



# Intervention Proposal

## Benzodiazepine Anxiolytic Duration of Use in Adults

Prepared for West Virginia Medicaid by Rx Delivery Services

Initial Study

Follow-up/Restudy

### EXECUTIVE SUMMARY

**Purpose:** To promote prudent prescribing of benzodiazepine anxiolytics in adults.

**Why Issue was Selected:** Benzodiazepine anxiolytic medications are generally well tolerated and very effective agents. However, most experts and available treatment guidelines do not recommend their use on a long-term basis.<sup>1-5</sup> In addition to potential adverse effects, such as psychomotor impairment and cognitive deficits, all benzodiazepines are controlled substances.<sup>1,6</sup> While true abuse of these agents is relatively rare, their long-term use may be associated with physical and/or psychological dependence.<sup>7-10</sup> Alternative, non-controlled medications are available for most conditions treated chronically with benzodiazepine anxiolytic medications.

Program Specific Information:	Performance Indicators	Exceptions
	<ul style="list-style-type: none"> <li>Use of a benzodiazepine anxiolytic for more than 60 of the last 90 days without a diagnosis of an anxiety disorder</li> </ul>	5,676
	<ul style="list-style-type: none"> <li>Use of a benzodiazepine anxiolytic in individuals with a history of substance abuse and/or dependence</li> </ul>	2,021
	<ul style="list-style-type: none"> <li>Chronic use of a benzodiazepine anxiolytic for anxiety (more than 180 of the last 200 days)</li> </ul>	7,287

**Setting & Population:** All patients 18 years of age or older with therapy with a benzodiazepine anxiolytic agent the in past 30 days  
*Medications discussed - approved*

**Type of Intervention:** Cover letter and modified profiles

**Main Outcome Measures:** The results of this intervention will be measured six months post-intervention. Targeted patient cases will be re-examined to determine whether changes in the performance indicators have been made.

**Anticipated Results:** Physician re-examination of the use of benzodiazepine anxiolytic medications in adults as a result of this mailing may reduce unnecessary or inappropriate drug therapy and decrease drug therapy expenditures.

## **WHY HAS THIS CLINICAL ISSUE BEEN SELECTED FOR REVIEW?**

Benzodiazepine anxiolytic medications are generally well tolerated and very effective agents. Since chlordiazepoxide was introduced in 1961 the benzodiazepines have been considered one of the safest classes of central nervous system medications. They are employed in the management of a wide variety of disorders, but are most commonly used to treat various anxiety disorders and sleep disturbances.<sup>1</sup> However, most experts and available treatment guidelines do not recommend their use on a long-term basis.<sup>1-5</sup>

Despite their relative safety, like all other medications benzodiazepines are associated with potential adverse effects. Their use is commonly associated with sedation, ataxia and other psychomotor impairments, and cognitive deficits.<sup>1,6</sup> In addition, all benzodiazepines are classified as controlled substances by the Drug Enforcement Administration (DEA).<sup>11</sup> While true abuse and addiction to these agents is relatively rare, their long-term use may be associated with physical and/or psychological dependence.<sup>7-10</sup> Alternative non-controlled medications are available for most conditions treated chronically with benzodiazepine anxiolytic medications.

For most anxiety disorders there are second generation antidepressants that have FDA approval and are now considered the treatment of choice for chronic pharmacologic management.<sup>2-5</sup> While a selective serotonin reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor (SNRI) may have a slower onset of action when compared to a benzodiazepine, they tend to be equally or more effective in the long-term. In addition, a dual benefit may be observed as depression is a frequent comorbid condition in patients with anxiety disorders.<sup>12</sup> If an antidepressant is not indicated, buspirone is another effective alternative. In addition, psychosocial and behavioral therapies are clearly effective for anxiety disorders and may provide a more definitive intervention in chronically anxious patients.<sup>13,14</sup>

## **PERFORMANCE INDICATORS**

### **Indicator #1: Long-Term Use of a Benzodiazepine Anxiolytic Without a Diagnosis of an Anxiety Disorder**

Why has this indicator been selected?	Benzodiazepine anxiolytics have many uses and are frequently employed short-term in the management of situational behavioral disturbances. Individuals without a diagnosis of an anxiety disorder should not use benzodiazepine anxiolytics for more than 60 days to minimize the development of psychological and/or physical dependence.
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How will the patients be selected?

Candidates (denominator):	All patients 18 years of age or older receiving a benzodiazepine anxiolytic within the past 30 days.
Exception criteria (numerator):	Candidates who received more than a 60 day supply in the last 90 days and do not have a diagnosis of an anxiety disorder. Individuals diagnosed with seizures or muscle disorders will be allowed chronic therapy with clonazepam, clorazepate, diazepam, or lorazepam.

### **Indicator #2: Use of a Benzodiazepine Anxiolytic with a History of Dependence**

Why has this indicator been selected?	All benzodiazepine anxiolytics are controlled substances and pose a risk of physical and psychological dependence in some patients.
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How will the patients be selected?

## Initiative Proposal

Candidates (denominator):	All patients 18 years of age or older receiving a benzodiazepine anxiolytic within the past 30 days.
Exception criteria (numerator):	Candidates who have a diagnosis of substance abuse in the past 720 days. Individuals diagnosed with seizures or muscle disorders will be allowed chronic therapy with clonazepam, clorazepate, diazepam, or lorazepam.

### Indicator #3: Chronic Use of a Benzodiazepine Anxiolytic for Anxiety

Why has this indicator been selected?	Benzodiazepine anxiolytics are recommended as short-term, adjunctive therapy in the management of anxiety by most experts and available treatment guidelines. Other FDA approved medications that are not controlled substances are recommended as treatments of choice for long-term use.
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How will the patients be selected?

Candidates (denominator):	All patients 18 years of age or older receiving a benzodiazepine anxiolytic within the past 30 days.
Exception criteria (numerator):	Candidates who have received more than a 180 day supply in the last 200 days. Individuals diagnosed with seizures or muscle disorders will be allowed chronic therapy with clonazepam, clorazepate, diazepam, or lorazepam.

## REFERENCES

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1. Moller HJ. Effectiveness and safety of benzodiazepines. *J Clin Psychopharmacol*. 1999; 19(Suppl 2): 2S-11S.
2. Ballenger JC, Davidson JR, Lecrubier Y, et al. Consensus statement on generalized anxiety disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry*. 2001; 62(Suppl 11):53-8.
3. Ballenger JC, Davidson JR, Lecrubier Y, et al. Consensus statement on post-traumatic stress disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry*. 2000; 61(Suppl 5):60-6.
4. Ballenger JC, Davidson JR, Lecrubier Y, et al. Consensus statement on social anxiety disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry*. 1998; 59(Suppl 17):54-60.
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13. Mitte K. Meta-analysis of cognitive-behavioral treatments for generalized anxiety disorder: a comparison with pharmacotherapy. *Psychol Bull*. 2005; 131:785-95.
14. Deacon BJ, Abramowitz JS. Cognitive and behavioral treatments for anxiety disorders: a review of meta-analytic findings. *J Clin Psychol*. 2004; 60:429-41.

Date

Joe Black  
2810 N. Parham Road  
Richmond, VA 23294

**RE: Caring for Your Adult Patients on Benzodiazepine Anxiolytics**

Dear Dr. Black:

The goal of this quality management program is to assist you in caring for your patients being treated with benzodiazepine anxiolytic medications. Benzodiazepine anxiolytics are generally well tolerated and very effective agents. However, most experts and available treatment guidelines do not recommend their use on a long-term basis.<sup>1-6</sup> This program targets duration of therapy and use in selected patients at increased risk for adverse outcomes.

Claims data indicates that in the West Virginia Medicaid program there are over 25,000 individuals with a recent drug claim for a benzodiazepine anxiolytic. Such drug therapy accounted for 76,687 prescriptions in a recent 90 day period at a total cost of \$618,702.

**West Virginia Medicaid Data**

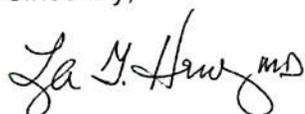
<b>Sedative/Hypnotic and Benzodiazepine Anxiolytic Indicators</b>	<b># of Patients with Opportunities*</b>
<ul style="list-style-type: none"><li>Identify patients using a benzodiazepine anxiolytic for more than 60 of the last 90 days without a diagnosis of an anxiety disorder</li></ul>	5,676
<ul style="list-style-type: none"><li>Promote use of non-controlled medications for the management of anxiety in individuals with a history of substance abuse and/or dependence</li></ul>	2,021
<ul style="list-style-type: none"><li>Encourage use of benzodiazepine anxiolytic agents as short-term, adjunctive measures as recommended by most experts and treatment guidelines rather than chronic therapy</li></ul>	7,287

\* based data through July 2012

**The enclosed patient profiles reflect one or more of the above issues and are provided as a chart reminder for when your patients return for their next appointments.**

We acknowledge that there may be clinical variables influencing an individual patient's management that are not apparent in claims data or that a patient may have been inadvertently identified as being under your care. We thank you for reviewing this information and caring for West Virginia Medicaid patients and welcome the opportunity to discuss any comments or concerns you may have about our quality management program. Please feel free to call our office at 1-866-923-7208 with questions or concerns.

Sincerely,



Lyle Henry, MD, FACS,  
Medical Director

### Benzodiazepine Anxiolytic Indicator Summary

- **Identify patients using a benzodiazepine anxiolytic for more than 60 of the last 90 days without a diagnosis of an anxiety disorder:** Benzodiazepine anxiolytics have many uses and are frequently employed short-term in the management of situational behavioral disturbances. Individuals without a diagnosis of an anxiety disorder should not use a benzodiazepine anxiolytic for more than 60 days to minimize the development of psychological and/or physical dependence.
- **Promote use of non-controlled medications for the management of anxiety as recommended by most experts and treatment guidelines in individuals with a history of substance abuse and/or dependence:** All benzodiazepine anxiolytics are controlled substances and pose a risk of physical and psychological dependence in some patients. Buspirone or one of the second generation antidepressants might be better choices in such patients.
- **Encourage use of benzodiazepine anxiolytic agents as short-term, adjunctive measures as recommended by most experts and treatment guidelines rather than chronic therapy:** Benzodiazepine anxiolytics are recommended as short-term, adjunctive therapy in the management of anxiety by most experts and available treatment guidelines. Other FDA approved medications that are not controlled substances, such as one of the second generation antidepressants or buspirone, are recommended as treatments of choice for long-term use. In addition, consideration should be given to the use of psychosocial and behavioral therapies as more definitive intervention in chronically anxious patients.<sup>7,8</sup>

#### References:

1. Moller HJ. Effectiveness and safety of benzodiazepines. *J Clin Psychopharmacol.* 1999; 19(Suppl 2): 2S-11S.
2. Ballenger JC, Davidson JR, Lecrubier Y, et al. Consensus statement on generalized anxiety disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry.* 2001; 62(Suppl 11):53-8.
3. Ballenger JC, Davidson JR, Lecrubier Y, et al. Consensus statement on post-traumatic stress disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry.* 2000; 61(Suppl 5):60-6.
4. Ballenger JC, Davidson JR, Lecrubier Y, et al. Consensus statement on social anxiety disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry.* 1998; 59(Suppl 17):54-60.
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6. Stevens JC, Pallack MH. Benzodiazepines in clinical practice: consideration of their long-term use and alternative agents. *J Clin Psychiatry.* 2005; 66(Suppl 2):21-7.
7. Mitte K. Meta-analysis of cognitive-behavioral treatments for generalized anxiety disorder: a comparison with pharmacotherapy. *Psychol Bull.* 2005; 131:785-95.
8. Deacon BJ, Abramowitz JS. Cognitive and behavioral treatments for anxiety disorders: a review of meta-analytic findings. *J Clin Psychol.* 2004; 60:429-41.





# Atypical Antipsychotics: Coordination of Care

Prepared for West Virginia Medicaid by Rx Delivery Services

Initial Study

Follow-up/Restudy

## EXECUTIVE SUMMARY

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**Purpose:** To assist physicians in the evaluation of atypical antipsychotic therapy, specifically when multiple prescribers and other health care providers may be involved. Commonly encountered situations include multiple prescribers and duplicate therapy, use in diabetic and/or obese patients, clinically significant drug interactions, and injectable options to improve adherence.

**Why Issue was Selected:** Newer atypical antipsychotics with fewer movement-related adverse effects have virtually replaced older antipsychotics.<sup>1,2</sup> However, they are associated with their own adverse effects and the potential for clinically significant drug-drug interactions.<sup>3,4</sup> Atypical antipsychotic related adverse effects often include both psychiatric and medical issues, so multiple providers may be involved in the optimal use of these agents. Additionally, even the benefits of treatments are limited when adherence is a problem. In patients with chronic psychosis who are nonadherent, long-acting injections of antipsychotic medications may decrease relapse.<sup>5</sup>

Program Specific Information:	Performance Indicators	Exceptions
	• Duplicate Therapy: Multiple Prescribers	247
	• Use in Type 1 or Type 2 Diabetic Patients	539
	• Use in Morbidly Obese Patients	136
	• Ziprasidone and Cardiac Concerns	268
	• Long-Acting Injection options for non-adherent, chronically psychotic patients	192

**Setting & Population:** All patients with a drug claim for an atypical antipsychotic in past 60 days

**Type of Intervention:** Cover letter and individual patient profiles.

**Main Outcome Measures:** The performance indicators will be re-measured when six months of outcome data are available.

**Anticipated Results:** Physician re-examination of atypical antipsychotic use as a result of this mailing may reduce potential adverse events, including metabolic-related complications, in selected patients and risk of relapse in non-adherent chronically psychotic patients. Improved outcomes and avoidance of unnecessary costs are possible if compliance is improved and adverse events are minimized.

**PERFORMANCE INDICATORS**

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**Indicator #1: Duplicate Therapy: Atypical Antipsychotics, Multiple Prescribers**

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Why has this indicator been selected? Concurrent use of more than one antipsychotic has not been adequately researched. Increased treatment efficacy has not been established, and increased adverse effects as well as decreased adherence are concerns.<sup>6,7</sup> Such use involves coordination of care issues when more than one prescriber is involved.

How will the patients be selected?

Candidates (denominator): All patients receiving atypical antipsychotics drugs in the past 60 days.  
Exception criteria (numerator): Candidates receiving more than one antipsychotic (multiple atypical antipsychotics or an atypical with a typical antipsychotic) agent for more than 35 of the 60 days from more than one provider.

**Indicator #2: Atypical Antipsychotics: Use in Diabetic Patients**

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Why has this indicator been selected? Atypical antipsychotics have been associated with metabolic side effects, including impaired glucose control. The literature indicates a hierarchal risk: clozapine & olanzapine > asenapine, iloperidone, paliperidone, quetiapine, & risperidone > aripiprazole, lurasidone, & ziprasidone. A history of diabetes should influence choice of agent and prompt monitoring of blood glucose levels.<sup>8,9</sup>

How will the patients be selected?

Candidates (denominator): All patients receiving an atypical antipsychotic in the last 30 days who have a diagnosis of diabetes in the past 2 years or history of an antidiabetic agent in the last 90 days.  
Exception Criteria (numerator): Candidates who are on clozapine or olanzapine and/or have not had a blood glucose level in the past 180 days if on one of the other atypical antipsychotics.

**Indicator #3: Atypical Antipsychotics: Use in Obese Patients**

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Why has this indicator been selected? Atypical antipsychotics have been associated with metabolic side effects, including increased body weight. The literature indicates a hierarchal risk: clozapine & olanzapine > asenapine, iloperidone, paliperidone, quetiapine, & risperidone > aripiprazole, lurasidone, & ziprasidone. Body weight (BMI) should influence choice of agent.<sup>8,9</sup>

How will the patients be selected?

Candidates (denominator): All patients prescribed clozapine or olanzapine in the past 30 days.  
Exception Criteria (numerator): Candidates who have a diagnosis of obesity in the past two years.

**Indicator #4: Ziprasidone Use: Potential Cardiac Concerns**

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Why has this indicator been selected? Based on approved prescribing information ziprasidone use is contraindicated in patients with a history congenital long QT syndrome or other QT prolongation, recent acute myocardial infarction, uncompensated heart failure, and in combination with other drugs known to prolong the QTc interval.<sup>10</sup> The literature also indicates an increased risk in patients who have bradycardia, are female and elderly, or when higher than recommended doses are used.<sup>11,12</sup>

How will the patients be selected?

Candidates (denominator): All patients prescribed ziprasidone in the past 30 days.  
 Exception Criteria (numerator): Candidates who have known contraindications or risk factors for QT prolongation (see Tables 1 and 2).

**Indicator #5: Coordination of Care: Long-Acting Injection Option for Chronic Nonadherent Patients**

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Why has this indicator been selected? Non-adherence is a major treatment issue in the maintenance therapy of schizophrenia and it may lead to hospitalization, increased physician office visits, and overall poor patient outcomes. In patients with a history of non-adherence to prescribed oral medication regimens, use of a long-acting injection of antipsychotic medication offers some hope that an extended period of medication usage might improve the patient’s insight and/or allow the development of a better therapeutic alliance with health care providers. During the initial phase of long-acting injection use the provider and healthcare team should initiate patient education, patient outreach, and other strategies to improve adherence.<sup>5,13,14</sup>

How will the patients be selected?

Candidates (denominator): All patients receiving chronic atypical antipsychotic therapy for the past 180 days and have a diagnosis of schizophrenia in the past 2 years.  
 Exception Criteria (numerator): Candidates who have received less than 60 days supply of an oral atypical antipsychotic agent in the last 90 days and have not been tried on a long-acting injection of antipsychotic medication in the past 180 days.

**REFERENCES**

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2. Alexander GC, Gallagher SA, Mascola A, et al. Increasing off-label use of antipsychotic medications in the United States, 1995-2008. *Pharmacoepidemiol Drug Saf.* 2011; 20:177-84.
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4. Frois Cm Guerin A, Saraogi A, et al. Preceptions and prescribing considerations among US psychiatrists regarding drug-drug interactions with oral atypical antipsychotics. *Curr Med Res Opin.* 2010; 26:2735-44.
5. Trihonen J, Haukka J, Taylor M, et al. A nationwide cohort study of oral and depot antipsychotics after first hospitalization for schizophrenia. *Am J Psychiatry.* 2011; 168:603-9.
6. Centorrino F, Goran JL, Hennen J, et al. Multiple versus single antipsychotic agents for hospitalized psychiatric patients: case-control study of risks versus benefits. *Am J Psychiatry* 2004; 161:700-6.

## Retrospective Intervention Proposal

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## APPENDIXES

**Table 1: Ziprasidone and QTc Prolongation: Potential Drug-Drug Interactions \***

Other Psychotropic Medications	Cardiac Medications	Antibiotic Agents	Misc. Medications
Chlorpromazine (Thorazine <sup>®</sup> )	Amiodarone (Cordarone <sup>®</sup> ),	Clarithromycin (Biaxin <sup>®</sup> )	Dolasetron Mesylate (Anzemet <sup>®</sup> )
Droperidol (Inapsine <sup>®</sup> )	Pacerone <sup>®</sup> )	Erythromycin (various)	Pentamidine (Pentam <sup>®</sup> ,
Levomethadyl (Orlaam <sup>®</sup> )	Bepidil (Vascor <sup>®</sup> )	Gatifloxacin (Tequin <sup>®</sup> )	NebuPent <sup>®</sup> )
Mesoridazine (Serentil <sup>®</sup> )	Disopyramide (Norpace <sup>®</sup> )	Moxifloxacin (Avelox <sup>®</sup> )	Tacrolimus (Protopic <sup>®</sup> )
Methadone (Dolophine <sup>®</sup> )	Procainamide (Pronestyl <sup>®</sup> )	Sparofloxacin (Zagan <sup>®</sup> )	
Pimozide (Orap <sup>®</sup> )	Quinidine (gluconate or sulfate)		
Thioridazine (Mellaril <sup>®</sup> )	Sotalol (Betapace <sup>®</sup> )		

\* Geodon (ziprasidone) prescribing information, revised 12/2010. Pfizer Inc. New York, NY. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=584> [last accessed July 7, 2012].

\* The International Registry for Drug-Induced Arrhythmias. Arizona Health Sciences Center, Tucson, AZ. Available at: <http://www.qtdrugs.org/medical-pros/drug-lists/drug-lists.htm> [last accessed July 7, 2012].

**Table 2: Contraindications and Risk Factors for Ziprasidone\***

Contraindications	Risk Factors
Congenital Long QT Syndrome	High Ziprasidone Dose
Recent Acute Myocardial Infarction	Bradycardia
Uncompensated Heart Failure	Elderly Females
Use with Other Drugs that Prolong the QT Interval	Pre-existing cardiac arrhythmias

\* Geodon (ziprasidone) prescribing information, revised 12/2010. Pfizer Inc. New York, NY. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=584> [last accessed July 7, 2012].

Date

Joe Black  
2810 N. Parham Road  
Richmond, VA 23294

**RE: Atypical Antipsychotics: Coordination of Care**

Dear Dr. <<NAME>>:

The goal of this quality management program is to assist you in caring for your patients using atypical antipsychotic (AA) medications. This program is based on recommendations for AA use from manufacturer product labeling, the American Psychiatric Association, the AHRQ PORT treatment recommendations, and recently published literature. These recommendations are designed to assist you in maximizing outcomes and promoting patient safety.<sup>1-5</sup>

Claims data indicate that in the West Virginia Medicaid Program there are approximately 9,000 individuals being treated with AAs. This treatment included 36,082 prescriptions for AAs in a recent 90 day period at the total cost of \$9,678,783.

**West Virginia Medicaid Specific Data**

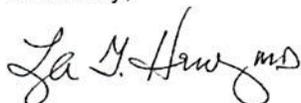
<b><i>Atypical Antipsychotic Indicators</i></b>	<b><i>Number of Patients with Opportunities*</i></b>
• Identify duplicate therapy with antipsychotic medications involving more than one prescriber	247
• Evaluate blood glucose levels in patients with Type I or Type II diabetes mellitus being treated with atypical antipsychotics	539
• Consider potential metabolic effects of atypical antipsychotics in obese patients	136
• Identify potentially significant cardiac risk factors that should be considered when using ziprasidone	268
• Identify chronically nonadherent patients who may be candidates for long-acting antipsychotic injection	192

\*Based on data through July 2012

**The enclosed patient profiles reflect one or more of the above issues and are provided as a chart reminder for when your patients return for their next appointments.**

We acknowledge that there may be clinical variables influencing an individual patient's management that are not apparent in claims data or that a patient may have been inadvertently identified as being under your care. We thank you for reviewing this information and caring for West Virginia Medicaid patients and welcome the opportunity to discuss any comments or concerns you may have about our quality management program. Please feel free to call our office at 1-866-923-7208 with questions or concerns.

Sincerely,



Lyle Henry, MD, FACS,  
Medical Director

### Atypical Antipsychotics: Coordination of Care

- Eliminate unintentional **duplicate therapy** with antipsychotic medications involving more than one prescriber. Use of more than one antipsychotic simultaneously has not been shown to improve outcomes and may increase adverse events.
- Consider potential destabilizing effects on blood glucose levels when selecting the most appropriate atypical antipsychotic for use in patients with **Type I or Type II diabetes mellitus** (see Table 1).
- Consider potential metabolic effects when selecting the most appropriate atypical antipsychotic for use in patients who are **obese** (see Table 1).
- Identify potentially **significant cardiac risk factors** that should be considered when using ziprasidone
- Identify **chronically nonadherent patients** who may be candidates for long-acting antipsychotic injection therapy to improve adherence and enhance potential outcomes.

#### Selected References (full reference list available upon request):

1. Center for Drug Evaluation and Research (CDER), United States Food and Drug Administration. Prescribing information by drug available at: [http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Search\\_Drug\\_Name](http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Search_Drug_Name) [last accessed July 2011].
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3. Practice Guidelines for the treatment of patients with schizophrenia. American Psychiatric Association web site. Available at [http://psych.org/psych\\_pract/](http://psych.org/psych_pract/). [last accessed July 2011].
4. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. Diabetes Care. 2004; 27:596-601.
5. Velligan DI, Weiden PJ, Sajatovic M, et al. Strategies for addressing adherence problems in patients with serious and persistent mental illness: recommendations from the expert consensus guidelines. J Psychiatr Pract. 2010; 16:306-24.

**Table 1: Side-Effect Profiles\*<sup>%</sup>**

Generic Name (Brand Name) [# = not first line]	Recommended Daily Dose (Max. Dose)	Adverse Effect Risk				
		Anticholinergic Effects	EPS	Orthostatic Hypotension	Sedation	Metabolic Changes
Aripiprazole (Abilify <sup>®</sup> )	5mg – 15mg (30 mg/day)	0	0 - +	+	+	0 - +
Asenapine (Saphris <sup>®</sup> )	10mg – 20mg (20 mg/day)	0	0 - ++	++	++	+ - ++
# Clozapine (Clozaril <sup>®</sup> )	300 mg - 600mg (900 mg/day)	++++	0	++++	+++	++++
Iloperidone (Fanapt <sup>®</sup> )	12mg – 24mg (24 mg/day)	0+	0 - +	+++	++	+ - ++
Lurasidone (Latuda <sup>®</sup> )	40mg – 80mg (120 mg/day)	0	0 - ++	++ - +++	++ - +++	0 - +
Olanzapine (Zyprexa <sup>®</sup> )	5mg – 20mg (20 mg/day)	++	0 - +	++	++	++++
Paliperidone (Invega <sup>®</sup> )	6mg – 9mg (12 mg/day)	0	0 - +++	++	+	++
Quetiapine (Seroquel <sup>®</sup> )	300mg – 800mg (800 mg/day)	0 - +	0	++	+++	++
Risperidone (Risperdal <sup>®</sup> )	0.5mg – 6mg (16 mg/day)	0	0 - +++	++	+	++
Ziprasidone (Geodon <sup>®</sup> )	80mg – 160mg (200 mg/day)	0	0 - ++	++	+	0 - +

0 = very rare effects, + = low incidence of side effects, ++ = moderate incidence of side effects,

+++ = high incidence of side effects, ++++ = very high incidence of side effects

\* Burnham TH, editor. Drug Facts and Comparisons. <http://www.drugfacts.com> [last accessed 07/11]

% Official Prescribing Information, available at: <http://www.fda.gov/Drugs/default.htm> [last accessed 07/11]