

# DUR Capsules

News and Information for West Virginia Providers from the West Virginia Bureau for Medical Services (WVBMS)

## Medicaid Integrity Provider Education Program Focus on Atypical Antipsychotics February, 2013

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### Introduction

The Deficit Reduction Act (DRA) of 2005, which was signed into law in February of 2006, created the Medicaid Integrity Program (MIP) under section 1936 of the Social Security Act (the Act). The MIP is the first comprehensive Federal strategy to prevent and reduce provider fraud, waste, and abuse in the \$300 billion per year Medicaid program. The Centers for Medicare and Medicaid Services (CMS) has two broad responsibilities under the MIP:

- To hire contractors to review Medicaid provider activities, audit claims, identify overpayments, and educate providers and others on Medicaid program integrity issues.
- To provide effective support and assistance to States in their efforts to combat Medicaid provider fraud and abuse.

Moreover, in November of 2009 the President signed Executive Order 13520 which called for the reduction of improper payments in the major programs administered by the Federal Government by intensifying efforts to eliminate payment error, waste, fraud, and abuse.<sup>1</sup> These two initiatives resulted in the need for a program that would enhance awareness of and educate providers and other stakeholders about Medicaid fraud, waste and abuse. More specifically, CMS was tasked with identifying ways to improve access to information necessary to ensure accurate coverage and reimbursement determinations and to find solutions to decrease fraud, waste, and abuse associated with prescription drug utilization and diversion.

As part of the MIP, the Center for Program Integrity, Medicaid Integrity Group (MIG), in collaboration with States, is providing education resources through its Education Medicaid Integrity Contractor (Education MIC) to promote best practices for therapeutic drug classes that have been identified as having high potential for improper payment.<sup>2</sup> These best practices are designed to combat overprescribing and/or overutilization while enhancing quality of care. Educational materials are focused on the importance of prescribing medications for the indications and within the dosage guidelines approved by the U.S. Food and Drug Administration (FDA). Five therapeutic drug classes that have been consistently found among the top ten highest potential improper payments in Medicaid have been identified as:

- atypical antipsychotics
- proton pump inhibitors (PPIs)
- stimulants
- anticonvulsants
- antidepressants

This newsletter will focus on the MIP / Education MIC materials related to the atypical antipsychotics.

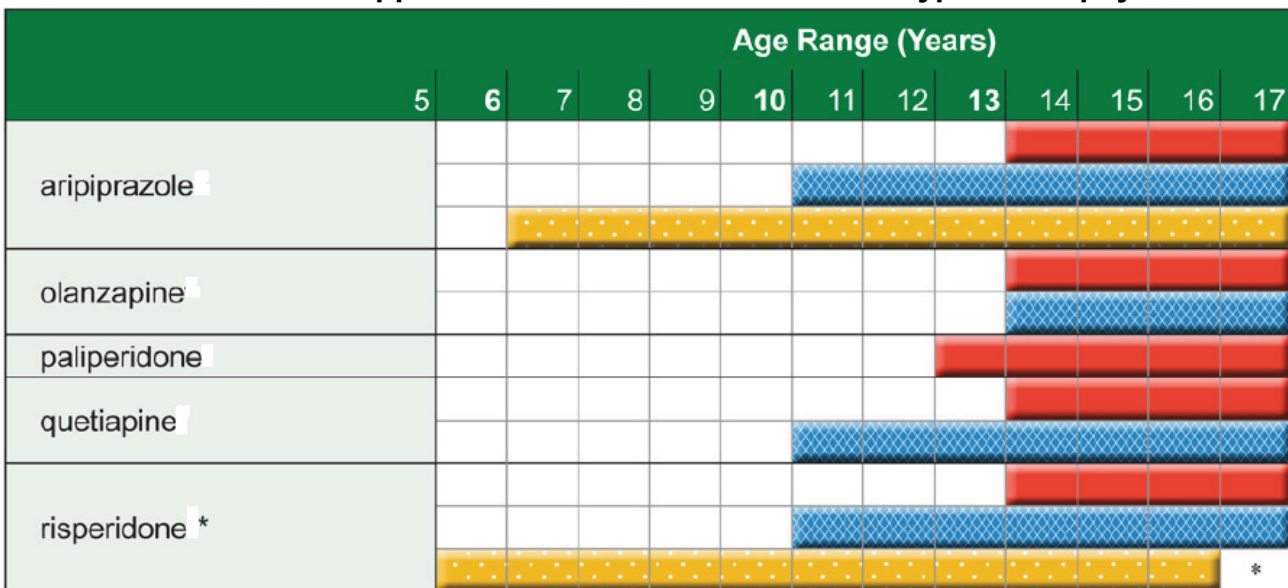
### Atypical Antipsychotics

Atypical antipsychotics (AAs), as their name implies, were originally researched and developed to treat psychosis, especially in schizophrenia. The first agent, clozapine, was introduced into the United States market in 1989, but its adverse effects profile limited its use. Other agents soon followed and, over the years since their introduction to the market, various AAs have been studied in conditions other than schizophrenia.<sup>3,4</sup> Currently there are ten AAs available and their FDA approved indications are shown in Table 1 (adults) and Table 2 (children).

**Table 1. FDA Approved Adult Indications for Atypical Antipsychotics<sup>5</sup>**

| Medication   | FDA Approved Indications |           |                 |                            |
|--------------|--------------------------|-----------|-----------------|----------------------------|
|              | Schizophrenia            | Bipolar I | Schizoaffective | Major Depression (adjunct) |
| Aripiprazole | X                        | X         |                 | X                          |
| Asenapine    | X                        | X         |                 |                            |
| Clozapine    | X                        |           |                 |                            |
| Iloperidone  | X                        |           |                 |                            |
| Lurasidone   | X                        |           |                 |                            |
| Olanzapine   | X                        | X         | X               | X                          |
| Paliperidone | X                        | X         | X               |                            |
| Quetiapine   | X                        | X         |                 | X (XR form only)           |
| Risperidone  | X                        | X         |                 |                            |
| Ziprasidone  | X                        |           |                 |                            |

**Table 2. FDA Approved Pediatric Indications for Atypical Antipsychotics<sup>5</sup>**



■ schizophrenia   ■ bipolar I disorder: manic or mixed   ■ irritability with autistic disorder

\*Risperidone should not be used by patients older than age 16 who have been diagnosed with irritability with autistic disorder.

**Clinical Use**

A review of clinical use of available AAs is beyond the scope of this newsletter, but the Schizophrenia Patient Outcomes Research Team (PORT) has published treatment recommendations for the use of atypical antipsychotics by patients with schizophrenia. Information on the PORT recommendations can be found at <http://www.ahrq.gov/clinic/schzrec.htm> on the Agency for Healthcare Research and Quality (AHRQ) website.<sup>6</sup> In addition, AHRQ hosts a database of treatment guidelines, the National Guideline Clearinghouse at <http://www.guideline.gov>.<sup>7</sup> It is a searchable site and searches can be done using “atypical antipsychotics,” or any of the conditions for which an atypical antipsychotic is an indicated treatment, for information on the available treatment guidelines. FDA approved dosing recommendations for various indications as well as other information about clinical use is available by drug in the official prescribing information.<sup>5</sup>

## Off-Label Use

Despite several of the AAs having multiple FDA approved indications, off-label use of these agents appears to remain quite common. AHRQ has evaluated off-label use of AAs and published two reviews of their findings, the first in 2007 and most recently in 2011.<sup>8,9</sup> Two populations where off-label use tends to be quite common are in the elderly and in children and adolescents.

In the elderly AAs (as well as older typical antipsychotics) have been quite commonly used in an attempt to manage behavioral disorders in the presence of dementia. The benefits of such use are marginal in the absence of overt psychotic symptoms and, especially for AAs, the risks are relatively high. In 2005 the FDA issued a public health advisory indicating that atypical antipsychotics have been associated with a 1.6 to 1.7 fold increased risk of death when used in this population.<sup>10</sup> None of the AAs are FDA approved for use in elderly dementia patients and at this time the official prescribing information for all agents includes a “Black Box Warning” cautioning against such use.

In children and adolescents one of the common areas of off-label use is in the management of behavioral symptoms of Attention Deficit/Hyperactivity Disorder (ADHD).<sup>9</sup> Unfortunately, most of the agents do not have published data available to support such use. Risperidone is the only agent with published trials and they show limited evidence of efficacy for such use. The same can be said for use of AAs in other childhood disorders that frequently involve behavioral problems such as conduct disorder, oppositional defiant disorder, or disruptive behavior not otherwise specified.<sup>11</sup> There is insufficient data at the present time to support such use as being safe and effective.

## Adverse Effects

AAs as a class are associated with common potential adverse effects, although the actual risk for individual problems varies from agent to agent. These common problems include: metabolic changes (weight gain and changes in blood glucose and lipid levels); extrapyramidal effects (EPS); sedation; orthostatic hypotension; changes in serum prolactin levels and menstrual problems. These effects should be monitored for in all patients. In addition, the agents used in the management of depression have the same “Black Box Warning” that appears on all antidepressant agents related to the risk of suicidality.

Specific agents also have unique adverse warnings in their official prescribing information related to risks identified in studies of their use that are not necessarily true of the class.<sup>5</sup> These include:

**Clozapine:** use is associated with agranulocytosis, seizures, myocarditis, and orthostatic hypotension. It has also been linked to respiratory arrest and cardiac arrest in patients taking benzodiazepines. Because of the risk of agranulocytosis, clozapine is only available through a distribution system that ensures monitoring of WBC count and ANC prior to delivery of the next supply of medication.

**Asenapine:** use is associated with the risk of serious Type I hypersensitivity reactions that may include anaphylaxis, angioedema, difficulty breathing, hypotension, rash, swollen tongue, tachycardia, or wheezing.

**Olanzapine Pamoate Injection:** a long-acting atypical antipsychotic that has been associated with delirium and sedation, such as that typically seen in a patient with an olanzapine overdose. Because of the severity of this potential adverse reaction, it may only be given in a registered healthcare facility, is only available through a restricted distribution program, and may not be dispensed directly to the patient.

## Specific to Pediatric Patients:

**Aripiprazole:** The incidence of EPS in adults diagnosed with schizophrenia who were being treated with aripiprazole monotherapy was 13 percent versus 12 percent for placebo. In pediatric patients (13 to 17 years old) the percentage of EPS-related events was 25 percent versus 7 percent for placebo.

**Olanzapine:** Adolescents who take olanzapine have an increased potential for weight gain and hyperlipidemia compared with adult patients who take olanzapine. Prescribing information for olanzapine states: “Clinicians should consider the potential long-term risks when prescribing to adolescents, and in many cases this may lead them to consider prescribing other drugs first in adolescents.”

**Quetiapine:** In clinical trials for quetiapine, an increased risk of hypertension existed for pediatric patients. Baseline blood pressure and periodic monitoring is recommended in children and adolescents.

## Conclusion

AAs have largely replaced the older, typical antipsychotics in clinical use, despite limited evidence that they are actually significantly more effective. They do have a lower incidence of EPS if used in recommended doses, but they are not free of that risk which includes the development of potentially irreversible Tardive Dyskinesia (TD). In addition, AAs have an increased risk of inducing undesirable metabolic changes compared to older agents. They have been demonstrated to be effective medications for several disorders, but also tend to be used for conditions for which data is lacking regarding safety versus efficacy. In addition, due to the generally linear relationship between dose and dopamine (and other) receptor occupancy, if they are used at higher than recommended doses their adverse effect profile may outweigh their potential benefits. It is therefore important to be aware of and attempt to follow official prescribing information guidelines when using these medications.

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The DUR Capsules is a quarterly newsletter published for West Virginia Medicaid Providers. Information concerning West Virginia Medicaid can be accessed online at <http://www.dhr.wv.gov/bms/>

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