SESLHD PROCEDURE COVER SHEET

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FUNCTIONAL GROUP(S)	Mental Health
KEY TERMS	Olanzapine Pamoate Long-Acting Injection Administration, Post-Injection Syndrome
SUMMARY	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.

Feedback about this document can be sent to SESLHD-Policy@health.nsw.gov.au

Olanzapine Pamoate Long-Acting Injection (LAI): Administration and Management

SESLHDPR/607

1. POLICY STATEMENT

South Eastern Sydney Local Health District (SESLHD) has the responsibility to provide employees, consumers and visitors with a safe and healthy workplace in accordance with the NSW Health Policy Directive PD2013_043 Medication Handling in NSW Public Health Facilities.

Olanzapine Pamoate Long-Acting Injection (LAI) will be prescribed under the direction of a psychiatrist in consultation with the site Clinical Director, drawn up by accredited nursing 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 consumer 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.

This medication is only to be administered by an appropriately accredited Mental Health Nurse who has been trained in the administration of, and post injection monitoring requirements specific to, Olanzapine Pamoate LAI.

2. BACKGROUND

Olanzapine Pamoate LAI is an atypical antipsychotic used in the maintenance treatment of schizophrenia. A rare serious adverse event related to the use of Olanzapine Pamoate LAI is post-injection syndrome (PIS) which is reported to occur in 0.07% of injections[1]. Unrecognised PIS has been linked to the unexpected deaths of a small number of consumers.

PIS is also referred to as Post Injection Delirium/Sedation Syndrome (PDSS) however for the purpose of this document the term PIS will be used.

PIS can result from inadvertent intravascular injection of Olanzapine or where there is contact with blood (eg if a haematoma occurs around the track of the injection), 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 84% of cases of PIS 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[2] .

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.

[1] Olanzapine 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

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 consumers 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 and Nursing staff of SESLHD.

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 PIS, its monitoring and management
- Have completed DETECT e-learning and the DETECT practical
- Be aware of the rapid response protocol SESLHDPR/697 - Management of the Deteriorating ADULT inpatient (excluding maternity)

3.5. Medical Staff will:

- Comply with this procedure
- Prescribe Olanzapine Pamoate under the direction of a Consultant Psychiatrist.
- Be competent in the recognition and management of the Olanzapine Pamoate LAI post-injection syndrome, including the rapid response protocol SESLHDPR/697 - Management of the Deteriorating ADULT inpatient (excluding maternity)
- Review consumer 3 hours post injection for sign of PIS

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 Clinical Director.

An Individual Patient Use (IPU) approval is required before new initiations (NB if a consumer has previously been prescribed Olanzapine Pamoate either from another LHD, or a previous admission within SESLHD, an IPU approval is not required)

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

Consumer 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 agents
- A management plan for the administration and observation of the consumer post injection
- A plan for the monitoring of the consumer's metabolic profile.

4.2. Prescription

The consumer 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 1. Recommended dose scheme between oral Olanzapine and Olanzapine Pamoate

Target oral Olanzapine dose	Recommended starting dose of Olanzapine Pamoate	Maintenance dose after 2 months of Olanzapine Pamoate treatment
10 mg/day	210 mg / 2 weeks *or* 405 mg / 4 weeks	150 mg / 2 weeks *or* 300 mg / 4 weeks
15 mg/day	300 mg / 2 weeks	210 mg / 2 weeks *or* 405 mg / 4 weeks
20 mg/day	300 mg / 2 weeks	300 mg / 2 weeks

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 consumers. A lower starting dose (150mg every four weeks) should be considered.

4.3. Pre-administration Check

- Right consumer, right drug, right dose, right route, right time
- Nursing staff who have received training in the correct injection technique and post-injection monitoring must be available to administer the injection and provide post-injection monitoring
- Injection administration must be performed by a Registered Nurse, and checked by a second nurse. The second person may be a Registered Nurse or Enrolled Nurse without notation. The check should include the drug, dose, calculation and fluid, consumer's identity and countersigning the administration on the medication chart or in eMEDS.
- A safe locked environment, with the local facility must be identified for the administration and monitoring of Olanzapine Pamoate LAI, to ensure continuous monitoring and immediate emergency medical assistance from a Code Blue 2222 response, if signs of PIS are identified.

- Olanzapine Pamoate LAI must only be administered in locations where a Code Blue 2222 response is available.
- Valid informed consent has been obtained and documented for each administration of Olanzapine Pamoate (see Appendix B). Where this is not possible, an appropriate and valid legal framework exists under the NSW Mental Health Act (2007).
- The consumer is aware of the potential side effects of PIS and is prepared to cooperate with a three hour monitoring period
- Outpatients and consumers being discharged or released on leave must be advised to:
  - Be vigilant for symptoms of post injection adverse reactions,
  - Obtain medical assistance if needed,
  - Not drive or operate heavy machinery for the rest of the day
- Consumers should be escorted home by a carer/responsible person
- The consumer and carer or responsible person must 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 consumer has left the healthcare facility.

- Standard precautions must be implemented, including sharps handling and disposal of waste
- Physical environment must be free from hazards
- Latex allergy risk must be assessed and recommended precautions utilised to prevent exposure to latex or known or suspected latex allergy in consumers and staff
- Ergonomic and manual handling principles must 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 consumer or Care Coordintaor.

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 3 mL vial of sterile diluent (for specific use with Olanzapine Pamoate only)
- One 3 mL syringe with pre-attached 38 mm safety needle
- One 19 gauge, 38mm safety needle
- Two 19 gauge, 50mm safety needles (for obese consumers)
- 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 2: Amount of diluent required for reconstitution and injection.

Dose	Olanzapine Pamoate Vial Strength	Volume of diluent to add	Final volume to Inject
150 mg	210 mg	1.3 mL	1 mL
210 mg	210 mg	1.3 mL	1.4 mL
300 mg	300 mg	1.8 mL	2 mL
405 mg	405 mg	2.3 mL	2.7 mL

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 without notation) 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 consumers, the 50mm needle is recommended
   - If the 50mm needle is to be used for the injection, attach the 38mm needle to the syringe to withdraw the required suspension volume

- 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 without notation) 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. Check the consumer's known allergies against the medication chart / EMR and with the consumer. If an allergy to the medication being administered is identified, do not administer the medication and contact the consumer's medical officer.
vii. Perform hand hygiene and don gloves before touching consumer.
viii. Select and prepare a site for injection in the gluteal area.

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

ix. 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 MUST BE USED TO ADMINISTER AFTER A FAILED FIRST ATTEMPT.

x. The injection should be performed with steady, continuous pressure. **Do not massage the injection site**
xi. Engage the needle safety device
xii. 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 consumer must be observed for sedation, confusion, agitation and other symptoms of PIS for three hours after administration and observations are to be documented using the
- The trained Registered Nurse should maintain continuous observation of the consumer for a period of 15 minutes immediately following the injection. The consumer should remain in sight of staff for the remainder of the three hour observation period for signs and symptoms of PIS
- The consumer 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 with observations documented in eMR on the GCS Assessment within the General Neurological Assessment
- Assess the consumer's level of sedation or agitation, and ask "How are you feeling?" Ensure the consumer is able to follow basic commands. Document observations and

consumer's response in eMR on the GCS Assessment within the General Neurological Assessment.

- **Visual monitoring is insufficient.** An assessment must ascertain that the consumer is not sedated, confused or anxious. Further questions to ascertain orientation need only be asked if signs and symptoms of PIS are observed
- Staff should remain alert for any signs of PIS, and ensure appropriate clinical handover to oncoming staff. If the consumer's condition deteriorates a clinical review or Code Blue 2222 response must be activated in accordance with SESLHDPR/697 - Management of the Deteriorating ADULT inpatient (excluding maternity)
- At the end of the three hour monitoring period, the allocated nurse must notify the prescribing medical officer or delegate medical officer for assessment prior to discharge to ensure no signs and symptom of PIS are displayed
- The three hour observation period should be extended as clinically appropriate for consumers who exhibit any potential signs or symptoms of PIS
- Immediately prior to leaving the facility, the staff member must confirm that the consumer is alert, orientated, and absent of any signs and symptoms of overdose.
- The staff member conducting post-injection monitoring must note in the consumer's medical records that the injection has been given and that the pre and post-injection physical observation monitoring has been carried out as per this procedure, including completion of the post-injection check list
- A Medical Officer must review the consumer to ensure no signs and symptoms of PIS are displayed, at the conclusion of the three hour observation period and prior to authorisation for discharge. NB if an inpatient, this review must occur and be document prior to the consumer being granted leave
- On discharge:
    - the consumer *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
    - the consumer must be provided with a consumer medicine information leaflet (CMI) after every administration of Olanzapine Pamoate LAI
    - Consumers must be reminded that they are not permitted to drive or operate machinery for the rest of the day after the injection.

4.5.1. Consumer insists on leaving prior to the three hour observation

- Refer to SESLHDPD/291 - Clinical Risk Assessment and Management and PD2017_015 - NSW Health Admission Policy **– Section 4 Discharge**
- Notify prescribing medical officer or their delegate medical officer
- All practices should align with the Mental Health Act (2007).

5. DOCUMENTATION / REPORTING

- An IMs+ report must be completed following any Post-injection Syndrome event as per SESLHDBR/009 - Incident Processes for Harm Score (HS) 2, 3 and 4 Incidents required to be reported to the MHS General Manager
- Any adverse drug reaction must be reported on IMs+, to the SESLHD MHS Drugs and Therapeutics Committee, 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 consumer's medical record indicating that the injection has been given and the pre and post-injection monitoring has been carried out as per this Procedure.
- A robust plan must be documented in eMR for the allocated three hours of PIS monitoring with appropriate/adequate resources.
- A plan detailing the process to gain emergency medical attention in the event of an adverse reaction must also be documented in eMR

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 Lily: Olanzapine Pamoate Long-Acting Injection (LAI) product information
- Eli Lilly: Zyprexxa Relprevv® Observation Checklist
- Mental Health Act (2007)
- NSW Health Safety Notice 019/21: Identification and Monitoring of Post-Injection Syndrome Olanzapine Pamoate Long Acting Injection (updated)
- 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
- PD2013_043 - Medication Handling in NSW Public Health Facilities
- PD2017_015 - NSW Health Admission Policy
- SESLHDPR/697 - Management of the Deteriorating ADULT inpatient (excluding maternity)
- SESLHDGL/082 - Clinical Risk Assessment and Management - Mental Health
- SESLHDBR/009 - Incident Processes for Harm Score (HS) 2, 3 and 4 Incidents required to be reported to the MHS General Manager

8. REVISION AND APPROVAL HISTORY

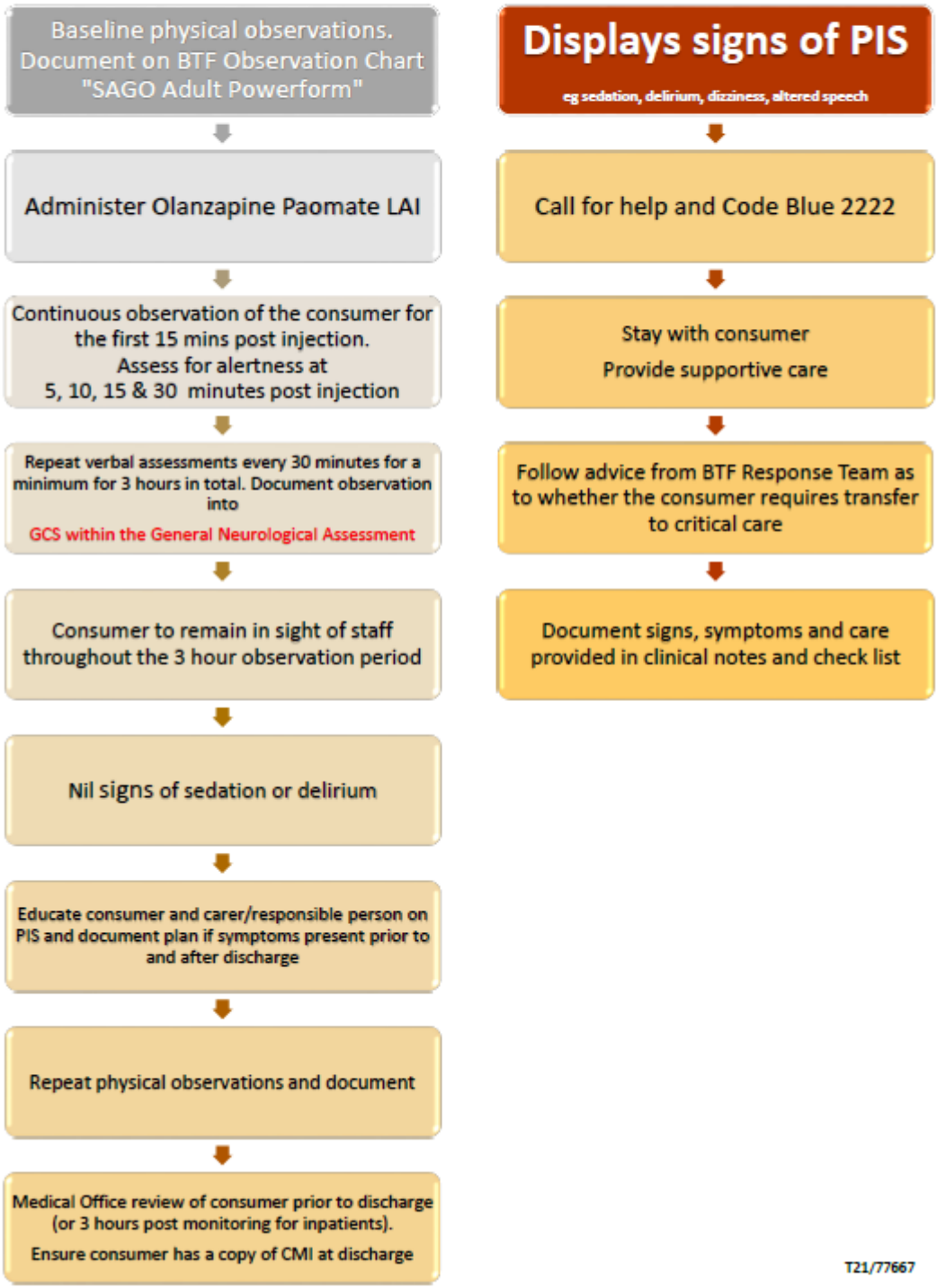
Date	Revision No.	Author and Approval
April 2017	1	First draft developed by Benjamin Chidester, SESLHD MHS Workplace Capabilities Mental Health Clinical Nurse Educator.
June 2017	2	Reviewed by Angela Karooz, SESLHD MHS Clinical Nurse Manager. Second draft updated by author upon feedback.
July 2017	3	Reviewed and updated by Lisa John, Pharmacist, POWH, and Peter Young, SESLHD MHS A/Chief Psychiatrist.
September 2017	4	Reviewed by District Document Development and Control Committee member (DDDCC). Feedback updated by author and MHS Policy Officer.

October 2017	5	Preliminary endorsed by DDDCC; required inclusion of audit process. Consulted Peter Young, A/Chief Psychiatrist and ESMHS Pharmacist on audit recommended process.
November 2017	6	Incorporate audit process feedback from ESMHS and District Lead Pharmacist. Reviewed by Ben Chidester and Angela Karooz.
January 2018	6	Endorsed by MHS Clinical Council.
May 2018	7	Reviewed by District QUMC. Reviewed and amended by District Mental Health Service: Peter Young, Angela Karooz and Trinh Huynh
May 2018	7	Processed by Executive Services prior to resubmission to SESLHD Quality Use of Medicine Committee.
July 2018	7	Endorsed by SESLHD Quality Use of Medicines Committee Endorsed by SESLHD Clinical and Quality Council
November 2021	8	Review commenced. Document updated to reflect that administration of Olanzapine Pamoate LAI can only be given in areas where a 2222 (not 000) response available. Appendix A expanded, Appendix B developed for testing. Post injection monitoring must be by an appropriately trained Nurse. Specification of post injection verbal observations to be recorded within the General Neurological Assessment chart (GCS) Endorsed MHS Drugs & Therapeutics Committee and Document Development and Control Committee.
December 2021	8	Endorsed SESLHD MHS Clinical Council. Approved by Executive Sponsor.
February 2022	9	Approved at SESLHD Quality Use of Medicines Committee.

APPENDIX A: OLANZAPINE LONG ACTING INJECTION (ZYPREXA RELPREVV): ADMINISTRATION MONITORING AND SAFETY FLOW CHART

OLANZAPINE LONG ACTING INJECTION (ZYPREXA RELPREVV): ADMINISTRATION, MONITORING AND SAFETY FLOW CHART

Trained health staff must maintain continuous observation of the consumer for 15 minutes immediately post injection. The consumer should remain in sight of staff for the remainder of the three hour observation period for signs and symptoms of PIS



APPENDIX B: CONSUMER INFORMED CONSENT

Health
South Eastern Sydney
Local Health District

Informed Consent for Olanzapine Pamoate Long Acting Injection (LAI)

I, _____.
(consumer name)

☐ I have read and understood the Consumer medicine Information for Zyprexa Relprevv (Olanzapine Pamoate LAI) and the nature of Post Injection Syndrome (also known as Post Injection Delirium/Sedation Syndrome (PDSS)) that may occur with this drug.

☐ All questions I have asked regarding the drug and post injection syndrome have been answered to my satisfaction.

☐ I agree to stay for three hours after the injection for observation purposes and I have organised an escort to accompany me home.

Name and contact number of escort: _____

☐ I agree to refrain from driving and operating heavy machinery for the rest of the day.

☐ I provide permission for the treating team to contact my family / carer if they have any concerns.

Name and contact number of family / carer _____

Signature of the participant: _____

Date: _____

Signature of administering clinician: _____

Name of administering clinician: _____

Name of Monitoring Health Professional: _____

Name of Attending Medical Officer: _____