Schizophrenia is a chronic debilitating disease that requires lifelong medical care and supervision. Even with treatment, the majority of patients relapse within 5 years, and suicide may occur in up to 10% of patients. The discontinuation rate for oral antipsychotics ranges from 26-44%, and as many as two-thirds are at least partially nonadherent, with increased risk for hospitalization.

Long acting antipsychotic injections (LAAI) are for maintenance therapy in the treatment of schizophrenia, mania and other psychoses. The LAAI are usually prescribed when the patient elects to have the medication administered this way, or where adherence to oral treatment has been unreliable.

LAAI were developed to allow the medicines to be delivered in a modified way, over time, following administration. This has the advantage of promoting a steady therapeutic concentration of the drug, while minimizing some of the side effect and variable effects on symptoms that may result when oral medications are used. The achievement of a steady therapeutic level from regular injections also affords protection from relapse beyond the time the last injection was received.

With the development of the second generation LAAIs, there was an expectation that the second generation long-acting medications would provide greater therapeutic efficacy and adherence over the first generation agents. All of the second generation antipsychotics remain on patent and can be up to ten times more expensive than the older drugs. In a recent study called the ACLAIMS (A comparison of long acting injectable medications for Schizophrenia), 311 patients with schizophrenia or schizoaffective disorder were randomly assigned to receive the LAI Paliperidone palmitate or Haldol decanoate. The study looked at efficacy of the drugs as well as metabolic markers and prolactin levels. The study found no evidence that paliperidone was superior to haloperidol in preventing efficacy failure, as defined by psychiatric hospitalization, a need for crisis stabilization, increased outpatient visits, or an inability to discontinue oral antipsychotics. When compared to haloperidol, paliperidone had no significant advantages in AIMS, Parkinsonism, or incidence of TD, though there was an increased incidence of akathisia.

Besides the good efficacy and safety profile of LAAIs, health care staff must also take into account the importance of establishing a therapeutic alliance with the patient and his/her relatives when selecting the most relevant treatment. The use of the LAAIs will also improve compliance, which is a key factor in promoting adherence and to establishing a therapeutic alliance between patients, families, and health care providers.

IN ACCORDANCE WITH THE NICE* CLINICAL GUIDELINES FOR SCHIZOPHRENIA:¹

- A risk assessment should be performed by the clinician and team, regarding concordance with medication and depot preparations should be prescribed when appropriate.

¹ National institute for health and Clinical Excellence (2009)
*National Institute for Health and Clinical Excellence
LONG ACTING ANTIPSYCHOTIC INJECTIONS

- Depot preparations should be a treatment option where a patient expresses a preference for such treatment because of its conveniences or as a part of a treatment plan in which the avoidance of covert non-adherence with antipsychotic drugs is a clinical priority.
- Depot preparations should be prescribed within the standard recommended dosage and interval range, for optimum effectiveness in preventing relapse.
- Following full discussion between the clinician and the patient, the decision to initiate depot should take into account the preferences and attitudes of the service user towards the mode of administration and organizational procedures.

PATIENT INFORMATION AND CONSENT

Patients and their caregivers must be offered clear and accessible information in a suitable format regarding the use and possible side effects of any injection being considered. A note should be placed in the patient's record of any information provided and in what format and also of any information offered but refused.

RELAPSE AND HOSPITALIZATION RATES

No head-to-head studies have actually demonstrated and adherence advantage of the LAIs.

A 2005 Cochrane review looked at 6 randomized controlled studies comparing injectable fluphenazine with oral antipsychotics and found that the depot medication did not reduce relapse more than oral neuroleptics. A more recent study focused specifically on risperidone with similar results.²

In another study, of a large Medicaid sample found that fewer than 10% of patients who started on LAIs in the hospital were still on them at six months post discharge.

Both randomized and naturalistic studies compared LAIs versus oral antipsychotic medications for treating schizophrenia to assess the efficacy and tolerability of LAIs. Overall LAIs were associated with a lower rate of relapse versus oral antipsychotics and the benefits of LAIs were greater in naturalistic studies.

TEST DOES PRIOR TO ADMINISTRATION

LAAs are long acting medications that take a long period to fully wash out of the body. Any adverse effects, then are likely to be long lasting.

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² Long Acting Injectable Antipsychotics: A Primer Psych Central Professional 2013.
*National Institute for Health and Clinical Excellence
With the exception of Risperdal Consta, it is recommended that patients are given a small test dose before the onset of the therapeutic dose before the onset of treatment to avoid severe and prolonged adverse effects.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Generic</th>
<th>Strength</th>
<th>Test dose</th>
<th>Maintenance dose</th>
<th>Maximum dose</th>
<th>Oral overlapping</th>
<th>Cost (Amerisource Bergen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluphenazine decanoate</td>
<td>Yes</td>
<td>25 mg</td>
<td>12.5 mg, 6.25 mg (&gt;60 years)</td>
<td>12.5 mg to 100 mg every 2-5 weeks</td>
<td>100 mg q 2 weeks</td>
<td>YES 7-14 days</td>
<td>5 ml vial=$70.00</td>
</tr>
<tr>
<td>Haloperidol decanoate</td>
<td>Yes</td>
<td>50 mg</td>
<td>50 mg, 12.5-25 mg (&gt;65 years)</td>
<td>50-300 mg q 4 weeks</td>
<td>300 mg q 4 weeks</td>
<td>No, but observe for response</td>
<td>50 mg 3 x 1 ml=$60.00 100 mg 5 x 1 ml=$170</td>
</tr>
<tr>
<td>Risperidone (Risperdal consta)</td>
<td>No</td>
<td>12.5 mg</td>
<td>25 mg, 37.5 mg, 50 mg</td>
<td>25-50 mg q 2 weeks</td>
<td>50 mg q 2 weeks, 25 mg q 2 weeks (&gt;65 years)</td>
<td>Yes 21 days</td>
<td>12.5 mg = $143 25 mg = $286 37.5 mg = $429 50 mg = $572</td>
</tr>
<tr>
<td>Paliperidone (Invega Sustenna)</td>
<td>No</td>
<td>39 mg</td>
<td>?</td>
<td></td>
<td></td>
<td>No</td>
<td>39 mg = $286 78 mg = $572 117 mg = $858 156 mg = $1144 234 mg = $1717</td>
</tr>
<tr>
<td>Aripiprazole (Abilify Mantena)</td>
<td>No</td>
<td>300 mg</td>
<td>400 mg</td>
<td></td>
<td></td>
<td>Yes 14 days</td>
<td>300 mg = $1055 400 mg = $1406</td>
</tr>
<tr>
<td>Olanzapine pamoate (Zyprexa Relprevv)</td>
<td>No</td>
<td>210 mg</td>
<td>300 mg, 405 mg</td>
<td>210 mg q 2 weeks, 405 q 4 weeks</td>
<td>After 2 mo.: 150 mg q 2 weeks 300 mg q 4 weeks (PO of 10 mg)</td>
<td>300 mg q 2 weeks</td>
<td>Maybe observe response</td>
</tr>
</tbody>
</table>

3 Patients who have suffered a relapse following cessation of depot therapy may be restarted on the same dose, although the frequency of the injections may need to be increased in the early weeks of treatment until satisfactory control is obtained.

4 National Registry required to document incidents of rare serious ADEs (hypotension, orthostasis, post-injection delirium/sedation syndrome. Patient should be observed for 3 hours after every dose.)

5 300mg q 2 weeks for 2 month (po Olanzapine 15-20 mg)
6 201 mg q 2 wks or 405 mg q 4 wks (PO 15 mg), 300mg q 2 wks (po 20 mg)

*National Institute for Health and Clinical Excellence*
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There are several factors to consider when electing to initiate treatment with a LAAI, particularly when the LAAI is given while a patient is in the inpatient treatment setting:

1. One of the factors determining the success of the LAAI is the development of a therapeutic alliance with the patient. If a patient has a different outpatient provider than the one giving care in the inpatient setting, the likelihood of compliance with additional follow up should be considered, particularly if the member is not currently engaged in outpatient treatment. If the patient is in outpatient treatment, the outpatient provider should be involved in the decision to initiate the LAAI. This is done to ensure that the medication will be continued in the outpatient setting.

2. The patient and or caregiver must be able to give informed consent when initiating treatment. This needs to be a separate consent signed or the information documented in the patient’s record.

3. Some of the LAAI require oral overlapping of meds to be effective. This must also be considered in those inpatients that are chronically noncompliant with meds and follow up. Consideration must be given as to the utility in preventing relapse in this population.

4. The LAAI medications can be very costly. There must be consideration as to how the patient will be able to obtain the medication and receive the injections on an outpatient basis. Though it is tempting to give a LAAI to a chronically recidivistic, noncompliant patient while in an inpatient setting, it may not prevent relapse if the patient is not invested in the treatment.

5. Since most hospitalized patients are admitted for rapid stabilization, it may not be realistic to administer a test dose and then wait an additional time for readministration of the medications.

6. The use of the LAAI is a therapeutic option with many benefits over oral administration. Patients should be carefully selected and be able to give informed consent for this type of therapy.

7. Given the fact that the LAAI, have a long period of wash out, it may be best to consider the use of the oral agents first-line, to be sure that they are well tolerated before progressing to the LAAI.
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References:


Sussex Partnership Guidelines for the Administration of Long Acting Antipsychotic Injections in Adults. NHS foundation Trust, Jan 2011

NIMH: Older Medication Just as Effective as Newer Medication for Patients with Schizophrenia