<table>
<thead>
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<th><strong>NAME OF DOCUMENT</strong></th>
<th>Olanzapine Pamoate Long-Acting Injection (LAI): Administration and Management</th>
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<td>Dr Peter Young A/ Chief Psychiatrist SESLHD Mental Health Service</td>
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<td><strong>POSITION RESPONSIBLE FOR THE DOCUMENT</strong></td>
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<tr>
<td><strong>KEY TERMS</strong></td>
<td>Olanzapine Pamoate Long-Acting Injection Administration, Post-Injection Syndrome</td>
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<tr>
<td><strong>SUMMARY</strong></td>
<td>This procedure is intended to provide clinicians with information required for the safe administration of Olanzapine Pamoate Long-Acting injection and management of the Post-injection Syndrome.</td>
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1. POLICY STATEMENT
South Eastern Sydney Local Health District (SESLHD) has the responsibility to provide employees, clients and visitors with a safe and healthy workplace in accordance with the NSW Ministry of Health Policy - PD2013_043 Medication Handling in NSW Public Health Facilities.

Olanzapine Pamoate Long-Acting Injection (LAI) will be prescribed under the direction of a psychiatrist, drawn up by accredited staff, and administered in accordance with this procedure. Measures must be in place before the medication is administered to ensure that staff with specific knowledge about post injection syndrome are available and able to monitor the client for three hours post injection, due to known serious adverse effects in some consumers. Early detection and management of post-injection syndrome will be carried out according to this procedure.

2. BACKGROUND
Olanzapine Long Acting Injection (LAI) is an atypical antipsychotic used in the maintenance treatment of schizophrenia. A rare serious adverse event related to the use of olanzapine LAI is post-injection syndrome (PIS) is reported to occur in 0.07% of injections. Non-recognition of PIS symptoms has resulted in the death of a patient.

PIS results from inadvertent intravascular injection of olanzapine, causing a range of olanzapine overdose-type symptoms. Post injection syndrome is not dose, frequency or time point specific, and the risk of occurrence exists following every administration. In most cases of PIS (84%) the initial signs and symptoms occur within the first hour after injection, but onset after three hours has been reported. Full recovery usually occurs within 24-72 hours.

The signs and symptoms of PIS include:
- Sedation (ranging from mild sedation to deep sleep and unconsciousness), and/or
- Delirium (including confusion/confused state, disorientation, anxiety and agitation)
- Other symptoms include dizziness, weakness, altered speech/dysarthria, altered gait, muscle spasms, possible seizures and hypertension.

Higher doses and therefore a larger final volume for injection and low body mass index (BMI) may present a higher risk for PIS; however, PIS has occurred in patients who do not have these risk factors.

3. RESPONSIBILITIES
3.1. Employees will:
- Comply with this procedure, and any related measures, to manage the safe use of Olanzapine Pamoate LAI. This includes all Medical, Nursing and Allied Health staff of SESLHD.

1Olanzapine depot injection (Zyprexa Relprevv) for schizophrenia
2 Post-injection delirium/sedation syndrome in patients with schizophrenia treated with olanzapine long-acting injection. I analysis of cases
3.2. **Line Managers will:**
- Disseminate, implement and comply with this procedure.

3.3. **District Managers/Service Managers will:**
- Ensure staff are aware of, and adhere to, this procedure.

3.4. **Nursing Staff will:**
- Comply with this procedure
- Be trained in the correct administration of Olanzapine Pamoate LAI
- Have received education on post-injection syndrome, its monitoring and management
- Have completed DETECT e-learning and the DETECT practical

3.5. **Medical Staff will:**
- Comply with this procedure
- Prescribe Olanzapine Pamoate under the direction of a consultant psychiatrist.

4. **PROCEDURE:**
This procedure outlines instructions for prescribing, monitoring and administering Olanzapine Pamoate LAI.

4.1. **Initiation**
Prior to the initiation of Olanzapine Pamoate, the consultant psychiatrist must obtain initial approval from the site Chief Psychiatrist/Clinical Director.

The capacity of the mental health service to administer the injection and provide required monitoring must be considered prior to initiation.

Client selection criteria includes:
- Demonstrated response to oral Olanzapine
- Evidence that a LAI is the preferred treatment option
- Evidence of failed response, or intolerable side effects, to other antipsychotic agent
- A management plan for the administration and observation of the client post injection
- A plan for the monitoring of the client’s metabolic profile.
4.2. Prescription
The client must have established tolerability and response to oral Olanzapine before a switch to Olanzapine Pamoate can be considered. Table 1 below outlines the dose recommendations of oral Olanzapine and Olanzapine Pamoate.

<table>
<thead>
<tr>
<th>Target oral Olanzapine dose</th>
<th>Recommended starting dose of Olanzapine Pamoate</th>
<th>Maintenance dose after 2 months of Olanzapine Pamoate treatment</th>
</tr>
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<tbody>
<tr>
<td>10mg/day</td>
<td>210mg / 2 weeks or 405mg / 4 weeks</td>
<td>150mg / 2 weeks or 300mg / 4 weeks</td>
</tr>
<tr>
<td>15mg/day</td>
<td>300mg / 2 weeks</td>
<td>210mg / 2 weeks or 405mg / 4 weeks</td>
</tr>
<tr>
<td>20mg/day</td>
<td>300mg / 2 weeks</td>
<td>300mg / 2 weeks</td>
</tr>
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</table>

Oral supplementation is not required at the start of treatment; however, an open label long-term clinical trial permitted doses of up to 20mg per day of oral Olanzapine, when clinically necessary. Peak plasma levels are reached within the first week after injection.

Dosage in older patients (65 years and over), hepatically or renally impaired patients:
Olanzapine has not been systematically studied in these patients. A lower starting dose (150mg every four weeks) should be considered.

4.3. Pre-administration Check
- Right patient, right drug, right dose, right route, right time
- Staff who have received training in the correct injection technique and post-injection monitoring must be available to administer the injection and provide post-monitoring
- A safe environment must be identified for the administration and monitoring of Olanzapine Pamoate LAI, within the local facility, to ensure immediate emergency medical assistance, if signs of PIS are identified
- Valid informed consent has been obtained and documented for the treatment course
- The client is aware of the potential side effects of PIS and is prepared to cooperate with a three hour monitoring period
- Outpatients and clients being discharged or released on leave are aware of, and consent to, the requirement to be accompanied home by a carer or responsible person and that they do not to drive or operate heavy machinery for the rest of the day
- The client and carer or responsible person accept education about symptoms that may indicate PIS, including actions to be taken and who to contact if there is any adverse event after the patient has left the healthcare facility.

- Standard precautions will be implemented, including sharps handling and disposal of waste
- Physical environment will be free from hazards
- Latex allergy risk will be assessed and recommended precautions utilised to prevent exposure to latex or known or suspected latex allergy in patients and staff
- Ergonomic and manual handling principles will be implemented.
4.3.1. Equipment
Required equipment:
- Olanzapine Pamoate (Zyprexa Relprevv®) injection pack
- Gloves
- Injection site dressing.

The Olanzapine Pamoate injection pack should be provided by the hospital pharmacy department for inpatients. For outpatients, the injection pack should be brought to the unit by the client or case manager, unless an IPU application has been approved for supply via the hospital pharmacy.

4.4. Reconstitution and Administration

4.4.1. Preparing Materials
The Olanzapine Pamoate injection pack includes:
- One vial of Olanzapine Pamoate powder (labelled Zyprexa Relprevv®)
- One 3ml vial of sterile diluent (for specific use with Olanzapine Pamoate only)
- One 3ml syringe with pre-attached 38 mm safety needle
- One 19 gauge, 38mm safety needle
- One 19 gauge, two 50mm safety needles (for obese patients)
- Package literature including product information, consumer medicine information, and reconstitution and administration instructions.

It is recommended by the manufacturer that gloves are used when reconstituting Olanzapine Pamoate, as it may irritate the skin.

4.4.2. Determining diluent volume for reconstitution
The Olanzapine Pamoate powder must only by reconstituted with the sterile diluent supplied in the injection package.

Table 2 below outlines the amount of sterile diluent required to reconstitute Olanzapine Pamoate powder.

Note: There is more diluent in the vial than is required.

<table>
<thead>
<tr>
<th>Dose</th>
<th>Olanzapine Pamoate Vial Strength</th>
<th>Volume of diluent to add</th>
<th>Final volume to Inject</th>
</tr>
</thead>
<tbody>
<tr>
<td>150mg</td>
<td>210mg</td>
<td>1.3mL</td>
<td>1mL</td>
</tr>
<tr>
<td>210mg</td>
<td>210mg</td>
<td>1.3mL</td>
<td>1.4mL</td>
</tr>
<tr>
<td>300mg</td>
<td>300mg</td>
<td>1.8mL</td>
<td>2mL</td>
</tr>
<tr>
<td>405mg</td>
<td>405mg</td>
<td>2.3mL</td>
<td>2.7mL</td>
</tr>
</tbody>
</table>

4.4.3. Reconstituting Olanzapine Pamoate
i. Loosen the powder by lightly tapping the vial
ii. Open packaging containing the syringe with pre-attached safety needle
iii. Withdraw the pre-determined volume of sterile diluent into the syringe (refer to Table 2). A second nurse (registered or enrolled) should perform a double check on the diluent volume

iv. Inject the diluent into the powder vial

v. Withdraw air to equalise the pressure in the vial

vi. Remove the needle, holding the vial upright to prevent any loss of solution

vii. Engage the needle safety device

viii. Tap the vial firmly and repeatedly on a hard surface until no powder is visible (protect the surface to cushion the impact and prevent breakage)

ix. Visually check the vial for clumps. Unsuspended powder appears as light yellow, dry clumps clinging to the vial. Additional tapping may be required if clumps remain

x. Shake the vial vigorously until the suspension appears smooth and is consistent in colour and texture. The suspended product will be yellow and opaque.

**Note:** If foam forms, let vial stand to allow foam to dissipate. If the product is not used immediately, it should be shaken vigorously to re-suspend. Do not refrigerate or freeze. The reconstituted product may be stored for up to six hours at room temperature.

4.4.4. Injecting Olanzapine Pamoate

i. Determine which needle will be used to administer the injection. For obese patients, the 50mm needle is recommended

   o If the 50mm needle is to be used for the injection, attach the 38mm needle to the syringe to withdraw the required suspension volume

   o If the 38mm needle is to be used for the injection, attach the 50mm needle to the syringe to withdraw the required suspension volume.

ii. Determine the amount that needs to be withdrawn from the vial for injection (from Table 2) and slowly withdraw the desired amount. **Some excess product will remain in the vial**

iii. A second nurse (registered or enrolled) must check the volume withdrawn for the injection

iv. Engage the needle safety device and remove needle from syringe

v. Attach a new safety needle to the syringe prior to injection. Once the suspension has been removed from the vial, it should be injected immediately.

vi. Select and prepare a site for injection in the gluteal area.

**NOTE:** FOR DEEP INTRAMUSCULAR GLUTEAL INJECTION ONLY. DO NOT ADMINISTER INTRAVENOUSLY OR SUBCUTANEOUSLY.

vii. After insertion of the needle into the muscle, aspirate for **several seconds** to ensure no blood appears.

**NOTE:** IF ANY BLOOD IS DRAWN INTO THE SYRINGE, DISCARD THE SYRINGE AND THE DOSE, AND CONSULT A MEDICAL OFFICER. A NEW INJECTION PACK SHOULD BE USED TO ADMINISTER AFTER A FAILED FIRST ATTEMPT.
viii. The injection should be performed with steady, continuous pressure. **Do not massage the injection site**

ix. Engage the needle safety device

x. Discard the vials, syringe, needles and any unused diluent into a sharps bin following injection. The vial is for single use only.

4.5. **Post-injection Observation**

- The patient must be observed for sedation, confusion, agitation and other symptoms of PIS for three hours after administration
- The trained health staff should maintain continuous observation of the patient for a period of 15 minutes immediately following the injection. The patient should remain in sight of staff for the remainder of the three hour observation period for signs and symptoms of PIS
- This may include allied health staff, providing they have had training in the safety precautions associated with PIS, and have immediate access to emergency response assistance
- The client should be assessed for alertness at 5 minutes, 10 minutes, 15 minutes and 30 minutes post injection, then at least every 30 minutes thereafter through direct verbal interaction
- Assess the patient’s level of sedation or agitation, and ask “How are you feeling?” Ensure the patient is able to follow basic commands. Document observations and patient’s response on the Standard Adult General Observations (SAGO)
- **Visual monitoring is insufficient.** An assessment must ascertain that the patient is not sedated, confused or anxious. Further questions to ascertain orientation need only be asked if signs and symptoms of PIS are observed
- Record baseline observations of vital signs on Standard Adult General Observations (SAGO) Chart. Observations should be repeated before discharge for any forms of clinical deterioration
- Staff should remain alert for any signs of PIS, and ensure appropriate clinical handover to oncoming staff. If the patient’s condition deteriorates local rapid response must be activated in accordance with SESLHDPR/283 Patient with Acute Condition for Escalation (PACE): Management of the Deteriorating ADULT & MATERNITY Inpatient
- At the end of the three hour monitoring period, the nurse or allied health member must notify the prescribing medical officer or after hours medical officer on-call
- The three hour observation period should be extended as clinically appropriate for patients who exhibit any potential signs or symptoms of PIS
- Immediately prior to leaving the facility, the staff member must confirm that the patient is alert, orientated, and absent of any signs and symptoms of overdose
- The staff member conducting post-injection monitoring must note in the patient’s medical records that the injection has been given and that the post-injection monitoring has been carried out as per this procedure, including completion of the post-injection check list
- A Medical Officer must review the patient to ensure no signs and symptoms of PIS are displayed, prior to authorisation for discharge
- On discharge, the client **and carer or responsible person**, must be instructed to remain vigilant for the onset of symptoms of PIS for the rest of the day, and have a documented plan for how to contact appropriate services should symptoms present...
Clients must be advised that they are not permitted to drive or operate machinery for
the rest of the day after the injection.

4.5.1. Patient insists on leaving prior to the three hour observation
- Refer to SESLHDPD/291 Clinical Risk Assessment and Management and
  PD2017_2015 NSW Health Admission Policy – Section 4 Discharge
- All practices should align with the Mental Health Act (2007).

5. DOCUMENTATION / REPORTING
- An IIMS report must be completed following any Post-injection Syndrome event
- Any adverse drug reaction must be reported on IIMS, to the local hospital Drug
  Committee, and to the Therapeutic Goods Administration (TGA) via the blue card
  adverse reaction reporting form
- An entry must be made in the client’s file indicating that the injection has been given
  and the post-injection monitoring has been carried out as per this Procedure.

6. AUDIT
Services where eMEDs and eMR2 have not fully been adopted will adhere to standard
monitoring process on documented paper annually using the SAGO chart or equivalent.
The service will conduct regular audits at least once per annum where eMEDs and eMR2
are available. An audit on compliance is to be consistent with the annual audit schedule
determined by local services.

7. REFERENCES
- Eli Lilly: Olanzapine Pamoate Long-Acting Injection (LAI) product information
- Eli Lilly: Zyprexxa Relprevv® Observation Checklist
- Mental Health Act (2007)
- NSW Health Safety Notice 002/17: Identification of Post-injection Syndrome
  Olanzapine Long Action Injection
- Olanzapine depot injection (Zyprexa Relprevv) for schizophrenia
- Post-injection delirium/sedation syndrome in patients with schizophrenia treated
  with olanzapine long-acting injection, I:analysis of cases
- Macquarie Hospital Olanzapine Pamoate Protocol: PR2010_312
- NSW Ministry of Health Policy - PD2013_043 Medication Handling in NSW Public
  Health Facilities
- SESLHDPR/283 Patient with Acute Condition for Escalation (PACE): Management
  of the Deteriorating ADULT & MATERNITY Inpatient

8. REVISION AND APPROVAL HISTORY

<table>
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<tr>
<th>Date</th>
<th>Revision No.</th>
<th>Author and Approval</th>
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<tbody>
<tr>
<td>April 2017</td>
<td>1</td>
<td>First draft developed by Benjamin Chidester, SESLHD MHS Workplace Capabilities Mental Health Clinical Nurse Educator.</td>
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<tr>
<td>June 2017</td>
<td>2</td>
<td>Reviewed by Angela Karooz, SESLHD MHS Clinical Nurse Manager. Second draft updated by author upon feedback.</td>
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<tr>
<td>July 2017</td>
<td>3</td>
<td>Reviewed and updated by Lisa John, Pharmacist, POWH, and Peter Young, SESLHD MHS A/Chief Psychiatrist.</td>
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<tr>
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<td>Review step</td>
<td>Notes</td>
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<td>Reviewed by District Document Development and Control Committee member (DDDCC). Feedback updated by author and MHS Policy Officer.</td>
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<tr>
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<td>Incorporate audit process feedback from ESMHS and District Lead Pharmacist. Reviewed by Ben Chidester and Angela Karooz.</td>
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<tr>
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<td>7</td>
<td>Reviewed by District QUMC. Reviewed and amended by District Mental Health Service: Peter Young, Angela Karooz and Trinh Huynh</td>
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<tr>
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<td>7</td>
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</tr>
<tr>
<td>July 2018</td>
<td>7</td>
<td>Endorsed by SESLHD Quality Use of Medicines Committee Endorsed by SESLHD Clinical and Quality Council</td>
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