Long-Acting Injectable Antipsychotics and Clozapine: Evidence-Based But Underutilized Treatments

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Key to Abbreviations

- AP: Antipsychotic(s)
- D/C: Discharge
- LAI: Long-Acting Injectables
- SE: Side effects
- SGA: Second generation antipsychotic
- SI: Suicidal ideation
- Sx: Symptom(s)
- TD: Tardive Dyskinesia
- NMS: Neuroleptic Malignant Syndrome
## Guidelines Regarding Clozapine Use

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>Basic Use</th>
<th>Specific Clinical Features</th>
</tr>
</thead>
</table>
| American Psychiatry Association (APA)   | • Persistent psychotic Sx after 2 AP trials – “should be given strong consideration” | • Persistent hostility, aggressive behavior  
• Persistent SI  
• TD |
| Schizophrenia Patient Outcomes Research Team (PORT) | • Persistent and clinically significant positive Sx after >2 AP trials (including >1 SGA) – “should be used” | • Persistent hostility/ violent behaviors – “should be used”  
• Marked and persistent SI/ behaviors – “should be offered”  
• NMS, persistent dystonia/severe or very distressing TD – “should be offered” |
| Texas Medication Algorithm Project (TMAP) | • No-response or partial response to 2 AP trials (including ≥1 SGA)       | • Recurrent suicidality, violence or substance abuse-”consider earlier trial”  
• Persistent positive Sx >2yrs-”warrants”  
• Persistent positive Sx >5yrs-”requires” (independent of # of AP trials) |
| National Institute for Health and Clinical Excellence (NICE) | • Sequential use of >2 APs (including ≥1 SGA) |  |

*Kishimoto et al. in preparation.*
Clozapine Prescription Rate for Schizophrenia
-International Comparison-

0.00% 5.00% 10.00% 15.00% 20.00% 25.00% 30.00% 35.00%

Japan 2011.6 total patients
Korea 2004 inpatients
USA 2006 outpatients
Norway 2004 outpatients
Italy 2003 outpatients
Germany 2004 outpatients
China 2004 outpatients
Australia 2007 outpatient
New Zealand 2004 outpatient

*Data were obtained from multiple studies. Population/settings is not standardized

What Psychiatrists Find Most Problematic About Clozapine and What They Think Patients Find Problematic

- What Psychiatrists Find Most Problematic
- What Psychiatrists Think Patients Find Most Problematic

Nielsen et al. 2010 J Psychopharmacol
Factors that Discourage Doctors from Prescribing Clozapine

Possible non-adherence
Possible refusal to try clozapine
Possible emergence of metabolic SE
Cost (Patients cannot afford)
Difficult linkage to next level care
Possible emergence of agranulocytosis
Possible emergence of seizure
Possible emergence of myocarditis
Hassle of blood draw/monitoring
Lack of experience
Hassle of administrative procedures
Cost (hospital not sufficiently reimbursed)

*Expressed mean with 95%CI

N=171

Kishimoto and Kane. In preparation
## Guidelines Regarding Long Acting Injection Use

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Psychiatry Association (APA)</td>
<td>Pts with recurrent relapses related to nonadherence are candidates, or pts who prefer LAI</td>
</tr>
<tr>
<td>Schizophrenia Patient Outcomes Research Team (PORT)</td>
<td>Consider LAI for pts who have a history of frequent relapse on oral medication, or history of problems with adherence, or who prefer LAI</td>
</tr>
<tr>
<td>Texas Medication Algorithm Project (TMAP)</td>
<td>Consider LAI when pts are inadequately adherent at any stage</td>
</tr>
<tr>
<td>National Institute for Health and Clinical Excellence (NICE)</td>
<td>Adherence doubtful or known to be poor</td>
</tr>
</tbody>
</table>

*Kishimoto and Kane. In preparation*
Number of Relapse Medication Intake

0-25% 
25-50% 
50-75% 
75-100%

LAI Selection Rate According to the Number of Relapses and Adherence

Kishimoto and Kane. In preparation
LAI indication (category 1):  

a) Index hospitalization due to non-adherence OR  
b) partial-adherence before index hospitalization AND ≥1 past hospitalization due to non-adherence

*Kishimoto et al. in preparation*
LAI indication (category 2): Index hospitalization due to non-adherence AND ≥1 past hospitalization due to non-adherence

Kishimoto et al. in preparation