescent Psychiatry Trials Network (CAPTN). He is an elected member of the American College of Neuropsychopharmacology (ACNP) and the Collegium Internationale Neuro-Psychopharmacologicum (CINP). He is also a member AACAP Workgroup on Research and a variety of scientific advisory boards. Widely published in the areas of OCD, PTSD, anxiety, depression, ADHD, and pediatric psychopharmacology, his most recent books, *OCD in Children and Adolescents: A*

Cognitive-Behavioral Treatment Manual and Phobic and Anxiety Disorders: A Clinician's Guide to Effective Psychosocial and Pharmacological Interventions define the state-of-the-art in the care of anxious youth. In addition to published and ongoing research, Dr. March is active in teaching and training in the treatment of child and adolescent mental disorders locally, nationwide, and internationally.

David Medvedeff, PharmD, MBA, has served as President of Informed Decisions, LLC, a Gold Standard Company, providing innovative end-to-end solutions for healthcare since 2005. Dr. Medvedeff also serves as Gold Standard's Vice President of Clinical Programs. Previously, he served as Gold Standard's Vice President of Government Business Development. Prior to joining the company in 2003, Dr. Medvedeff worked with The Florida Agency for Health Care Administration, where he coordinated the State's Pharmacy and Therapeutics Committee. His responsibilities also included the supervision and continuous development of the State's Preferred Drug List, with a budget of two billion dollars annually. Dr. Medvedeff's professional background includes a variety of positions within the Eckerd Corporation, where while serving as Director of Clinical Services, he led a team of pharmacists who were recognized with the APhA Pinnacle award for innovative patient care services. In 2006, Dr. Medvedeff became the only two-time APhA Pinnacle Award recipient in the history of the program when he and his Informed Decisions' team received the award for their role in the development and implementation of KatrinaHealth, an unprecedented online source of comprehensive medical and prescription histories for healthcare providers treating evacuees of Hurricane Katrina. Dr. Medvedeff also received Laureate recognition by IDG's Computerworld Honors Program for the KatrinaHealth project, which named Informed Decisions as a Finalist in the Medicine category for the 21st Century Achievement Award. He received both his PharmD and MBA from the University of Florida, where he also serves as an Associate Clinical Professor in the College of Pharmacy and has been recognized by the University as an Outstanding Young Alumnus.

Edward Mobley, MD, is currently involved in three professional activities. Since 1987 he has been in the private practice of psychiatry in Pensacola, Florida, he is an adult psychiatrist and a Diplomat of the American Board of Psychiatry and Neurology, and he is the Education Director of Psychiatry for Florida State University College of Medicine in Tallahassee and the Clerkship Director of Psychiatry at the Pensacola Regional Campus of FSUCOM. He has the academic appointment of Assistant Clinical Professor of Clinical Sciences / Psychiatry at FSUCOM. He has been affiliated with the College of Medicine since August of 2002. In November of 2002, he became the Medical Director of Access Behavioral Health, a subsidiary of Lakeview Center. Access Behavioral Health is the managing entity for the prepaid mental health plan in District One of Florida. Since September of 2003, he has been involved in Florida's statewide effort to implement evidence-based pharmacology guidelines for treating psychiatric illnesses.

J. David Moore, MD, is the Medical Director for the Tampa Service Center for Value Options and Florida Health Partners, Inc. Dr. Moore was in private practice in Tallahassee from 1975 through 1996. His roles encompassed both private practice and Public Psychiatry. His function as Medical Director and owner of a large outpatient practice involved supervision and direction of care for over 3,000 patients in active treatment. This practice served as the provider of Behavioral Health Care carve-out for MetLife (average 15,000 covered lives) for two years in the mid-1980s. Dr. Moore was the clinical Director for the Child and Adolescent Unit at the Psychiatric Center of Tallahassee Memorial Regional Medical Center for five years and was on the Medical Staff for 21 years. He is now on the honorary medical staff.

Emilio M. Roig, MD, was born in Cuba and immigrated to Florida with his family as a young child. After graduating with an MD degree from Central Eastern University in the Dominican Republic, he completed a residency in Pediatrics at the Mount Sinai School of Medicine Hospital and its affiliate, Elmhurst Hospital In New York. Dr. Roig worked as an attending pediatrician supervising pediatric residents in the emergency room at Elmhurst Hospital for two years. He completed an adult psychiatry residency at Albert Einstein College of Medicine also in New York. Dr. Roig moved to Florida and married in 1992. He completed his training with a fellowship in child and adolescent at the University of Miami / Jackson Memorial Hospital. After completing training in 1994, Dr. Roig and his wife moved to Georgia to work as assistant professors of psychiatry and pediatrics at Mercer University School of Medicine in Macon. He and his wife moved to Orlando in 1995. He has been working as a psychiatrist for the Devereux Intensive Residential Treatment Center in Viera, Florida for the past ten years. During his tenure at Devereux, Dr. Roig has worked with a myriad of child and adolescent clients with multiple diagnoses who had ailed all less restrictive placements and interventions. Dr. Roig continually strives to improve his treatment interventions by reducing polypharmacy, the need for seclusion / restraint, and PRN usage. Dr. Roig has been the Medical Director for Devereux since 1999.

Darren M. Rothschild, MD, has a private practice in Forensic and General Psychiatry in Palm Harbor, Florida. Additionally, he serves as medical director and staff psychiatrist at Turning Point of Tampa, Inc. and is an Assistant Clinical Professor at Florida State University's College of Medicine in Sarasota, Florida. He obtained his medical degree from the University of South Florida College of Medicine, where he was elected to the Alpha Omega Alpha Honors Medical Society. He completed medical internship and psychiatry residency training at Duke University Medical Center, followed by a fellowship in Forensic Psychiatry at Emory University School of Medicine.

Bhagirathni Sahasranaman, MD, has been serving as Medical Director at Henderson Mental Health Center in Fort Lauderdale, Florida for over four years. She is board certified in general psychiatry, as well as in child and adolescent psychiatry, and functions as a consultant child psychiatrist to Camelot Community Care, Inc. and Brookwood Group Home for Girls in Broward County. As Clinical Assistant Professor, Department of Psychiatry, Nova Southeastern University College of Osteopathic Medicine, she is also involved in teaching medical students and coordinating their psychiatry rotations at Henderson Mental Health Center.

Sandra Stock, MD, currently serves as an Assistant Professor of Psychiatry at the University of South Florida. She attended the University of Central Florida from 1986 to 1990, where she received a BS in Biology. She attended the University of South Florida School of Medicine from 1990 to 1994. Dr. Stock completed a General Psychiatry residency at USF in 1997 and a Child and Adolescent Psychiatry fellowship in 1999. She is the recipient of the 2003 Office of Curriculum and Medical Education teaching award, 2000-01 Educator of the Year Award from the USF Department of Psychiatry, GlaxoWellcome Fellowship to the American Psychiatric Association 1996-1998, and the John & Adams Award for the Florida Psychiatric Society for Outstanding research by a Psychiatric Resident in 1995. Her interests are medical student education, childhood anxiety disorders, and psychiatry resident education.

Mary Elizabeth Seay, MD, graduated from Ocala High School, Ocala, Florida in 1961. She received her BS from the University of Florida with majors in biology and chemistry in 1964. She then continued at University of Florida School of Medicine and graduated in 1968. She completed her residency and internship in Pediatrics at Shands Teaching Hospital in 1971. Dr. Seay completed her fellowship in Adolescent Medicine at the University of Colorado Health Services Center and went on to become the Medical Director and founder of Consultative Pediatrics, a private holistic pediatric practice treating children with behavioral, developmental, and emotional issues. She retired from private practice in 2000 and presently serves as the Medical Director of Children's Medical Services at the Tallahassee office, Medical Director of Early Steps Program and Clinical Associate in Pediatrics at the FSU College of Medicine.

Rajiv Tandon, MD, is currently the Chief of Psychiatry at the Florida Department of Children and Families. He was on the faculty of the Department of Psychiatry at the University of Michigan Medical Center, Ann Arbor, Michigan, from 1987-2004, where he was a tenured Professor of Psychiatry. He is currently the Chairman of the Board of Directors of the National Schizophrenia Foundation and a member of the Scientific Council of the National Alliance for the Mentally Ill. He was a member of State of Michigan Mental Health Commission in 2003-2004. Dr Tandon has authored more than 200 scientific publications and given over 500 national and international scientific presentations. He has received several awards for research and teaching in schizophrenia, including the American Psychiatric Association Young Psychiatrist of the Year award in 1993 and the 1997 FuturPsych award for outstanding achievement in schizophrenia research. He has been included in every edition of THE BEST DOCTORS IN AMERICA since 1995.

Shairi Turner, MD, primary focuses on the relationship between mental illness, substance abuse, and the disproportionate number of minority adolescents in the U.S. juvenile justice system. She recently became the first Chief Medical Director in the ten-year history of the Florida Department of Juvenile Justice in Tallahassee, where she is responsible for the health, mental health, and substance abuse issues for the over 10,000 children per year who are committed. Previously, Dr. Turner provided medical care to underserved adults and children at The Massachusetts General Hospital Medical Walk-In Clinic in Chelsea, MA. Also, working to address the issue of disproportionate minority confinement for the Governor's Juvenile Justice Advisory Committee, Dr. Turner served on Massachusetts' Disproportionate Minority Confinement (DMC) subcommittee. In addition, she was on the Board of Directors for homeless shelter, Bridge Over Troubled Waters.

A native of New York City, Dr. Turner received the Doctor of Medicine degree from Case Western University School of Medicine in Cleveland, OH in 1996. Dr. Turner then completed the four-year Harvard Combined Internal Medicine and Pediatrics Residency Program at the Massachusetts General Hospital and the Children's Hospital of Boston in 2000. She earned an MPH from the Harvard School of Public Health as a CFHU Fellow in 2002. She most recently finished a two-year Yerby Post-Doctoral Research fellowship at the HSPH in the Harvard Injury Control Research Center and Youth Violence Prevention Center.

Expert Panel Disclosure Information

Leigh A. Anderson, PharmD

Disclosed a financial interest / arrangement: Stock Shareholder, GlaxoSmithKline.

Jorge Armenteros, MD

Disclosed a financial interest / arrangement: Speakers Bureau, Janssen Pharmaceuticals.

Louis B. Antoine, MD

Disclosed no financial interest / arrangements with any corporate organizations, whose products, services, or research may be addressed in the discussions at the expert panel.

R. Scott Benson, MD

Disclosed no financial interest / arrangements with any corporate organizations, whose products, services, or research may be addressed in the discussions at the expert panel.

Naakesh A. Dewan, MD

Disclosed no financial interest / arrangements with any corporate organizations, whose products, services, or research may be addressed in the discussions at the expert panel. Formerly on Speakers Bureau for Lilly and Pfizer and Bristol-Myers in 2005.

Wayne Goodman, MD

Disclosed no financial interest / arrangements with any corporate organizations, whose products, services, or research may be addressed in the discussions at the expert panel.

Catherine Goldsmith, PhD, LCSW

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Daniel Castellanos, MD

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Tanya K. Murphy, MD

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J. David Moore, MD

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Lawrence E. Mobley, MD

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Darren Rothschild, MD

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Emilio Roig, MD

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Bhagirathy Sahasranaman, MD

Disclosed a financial interest / arrangement: Speakers Bureau, Janssen (previously Lilly and Pfizer), Consultant (previously Janssen, Pfizer, Bristol-Myers).

Mary E. Seay, MD

Disclosed no financial interest / arrangements with any corporate organizations, whose products, services, or research may be addressed in the discussions at the expert panel.

Kailie R. Shaw, MD

Disclosed no financial interest / arrangements with any corporate organizations, whose products, services, or research may be addressed in the discussions at the expert panel.

Sandra Stock, MD

Disclosed a financial interest / arrangement: Speakers Bureau, Janssen and Abbott.

Shairi R. Turner, MD, MPH

Disclosed no financial interest / arrangements with any corporate organizations, whose products, services, or research may be addressed in the discussions at the expert panel.

The panel had access to a summary of a literature review conducted by Dr. Rajiv Tandon, Department of Children and Families, Tallahassee, Florida, the resources referenced in the Gold Standard Drug Monographs for Mental Health Drugs, and the results of a literature summary prepared by CMHI, Clearwater, Florida. Each expert panelist received the Journal of Lifelong Learning in Psychiatry FOCUS Fall 2004, Volume II, Number 4 which included the Treatment Recommendations for the Use of Antipsychotics for Aggressive Youth (TRAAY) Parts I and II. Additionally, the 2006 draft AACAP guidelines for the treatment of children and adolescents with mental health disorders were reviewed and made available for the panel. Every effort was made to provide the panel the most current information on the treatment of and the use of psychotropic medications in children and adolescents.

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