Utilization of Long-Acting Injectable Medications

• For Mental Health Conditions – Schizophrenia.
• For addictions – patients with alcohol and opioid dependency.
• The cost of these long-acting medications may significantly surpass the cost of oral medications.
• Multiple payers could cost-shift to other payment options.
Utilization of Long-Acting Injectable Medications

• Use of long-acting injectable preparations has been shown to reduce rate of both admissions to inpatient, readmissions and to improve personal functioning.
• Utilization of long-acting injectable medications is low among persons with substance use disorders and mental illnesses such as schizophrenia.
• Why is usage low? Cost is often given as one of the reasons for low usage.

The Business Case for Long-Acting Injectable Agents

1. Would we see higher utilization of lower levels of care?
2. Would we see a reduction in higher cost care?
3. Would we see lower readmission rates?
4. Would we see higher medication adherence rates and lower medication holidays?
5. Are health care expenditures redirected and/or conserved?
**Long-Acting Injectable Agents Show Increased Abstinence from Alcohol**

For alcohol dependent patients, when they achieved abstinence before treatment begins, patients using LAI’s maintained abstinence significantly longer and reported a greater reduction in alcohol consumption and craving than a placebo group.


**Long-Acting Injectable Agents Show Increased Abstinence from Opioids**

In opioid dependent subjects, non-randomized investigations have shown the ability of long-acting injections to block opioid effects and help maintain abstinence in different populations of opioid dependent patients.

Medical Conditions Associated With the Highest 30-Day Rehospitalization Rates

<table>
<thead>
<tr>
<th>Condition at Index Discharge</th>
<th>0%</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychoses*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td></td>
<td></td>
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<tr>
<td>Pneumonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GI Problems</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The DRG category 430 (Psychoses) includes various psychotic disorders. In a separate analysis of Medicare admissions during 2003-2004 associated with a primary diagnosis of DRG 430 (n=339,356), 52% were associated with the primary ICD-9 diagnosis episodic mood disorders with psychotic features, and 7% with psychotic psychoses.

In an analysis of approximately 12 million Medicare Fee for Service Program patients discharged from hospitals during 2003-2004, about 580,000 (19.6%) patients were readmitted within 30 days of discharge. The five medical reasons for the index (initial) hospitalization that were associated with the largest number of rehospitalizations are shown above.


Partial Adherence After Discharge from an Inpatient Center

<table>
<thead>
<tr>
<th>Time Since Discharge</th>
<th>7 to 10 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonadherence</td>
<td>50%</td>
<td>Up to 25%</td>
</tr>
</tbody>
</table>

Nonadherence can begin within 7 to 10 days of discharge from the hospital.1,2

Within 1 year, about half of patients may be nonadherent.3

Note: Nonadherence can be defined as a situation in which a person takes some, but not all, of his or her prescribed medication. It includes taking an amount that is consistently less than recommended, irregular (“on and off”) dosing behavior, and having discrete gaps in antipsychotic therapy.4

LAI Rationale—An Opportunity to Impact Adherence and Reduce Costs

QD or BID Therapy (365-730 doses per year)

Maintenance Dosing: Patient takes oral medication once or twice daily.

Long-Acting Injectables (12-26 doses per year)

Maintenance Dosing: Patient receives injection every 2 to 4 weeks.

Injection 1  2-4 weeks  Injection 2  2-4 weeks  Injection 3

EPIDEMIOLOGY AND ECONOMIC IMPACT

- Prevalence of schizophrenia: 4.6 per 1000 population
- Lifetime morbid risk: 7.2 per 1000
- Standardized mortality ratio: 2.3
- Direct healthcare costs of schizophrenia in the US: $22.7 billion
- Average acute-care hospitalization:
  - 8.7 days
  - $1565 per day

Wu EQ, et al., J Clin Psychiatry. 2005
Sclar DA, Robinson LM. Prim Care Companion J Clin Psychiatry. 2010
BACKGROUND

• Schizophrenia is a burden for patients and society
  – An estimated 1.1% of adults (2.6 million) in the USA have schizophrenia (1-year prevalence rate; based on 2010 census data)
  – This high prevalence is generally attributed to onset in early adulthood and a long natural history of the disease

• Schizophrenia relapse rates are 40–50% at 1 year and 80% at 5 years and although antipsychotic drug therapy remains the cornerstone of schizophrenia management
  – Up to 74% of patients are non-adherent to prescribed antipsychotics
  – Non-adherence to oral antipsychotics is associated with increased incidence of relapse and hospitalization, increasing the health care resource utilization and cost
  – Relapse prevention is an important treatment outcome

• The overall cost burden of schizophrenia in the USA was estimated to be $22.7 billion in 2002 based on direct health care costs (drug acquisition, inpatient, outpatient, and long term care) for patients with schizophrenia, which is equivalent to $46.7 billion in 2012 (when adjusted for inflation using the US Consumer Price Index Medical Care Category)

Karson C., et al. APA 2013

BACKGROUND CONTINUES

• Treatment adherence among patients with schizophrenia is identified as an important metric and captured via the Healthcare Effectiveness Data and Information Set (HEDIS)
  – HEDIS is a set of managed care and performance measures which are utilized by various agencies to assess USA health plans

• Long-acting injectable (LAI) formulations of antipsychotic agents were developed with the primary aim of improving adherence of patients with schizophrenia
  – Observational studies provide evidence that LAI antipsychotic therapy can improve the management of patients with schizophrenia, and the American Psychiatric Association (APA) Practice Guidelines recommend using these agents for patients who are not adherent to treatments

• LAIs may add value to the unmet medical need of treatment adherence in patients with schizophrenia and additionally reduce health care resource utilization and cost

Karson C., et al. APA 2013
PATIENTS OUTCOMES FROM REAL-WORLD STUDIES FAVOR THE USE OF LAIs vs ORAL IN TREATING PATIENTS WITH SCHIZOPHRENIAS

An analysis that evaluated 13 studies showed that LAI antipsychotics display increasing effectiveness compared with oral formulations as study design shifts from tightly controlled RCTs toward real-world clinical settings (see Figure 2-2) indicating that after factoring in the research design, the use of LAIs is associated with improved patient outcomes vs oral treatments.

Karson, C., et al., APA 2013

REDUCTION OF HOSPITALIZATIONS AND COSTS AMONG MEDICAID-INSURED SCHIZOPHRENIA PATIENTS AFTER INITIATING LONG-ACTING INJECTABLE ANTIPSYCHOTICS

Figure 1. Distribution of LAI Antipsychotic Agents Initiated (Percentage of Total Number of Patients, N = 3,841)

Karson, C., et al., APA 2013
REDUCTION OF HOSPITALIZATIONS AND COSTS AMONG MEDICAID-INSURED SCHIZOPHRENIA PATIENTS AFTER INITIATING LONG-ACTING INJECTABLE ANTIPSYCHOTICS continues

**CONCLUSIONS**

- For Medicaid-insured patients with schizophrenia, there was a 26.9% reduction in number of all-cause and 20.6% reduction in schizophrenia-related hospitalizations and a 30.6% reduction in all-cause and 29% reduction in schizophrenia-related total inpatient days
- These reductions in inpatient resource use were associated with a 26.5% reduction of all-cause and a 23.5% reduction in schizophrenia-related inpatient costs
- These results are consistent with previous national Medicaid and Commercial claims analyses that document significant reductions in resource use and costs among patients switching from oral to LAI treatment
- In accordance with the APA guidelines and results of this study, LAI antipsychotic agents offer an effective treatment option among patients with schizophrenia

**Table 3. Reduction in All-cause and Schizophrenia-related Inpatient Costs**

<table>
<thead>
<tr>
<th>Hospital payment ($) - Total mean (SD)</th>
<th>Baseline-index period</th>
<th>Follow-up period</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause</td>
<td>14,951.18 (30,290.16)</td>
<td>10,987.64 (28,598.82)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Schizophrenia-related</td>
<td>11,295.26 (23,072.07)</td>
<td>8,643.16 (23,053.21)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

*P-values determined by paired t test; SD: standard deviation*
Benefits of LAIs vs Oral Treatments

Non-adherence resulting in even a few days of gap in therapy increases the risk of rehospitalization (Weiden 2004).
- 1–10 days gap in therapy doubled the risk of hospitalization
- 11–30 days tripled it and greater than 30 days quadrupled

Percentage of Patients with Schizophrenia Rehospitalized by Maximum Gap in Therapy
Reduction in schizophrenia related hospitalizations and LOS after LAI initiation

ADHERENCE TO ANTIPSYCHOTIC TREATMENT AND CLINICAL OUTCOMES

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Adherent vs Non-adherent</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascher-Svanum 2009</td>
<td>Sub-analysis of a non-interventional study</td>
<td>Adherent (MPR&gt;80%) vs Non-adherent patients (MPR&lt;60%)</td>
<td>Significant fewer hospital admissions among patients who adhered to their antipsychotic treatment (hospital admissions: 17.1% vs 29.6% non-adherent; P&lt;0.05) - Adherent patients reported shorter hospital stay, less frequent uses of emergency services, and better participation in individual and group therapy</td>
</tr>
<tr>
<td>Ahn 2008</td>
<td>US claims database analysis (the California Medicaid program)</td>
<td>Adherent vs Non-adherent and partially adherent patients</td>
<td>- Non-adherent and partially adherent patients more likely to use long-term care, hospital admissions, ambulatory outpatient care - Non-adherent and partially adherent patients had significantly higher number of episodes per year, more frequent use of CMHCL, and more frequent suicide attempts (P=0.004 vs adherent patients)</td>
</tr>
<tr>
<td>Sun 2007</td>
<td>Systematic review; studies published between 1995 and 2007</td>
<td>Non-adherence to treatment</td>
<td>Non-adherence associated with increase in relapse rates, more frequent hospital admissions, and prolonged hospital stay</td>
</tr>
<tr>
<td>Morken 2008</td>
<td>Recent onset schizophrenia (&lt;2 years)</td>
<td>Adherent vs Non-adherent patients</td>
<td>Non-adherent patients: more likely to have persistent psychotic symptoms (OR: 3.63), relapse (OR: 10.27), and hospital admissions (OR: 4.0)</td>
</tr>
<tr>
<td>Kozma 2009</td>
<td>US claims database analysis (PharMetrics)</td>
<td>Adherent vs Partially adherent patients</td>
<td>Partially adherent patients (measured by MPR, consistency, and gaps) had greater risk of having ≥1 mental health hospitalization</td>
</tr>
</tbody>
</table>
• Out of approximately 300 patients, 44% of patients are on Typical Long-Acting Antipsychotic medications & 56% are on Atypical Long-Acting Antipsychotic medications

• Out of approximately 300 patients, 64% of patients did not have any inpatient admissions within 24 months period (10/01/2011-09/30/2013)

• Out of approximately 300 patients, 76% of patients did not have any inpatient admissions within 12 months period (10/01/2012-9/30/2013)

• Out of all inpatient admissions to the Center within 24 months period, 95% of admissions were for patients on oral antipsychotic medications

The Business Case

1. Effective and appropriate use of LAIs increases adherence.
2. When adherence is increased, relapse and/or acute episodes may be reduced.
3. When substance dependent patients have greater abstinence from alcohol or opioids, crisis events and emergency services may be reduced.
4. Readmissions to high cost care (e.g. inpatient care) are reduced thereby decreasing costs.
5. In a coordinated payer healthcare system, savings may be redirected to other healthcare services such as preventative health care or the total cost of healthcare may be controlled in growth or reduced.
Questions

Share your business case.
Further thoughts.