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Review of Atypical Anti-psychotics under the Ontario Drug Benefit Program and Drug Class Review

Placing limits on drug coverage has become a popular cost-containment strategy for both public and private health care programs in the United States and other countries, including Canada.[1] *However, many programs have excluded procedural barriers to medication access for the most vulnerable, high-risk patients with severe and long-term physical and mental illnesses for whom careful selection of medications can prevent relapses, hospitalization, incarceration or even death.*

Ontario Drug Benefit Reviews

The provincial government is planning a review of all atypical antipsychotic medications in the provincial formulary for the treatment of schizophrenia and other psychotic disorders: [2]

- risperidone (1995) *Risperdal*
- olanzapine (1996) *Zyprexa*
- quetiapine (1998) *Seroquel*

Drug reviews are performed by the Drug Quality and Therapeutics Committee, a sub-committee of the Ministry of Health and Long Term Care, to ensure that the medications in the Ontario Drug Benefit (ODB) program meets current standards of **safety**, **efficacy** and **cost-effectiveness** in light of the most recent clinical knowledge and practice guidelines. [3]

The Burden of Mental Illness

The economic, clinical and personal burdens associated with serious psychiatric disorders makes them a leading health problem in our society. Persons experiencing a psychotic episode usually suffer tremendous distress and may engage in actions that are dangerous to themselves and others. Their lives are already at risk and the inappropriate and sub-optimal choice of treatment can have devastating consequences, not only for the individual but also his/her family and friends as well as the community.

- Both schizophrenia and bipolar disorder are life-threatening diseases with severe and persistent symptoms.
- Schizophrenia accounts for the use of 1 in 12 hospital beds in Canada.
- Overall annual costs of the disease are estimated at $2.3 billion in direct costs and an additional $2 billion in indirect costs.
- A large percentage of our homeless population has a mental illness.

[1] Ontario spends $2.6 billion on its drug program, which still represents just 9% of its health care budget. (2002/03 Report Card for the Ontario Drug Program).

[2] There are more than 100 potential pharmaceutical agents for a variety of mental disorders that are either in human clinical testing or waiting approval. Persons in the United States already have access to two new antipsychotics, ziprasdinone (2001) *Geodon* and aripiprazole (2002) *Abilify*.

[3] Rapidly rising spending for psychotropic drugs, particularly antipsychotics and antidepressants, is a growing concern for provincial and state drug programs.

The Right Choice at the Right Time

Atypical psychotropic drugs are the most effective treatment for acute episodes or exacerbations of serious mental illnesses such as schizophrenia and bipolar disorder.

- Antipsychotics have revolutionized the treatment of both schizophrenia and bipolar disorder enabling many patients to return to a productive life.
- The new generation of psychotropic medications is more efficacious (i.e., they reduce symptoms and have fewer side effects), encouraging patient compliance and reducing the frequency of relapses.
- Although the three agents are grouped together as "atypical antipsychotics," they have distinct pharmacological profiles and are not interchangeable.
- These drugs target different chemical imbalances within the brain resulting in different clinical outcomes.
- The routine substitution of one drug for another may have disastrous effects.
- Physicians determine choice based on the profile of each individual patient and expected best outcomes.
- It is impossible to predict which medication will ultimately be effective.
- Timely use of the most effective drug therapies, as determined by the treating physician can result in fewer relapses and hospitalizations, reduced risk of suicide, reduced disability, reduced family and relationship disruptions.
- Creating barriers by denying or delaying access to appropriate first-line treatment can have significant harmful effects on the functioning and long-term benefit for psychiatric patients.
- The longer it takes to have access to the right medication, the more severe the symptoms of the illness.
- Each relapse is followed by further deterioration in the patient's functioning.
- If treatment fails, the chance of recovery diminishes significantly..

Limiting access

While the atypical antipyschotics are more effective providing better outcomes and fewer side effects,[4] they are also more costly than the first-generation of antipsychotics developed 40 years ago because of the complexity of their chemical properties.[5] There is also better adherence to the new medications and therefore their overall usage has increased substantially. As a result, atypical antipsychotic drugs are particularly vulnerable within the following cost-cutting programs:

1. *Formulary listings*: Virtually all health care programs (public and private) have "formulary" lists of prescription drugs that have been approved for reimbursement under a drug benefit program.

[4] Historically, outcomes for persons with serious psychiatric disorders have been poor due to non-adherence to treatment because of intolerable side effects.

[5] The average monthly cost of treating a patient with schizophrenia is approximately $200, still considerably less than the average monthly cost of treating individuals with HIV-AIDS and many cancer patients. The variance in the average cost per day (for the average patient with schizophrenia) of the three antipsychotics in the provincial formulary is less than $1.25 per day.

2. *Special authorization*: Physicians may also request reimbursement for a drug not listed in the formulary if it is a medical necessity.

3. *Cap*: Some programs have imposed a limit on the number of prescriptions for reimbursement that can be written within a 12-month period.[6]

4. *Fail-first system:* This has become a common approach to limit the expenditures for newer, more expensive medications. Newfoundland changed its coverage status in August 2004 denying its physicians open access to olanzapine [7] with the following exceptions: failure or intolerance to an adequate trial of no less than four weeks each of risperidone **and** quetiapine. [8]

Failure is defined by the government as a lack of satisfactory clinical response to prior treatments after an adequate trial period at maximum recommended therapeutic dosages.

Intolerance is defined as the inability to achieve adequate benefit because of intolerable adverse side effects.

The fail-first system creates unacceptable delays in treatment that may result in:
- poor clinical outcome with intolerable side effects
- non-compliance in the use of medications
- significant increase in emergency visits, hospital admissions and lengthier stays
- greater pressure on the case management system and community services
- increased risk of death by suicide during a psychotic or delusional phase.
- increased risk of entering the criminal justice system
- increased risk of becoming homeless

Best Medicines Approach

Creating barriers by denying or delaying access to appropriate first-line treatment for persons suffering from schizophrenia or bipolar disorder clearly is not in the patient's best interest when time is of the essence to reduce their symptoms, prevent a relapse requiring hospitalization, incarceration or even death.[9] However, not all medications work for all people. Individual responses are highly variable. Therefore, physicians who have the medical training and expertise as well as the scientific evidence and knowledge must have access to the most appropriate psychotropic medications in their clinical judgment for the most effective treatment of each patient.

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[6] In New Hampshire, the cap was discontinued when there was an immediate drop in the use of antipsychotics and a sharp increase in the use of emergency mental health and hospital services.

[7] Doctors in British Columbia, Saskatchewan, Nova Scotia, Prince Edward Island and New Brunswick are also faced with restrictions when determining which antipsychotics is the best choice for their patient.

[8] Olanzapine may be prescribed to patients with a diagnosis of bipolar disorder who are in a manic phase for an initial approval of a maximum of 12 weeks.

[9] In the United States, several states have included exemptions in their health care policies and some have enacted legislation to protect mental health medications, including all antipsychotics and anti-depressants, from cost controls.