

Wyoming Drug Utilization Review

Treatment with Multiple Antipsychotic Medications

Ashley Stromberg, PharmD

In patients that have been diagnosed with a psychological disorder, such as schizophrenia, pharmacological treatment is the mainstay of therapy. There is no cure for psychological illnesses at the current time; therefore, symptom control is the goal of treatment with antipsychotic medications. The majority of patients with psychological illness will experience a significant decrease in function within the first five years; consequently, aggressive

pharmacological therapy is essential within this time frame.¹ Many patients will not receive adequate response to the initial prescription of a single medication. A patient will be deemed to have treatment resistance once the patient has failed two separate treatments with antipsychotic medications, including a first generation and a second generation antipsychotic. Once a patient has failed two antipsychotic medications, a second medication is often added to an initial medication in order to increase efficacy. Even though treatment with multiple antipsychotic medications is frequently seen in clinical practice, it is not fully described in the treatment guidelines.^{1,2}

According to the National Institute for Health and Clinical Excellence (NICE)

guidelines, several factors should be considered prior to implementation of multiple antipsychotic medications.² First, the initial diagnosis of the patient's psychological illness should be reviewed. If the initial diagnosis was incorrect and the patient was experiencing psychosis from a secondary origin, then this could explain the reason for treatment failure. If the patient is experiencing psychosis from a secondary origin, the underlying cause should be treated, and then the patient should be reevaluated. Second, patient compliance should be investigated, as well as determining if the patient's dose and duration of initial antipsychotic medication is appropriate.² Patients with psychological illnesses often have poor compliance with their medications due to denial of psychological illness, inadequate information about illness or medication, symptoms of paranoia or grandiosity, no supposed need for medication, experienced side effects, theoretical "allergies", or an increased number of prescribed medications or daily doses.¹ Lastly, patients should be involved with cognitive behavioral therapy (CBT), which helps patients to restore improper thoughts with healthy, reasonable ways of thinking.¹

Adding a second antipsychotic medication for patients that have failed with a single treatment is seen in up to 60% of patients clinically.^{3,4} However, a number of patients may continue to have inadequate response after the implementation of multiple antipsychotics. Concerns that are seen with treatment of multiple antipsychotic medications include: a higher total medication dose; an increased side effect profile; decreased patient compliance; and providers' hindered ability to determine which medication the patient is responsive to.^{5,6} In order to optimize treatment with multiple antipsychotics, medications with different mechanisms of action should be implemented, such as a first-generation medication in combination with a second-generation medication. The patient

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Wyoming Drug Utilization Review
University of Wyoming
School of Pharmacy
Dept. 3375
1000 E. University Ave
Laramie, WY 82071
307-766-6750

www.uwyo.edu/DUR

Edited by
Aimee Lewis, PharmD, MBA
Laura Miller, MS

P & T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on February 16, 2012. Highlights of this meeting include:

The following prior authorization was approved:

Berinert and Firazyr will require prior authorization and will be approved only with lab-confirmed diagnosis and following 6 – 12 months of treatment in the physician’s office.

Ferriprox will be limited to patients with transfusional iron overload due to thalassemia syndromes.

Onfi will be limited to patients with Lennox-Gastaut syndrome.

Edluar, Zolpimist, Intermezzo will require prior authorization and will be approved for those who are unable to swallow zolpidem tablets.

Ivermectin will require prior authorization and will be approved in patients with strongyloidiasis of the intestinal tract, onchocerciasis and resistant head and body lice.

All proposed prior authorization criteria will be posted for public comment at www.uwyo.edu/DUR. Comments may be sent by email to alewis13@uwyo.edu or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to March 31, 2012.

The next P&T Committee meeting will be held May 17, 2012 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

WYDUR Mission Statement

The mission of Wyoming Drug Utilization Review (WYDUR) is to enhance quality of patient care by assuring appropriate drug therapy, optimal patient outcomes, and education for health care providers.

Goal 1:

Criteria and standards developed by WYDUR shall be clinically relevant and derived through evaluation of peer-reviewed literature, compendia, guidelines obtained from professional groups, health care providers, data and experience obtained by WYDUR.

Goal 2:

Criteria and standards developed by WYDUR shall be non-proprietary and shall be developed and revised through a consensus process. The criteria and standards development and revision process shall consider timely public comment before adoption.

Goal 3:

The costs of drug therapy shall be considered after clinical and patient considerations are addressed.

Goal 4:

WYDUR shall provide consistent education to providers and the public.

2012 P & T Committee Meeting Dates

May 17, 2012

August 30, 2012

November 15, 2012

Meeting time: 9 am - 1 pm

Location: Laramie County Community College,
Cheyenne

All meeting dates and times are subject to change.

Treatment with Multiple Antipsychotic Medications, continued

should be treated with monotherapy lasting for no less than four to nine weeks to determine treatment failure before addition of a second antipsychotic medication.^{6,1} It should be documented in the patients profile as to which medications have been previously used and deemed ineffective. When the clinician is to implement a polytherapy regimen, it is recommended that medications that have not been attempted prior be used.

Many studies have evaluated the efficacy and safety of treatment with multiple antipsychotic medications. Kreyenbuhl et al. showed that patients that were most likely to be prescribed treatment with multiple antipsychotics were younger, unmarried, admitted to the hospital within the last year for a psychological related issue, and had military service-connected disability or co-morbid depression or substance abuse.⁷

Most studies have implied that the addition of clozapine will add the most response for a patient that has shown no benefit from other medications.^{4,6} The NICE guidelines state that clozapine should be implemented with a second-generation antipsychotic medication to optimize the use of multiple mechanisms of action.² Many clinicians often choose not to follow the recommendation to combine medications with different mechanisms of action; it depends on clinical response of the patient as well as clinician preference. Centorrino et al. state that the most commonly seen combinations of antipsychotic medications were olanzapine with haloperidol, olanzapine with quetiapine, and olanzapine with risperidone.³ It is recommended that combination therapy be limited to a twelve weeks.³ If no improvement is seen, one medication should be tapered off and a different medication be implemented. If the medication combination does illicit a response, both of the medications can be titrated to the upper end of the dosage range and the patient should be reevaluated within twelve weeks.¹

In conclusion, treatment with multiple antipsychotic medications is not covered in the treatment guidelines for psychological illnesses, but is becoming more commonly seen in clinical practice. In order for implementation of multiple

antipsychotic medications to be practical, a patient must have failed four to nine weeks of treatment with two different medications including a first-generation medication and a second-generation medication. It is recommended that clozapine be first-line for the addition of a secondary antipsychotic medication. Included in the treatment with multiple medications should be a first-generation and a second-generation medication in order to optimize the use of multiple mechanisms of action. Many patients will not benefit from treatment with a single antipsychotic medication, therefore, upon clinician judgment; multiple antipsychotic medications may be prescribed to control patient symptoms.

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6. Schumacher JE, Makela EH, Griffin HR. Multiple antipsychotic medication prescribing patterns. *Ann Pharmacother*. 2003;37:951-955.
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University of Wyoming
School of Pharmacy
Dept. 3375
1000 E. University Avenue
Laramie, WY 82071

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