THE OREGON STATE DRUG REVIEW©
AN EVIDENCE BASED DRUG THERAPY RESOURCE http://pharmacy.oregonstate.edu/drug-policy/newsletter
July 2019 Volume 9, Issue 5

Oregon Health Authority Mental Health Clinical Advisory Group (MHCAG) Recommendations for the Treatment of Schizophrenia

Kathy Sentena, Pharm. D., Drug Use and Research Management Program, Oregon State University College of Pharmacy

There is an expansive need for quality behavioral and mental health services across Oregon. In response, the 2017 Oregon Legislature passed House Bill 2300 which directs the Oregon Health Authority (OHA) to convene a Mental Health Clinical Advisory Group (MHCAG) to develop evidence-based treatment algorithms.[1] Their recommendations are designed to improve access to care for medication assistance recipients with behavioral health disorders and to standardize treatment recommendations. In March of 2019, the MHCAG released their first set of recommendations focusing on the treatment of schizophrenia.[1] This newsletter will summarize their recommendations, describe opportunities with the Oregon Psychiatric Access Line (OPAL) and provide cost-comparison data.

MHCAG Schizophrenia Treatment Recommendations

The MHCAG was asked to develop criteria for managing schizophrenia, specifically focusing on the following:

- Efficacy of the drug
- Cost of the drug
- Potential drug side effects
- Patient's history of the drug

The group advocates for a collaborative approach between providers and patients to choose evidence-based medication therapies that provide efficacy and value.[1] Previous reviews of the literature have found a lack of high-quality evidence in differences between the comparative efficacy or harms, or benefits of oral versus injectable dosage forms, of antipsychotics in the management of schizophrenia.[2] Therefore, MHCAG recommendations were based on evidence and incorporation of expert opinion.

The MHCAG recommendations for schizophrenia are separated into: 1. acute psychosis and 2. stabilization and management.[1] Medications are an integral component of both scenarios. Factors that assist in choosing the most appropriate treatment are based on patient response and adherence to their current medication regimen.[1] The MHCAG treatment algorithms are divided into: starting second generation antipsychotics, use of first generation antipsychotics and alternative medication treatments in schizophrenia.

Antipsychotic recommendations are based on therapies that provide the greatest value and cost-effectiveness.[1] First-line treatment recommendations for generic second-generation antipsychotics include aripiprazole, risperidone, or paliperidone.[1] These agents are available as both oral formulation and long-acting injectable (LAI). Due to its improved safety profile, aripiprazole is recommended for patients who want to minimize the following:

- Weight gain and diabetes
- Pseudoparkinsonism and tardive dyskinesia
- High cholesterol
- Prolactin elevation

Risperidone or paliperidone are recommended for patients who want to minimize the risk of:

- Akathisia
- Treatment emergent activation or agitation

Patients who have an inadequate response after 2 to 6 weeks of therapy should switch to one of the other first-line treatments.[1] If an adequate response is obtained after 2 to 4 weeks then a LAI can be considered, especially in those patients who have the potential for nonadherence or a history of serious antipsychotic episodes that resulted in admission (**Table 1**). Additionally, LAIs are associated with a higher cost, which could be a potential barrier for some patients (**Figure 1**). Long-acting injectables should only be started if the patient has used the oral form and received a benefit with no or tolerable side effects.[1] The dose of LAI should be approximated based on the oral medication dose. Depending on the LAI, the oral form may be discontinued immediately or continued for 2 to 4 weeks.[1]

Table 1. Long-acting Second Generation Antipsychotic Injectables[1,3]

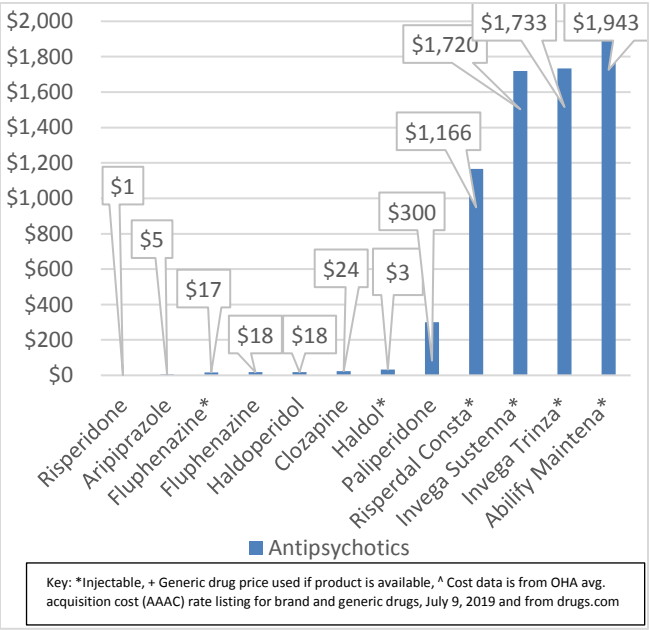
Generic Name*	Brand Name	Maintenance Dosing Interval	Oral supplementation during LAI initiation
Aripiprazole	Abilify Maintena®	Monthly	14 days of concurrent oral antipsychotic
Aripiprazole lauroxil	Aristada®	Monthly, every 6 weeks or every 8 weeks	A single 30 mg oral aripiprazole dose‡ or 21 days of oral aripiprazole
Risperidone	Risperdal Consta®	Every 2 weeks	3 weeks of concurrent oral antipsychotic
Paliperidone	Invega Sustenna®	Monthly	None

Paliperidone pamitate	Invega Trinza®	Once every 3 months	None
Risperidone	Perseris®)	Monthly	None

Abbreviation: LAI – long-acting injectables
* All treatments are preferred therapies on the OHA preferred drug list
ǂ In conjunction with Aristada Initio injection

Patients with predominately positive symptoms and need to minimize cardiometabolic risk, may be considered for a first generation antipsychotic. Fluphenazine or haldoperiodol are recommended first-line by the algorithm.[1] Two to four weeks of therapy are required to determine if an adequate response is obtained. If appropriate, a 2-week LAI (fluphenazine) or 4-week LAI (haldoperidol or Haldol Decanoate®) may be an option.[1]
If the patient fails two first-line therapies, of either first or second generation antipsychotic, then clozapine is recommended.[1] Clozapine is a viable alternative even though it is often underutilized due to monitoring requirements and risk of adverse reactions (e.g., central nervous system [CNS] and agranulocytosis). A six month trial is required to determine an adequate response to clozapine. Clozapine should not be used in patients with a history of clozapine-induced agranulocytosis, severe CNS depression or delirium, coma, history of clozapine-induced myocarditis or cardiomyopathy, pretreatment absolute neutrophil count (ANC) less than 1500 cells/cubic mm^3, uncontrolled seizure disorder or inability to adhere to lab monitoring.[1] Clozapine is also associated with multiple drug interactions mediated through cytochrome P450 enzymes and a full review of the patient's medication profile should be completed before drug initiation. Comparative costs of select antipsychotics are presented in **Figure 1**.

Figure 1. Thirty-Day Cost of Common Antipsychotics[+^]



Key: *Injectable, + Generic drug price used if product is available, ^ Cost data is from OHA avg. acquisition cost (AAAC) rate listing for brand and generic drugs, July 9, 2019 and from drugs.com

Antipsychotic use may cause serious and/or bothersome adverse reactions, which may be minimized by using the lowest effective dose. Regular laboratory monitoring (e.g., hemoglobin A1c [HbA1c], complete blood count [CBC], lipids, thyroid screen) will aid in detection and management of potential adverse reactions.[1] Patients should be monitored for indicators of parkinsonism, acute dystonia, akathisia and tardive dyskinesia.[1] Validated assessment tools and detailed options for the management of adverse reactions associated with antipsychotics are available in the full MHCAG report.[1]

Dosing Management

The MHCAG recommends that a 6 to 8 week titration up to the maximum tolerated antipsychotic dose is considered an adequate trial for acute treatment.[1] The FDA maximum daily dose should not be exceeded. Patients who have been stable on a medication regimen for 6 to 12 months can be considered for dosage reduction and possibly discontinuation of their antipsychotic. A maintenance dose of an antipsychotic is often lower than the acute treatment dose. The general recommendation for dose lowering is to gradually decrease the dose over 3 months until medication is discontinued or symptoms of psychosis return.[1] Clozapine can be associated with rebound psychosis, and therefore, should be tapered slowly. Tapering LAI can be difficult because clinical changes often lag 1 to 3 months after a dose has been changed. Oral supplementation may be needed for symptom reoccurrence.[1]

The Oregon Psychiatric Access Line (OPAL)

Optimal management of patients with behavioral mental health conditions often requires utilization of a variety of health care resources. In additional to standardized care through treatment algorithms, access to psychiatric consultation is a vital resource to improve care. The Oregon Psychiatric Access Line offers medication consultation for providers provided by Oregon Health and Science University (OHSU).[1] The purpose of OPAL is to allow high quality behavioral advice for Oregon youth and adults via timely psychiatric consultation, medical practitioner education and connections with mental health professionals throughout the state.[2] Providers must register with OPAL, which allows access to the following services:

- Free, same-day adult and child psychiatrist phone consultation
- Medical practitioner education
- Connection to mental health professionals around the state of Oregon

OPAL Consultation Line
Phone: 503-346-1000 (providers only)
Web: www.ohsu.edu/school-of-medicine/child-and-adolescent-psychiatry/oregon-psychiatric-access-line

Conclusion

There are many opportunities for improvements in the care and treatment of behavioral health conditions in the state of Oregon. The recommendations provided by MHCAG, along with the collaborative expertise provided by OPAL, is a viable pathway to improve the access and quality of care provided to patients with schizophrenia. Treatment algorithms and detailed guidance on the recommendations summarized in this newsletter are available at: https://apps.state.or.us/Forms/Served/le7548.pdf .[1]

References:

1. Mental Health Clinical Advisory Group. Mental health care guide for licensed practitioners and mental health professionals. Salem, OR: Oregon Health Authority; March 2019. OHA 7548. Available at: https://apps.state.or.us/Forms/Served/le7548.pdf . Accessed on July 9, 2019.
2. Oregon State University Drug Use Research and Management Program. Literature Scan: Antipsychotics. March 2019. Available at: https://www.orpdl.org/durm/meetings/meetingdocs/2019_03_21/archives/2019_03_21_Antipsychotics_LitScan.pdf. Accessed July 13, 2019.
3. Perseris prescribing information. Indivior Inc., North Chesterfield, VA. 2018.