From October 2012 through October 2013, 360,435 claims were dispensed for antipsychotic agents for the Connecticut Medical Assistance Program. Those claims represent 42,071 unique patients who received at least one claim for an antipsychotic agent.

Out of the 42,071 patients receiving an antipsychotic agent, 2,479 patients received at least 2 different agents concurrently for at least 90 days. It is typically recommended that cross titration between antipsychotic agents be finished in 8 weeks or less; the concurrent use for more than 90 days likely represents longer term polypharmacy. There were 152 patients who received 3 different agents concurrently for at least 90 days and 9 patients who received 4 different agents concurrently for at least 90 days. Since these patients are taking multiple antipsychotic agents concurrently, they are at an increased risk for negative outcomes, including increased risk for adverse drug reactions.

The table on the second page shows the number of patients, stratified by age, taking 2 or more different antipsychotic agents concurrently for at least 90 days. This data excludes duplications of the same ingredient. For example, if a patient was receiving two different strengths of risperidone, or if a patient was receiving quetiapine regular release and quetiapine extended release, those claims would not be counted as different therapies.

Even with limited data available to support the concurrent use of multiple antipsychotic agents for an extended period of time, this practice is commonly seen. Antipsychotic polypharmacy has multiple drawbacks, including some of the following:

- Higher mortality
- Increased risk for drug interactions
- Increased risk for adverse drug reactions
- Decreased medication adherence
- Greater cost

The following examples describe the most common reasons for antipsychotic polypharmacy and provide recommendations regarding use and administration:

**Switching between antipsychotic agents**

When switching from one antipsychotic agent to another, it is often recommended to cross-titrate over several weeks. During cross titration, patients receive both antipsychotic medications. Cross-titration should typically be completed within 8 weeks.

**Interrupted cross-titration**

Cross-titration is often interrupted because a patient appears better while taking both medications. It is likely that the second agent alone may explain the improvement, and the patient should continue to titrate off of the first agent. Once the process of switching agents has been initiated, it should be completed.

**Failure of antipsychotic monotherapy**

The effectiveness of an antipsychotic medication can only be determined if the patient has an adequate dose and trial duration. Before concluding that antipsychotic monotherapy “will not work” in a patient, the patient should have received adequate trials of at least two antipsychotic agents for at least six weeks each. Studies indicate that clinicians often go to antipsychotic polypharmacy without trying an adequate number of different agents at adequate doses.

**Different mechanism of action**

From an efficacy perspective, there is currently no rationale for combining multiple antipsychotic agents. The only mechanism of action directly linked to antipsychotic efficacy is the effect on the dopamine D-2 receptor. All antipsychotic agents have an effect on the D-2 receptor but vary in other pharmacological properties. The relationship between other pharmacological properties and side effects is well understood; however, their relevance to efficacy is unknown.

**To reduce the side effects of a single agent**

Data from clinical trials to evaluate the benefit of antipsychotic combinations yield mixed results, but generally suggest that the addition of a second antipsychotic agent rarely reduces side effects or allows a dose reduction of the first agent.

**Different route of administration**

Transition to appropriate monotherapy is the preferred option, but targeted use of two antipsychotics with different routes of administration may occasionally be appropriate. However, this scenario should generally be limited in duration.

**To treat comorbid conditions**

A frequent justification for use of multiple antipsychotic agents is that one of the agents is being utilized for its antipsychotic effect, and the second agent is targeting a comorbid condition such as insomnia or agitation. The use of a non-antipsychotic agent for the comorbid condition is recommended, for example, the use of benzodiazepine for agitation. Typically, the non-antipsychotic agent is more targeted, has fewer side effects, and is less costly.

The practice of long-term concur-
During October 2013, 21,518 patients received a prescription for an anticonvulsant. Following a routine query in October 2013, 1192 adults were found to be non adherent to their anticonvulsant therapy. Therefore, approximately 5.5% of patients who received anticonvulsant prescriptions during October 2013 were found to be non adherent to the therapy.

Non-adherence to anticonvulsant therapy can negatively impact patients and lead to:

- Inadequate seizure control
- Increases in breakthrough seizures
- Increases in overall healthcare costs associated with non adherent seizures
- Decrease in quality of life of patient

It is important for the healthcare community to counsel patients about the importance of adhering to their medication regimens. Physician pill counts, self adherence reporting, and pharmacy refill records are all possible tools that can be used to improve medication adherence.