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Medicine Guideline

Olanzapine Pamoate Long-Acting Injection (LAI)

Areas where Protocol/Guideline applicable	SESLHD Mental Health Services Olanzapine Pamoate LAI may only be administered in an area where a Code Blue 2222 response is available.
Authorised Prescribers:	Consultant Psychiatrist in consultation with the site Clinical Director
Important Safety Considerations	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. Unrecognised PIS has been linked to the unexpected deaths of a small number of consumers. 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 a **minimum of two hours post injection.** The observation period is to be determined by the site Clinical Director – it must be no less than two hours.
Indication for use	Maintenance treatment of schizophrenia
Proposed Place in Therapy	• Demonstrated tolerability and 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
Consumer selection	Criteria includes: • A willingness to comply with post injection monitoring requirements • A management plan for the administration and observation of the consumer post injection • A plan for the monitoring of the consumer's metabolic profile.
Adjunctive Therapy	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.
Contra-indications	Patients with a known hypersensitivity to Olanzapine Pamoate LAI or its ingredients.
Precautions	• 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.

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Dosage

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

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.

Prescribing Instructions

Prior to the initiation of Olanzapine Pamoate, the Consultant Psychiatrist must obtain initial approval from the site Clinical Director.

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

Olanzapine Pamoate LAI must be prescribed on the eMR or eRIC. In the absence of eMM systems, the appropriate paper medication chart may be used.

Pre-administration checks

Safe and accurate medication administration in the **5 Rights**: 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.

A safe 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.

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 minimum two-hour monitoring period as determined by the site Clinical Director.

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Equipment	• Olanzapine Pamoate (Zyprexa Relprevv®) injection pack • Gloves • Injection site dressing. *The Olanzapine Pamoate injection pack should be provided by the hospital pharmacy department in all inpatient settings.*
Olanzapine Pamoate injection pack	• 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, 38 mm safety needle • Two 19 gauge, 50 mm 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.
Administration Instructions	**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** 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. The Olanzapine Pamoate powder must only by reconstituted with the sterile diluent supplied in the injection package. 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

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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.

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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.

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Adverse effects	**Post Injection Syndrome (PIS) also referred to as Post Injection Delirium/Sedation Syndrome (PDSS)** can result from inadvertent intravascular injection of Olanzapine or where there is contact with blood (e.g., if a haematoma occurs around the track of the injection), causing a range of Olanzapine overdose-type symptoms. PIS is not dose, frequency, or time point specific, and the risk of occurrence exists following every administration. 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. In 91% of cases of PIS the initial signs and symptoms occur within the first hour, 96% of cases within 2 hours and 98% of cases within 3 hours. The remaining 2% of cases were identified beyond 3 hours. 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.

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Monitoring requirements	A plan for the monitoring of the consumer's metabolic profile is required. The consumer must be observed for sedation, confusion, agitation and other symptoms of PIS for a minimum of two hours duration as determined by the site Clinical Director after administration: • 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 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?" "Do you feel sedated?", "Open your eyes, take my hand". 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 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 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 and neurological observation monitoring has been carried out as per this procedure outlined in Appendix A. • A Medical Officer must review the consumer to ensure no signs and symptoms of PIS are displayed, at the conclusion of the observation period and prior to authorisation for discharge. Note: if an inpatient, this review must occur and be documented prior to the consumer being granted leave

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	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 • Consumers should be escorted home by a carer/responsible person • 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. **Consumer insists on leaving prior to the observation period being completed:** • Refer to SELSHDGL/082 Clinical Risk Assessment and Management – Mental Health and PD2025_012 Patient Admission and Discharge to NSW Health Facilities **– Section 4 Discharge** • Notify prescribing medical officer or their delegate medical officer • All practices should align with the NSW Mental Health Act (2007).
Management of Complications	A clinical review or Code Blue 2222 response must be activated in accordance with SESLHDPR/697 -Management of the Deteriorating ADULT inpatient (excluding maternity) Patients with Post Injection Syndrome (PIS) should be treated symptomatically.
Documentation and reporting	• An IMs+ report must be completed following any Post-injection Syndrome event as per SESLHDPR/748 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 National Standard 4 Committee and the SESLHD Drugs and Therapeutics 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 duration 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

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Basis of Protocol/Guideline:	1. Eli Lily: Olanzapine Pamoate Long-Acting Injection (LAI) product information 2. Eli Lilly: Zyprexxa Relprevv® Observation Checklist 3. NSW Mental Health Act (2007) 4. NSW Health Safety Notice 016/21: Identification and Monitoring of Post-Injection Syndrome Olanzapine Pamoate Long Acting Injection (updated) 5. Olanzapine depot injection (Zyprexa Relprevv) for schizophrenia 6. Post-injection delirium/sedation syndrome in patients with schizophrenia treated with olanzapine long-acting injection, I:analysis of cases 7. Macquarie Hospital Olanzapine Pamoate Protocol: PR2010_312 8. PD2022_032 Medication Handling 9. PD2025_012 Patient Admission and Discharge to NSW Health Facilities 10. SESLHDPR/697 - Management of the Deteriorating ADULT inpatient (excluding maternity) 11. SESLHDGL/082 - Clinical Risk Assessment and Management - Mental Health 12. SESLHDPR/748 Incident Processes for Harm Score (HS) 2, 3 and 4 Incidents required to be reported to the MHS General Manager 13. Meyers KJ, et al. Postinjection delirium/sedation syndrome in patients with schizophrenia receiving olanzapine long-acting injection: results from a large observational study. BJPsych Open. 2017; 3:186-92 14. SESLHDPR/607 Olanzapine Pamoate Long-Acting Injection (LAI): Administration and Management (replaced by Medicine Guideline)
Groups consulted in development of this guideline	MH National Standard 4 Committee (MHNS4C)

AUTHORISATION	
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Chairperson, DTC Committee	Stuart Binns, A/Chair DTC
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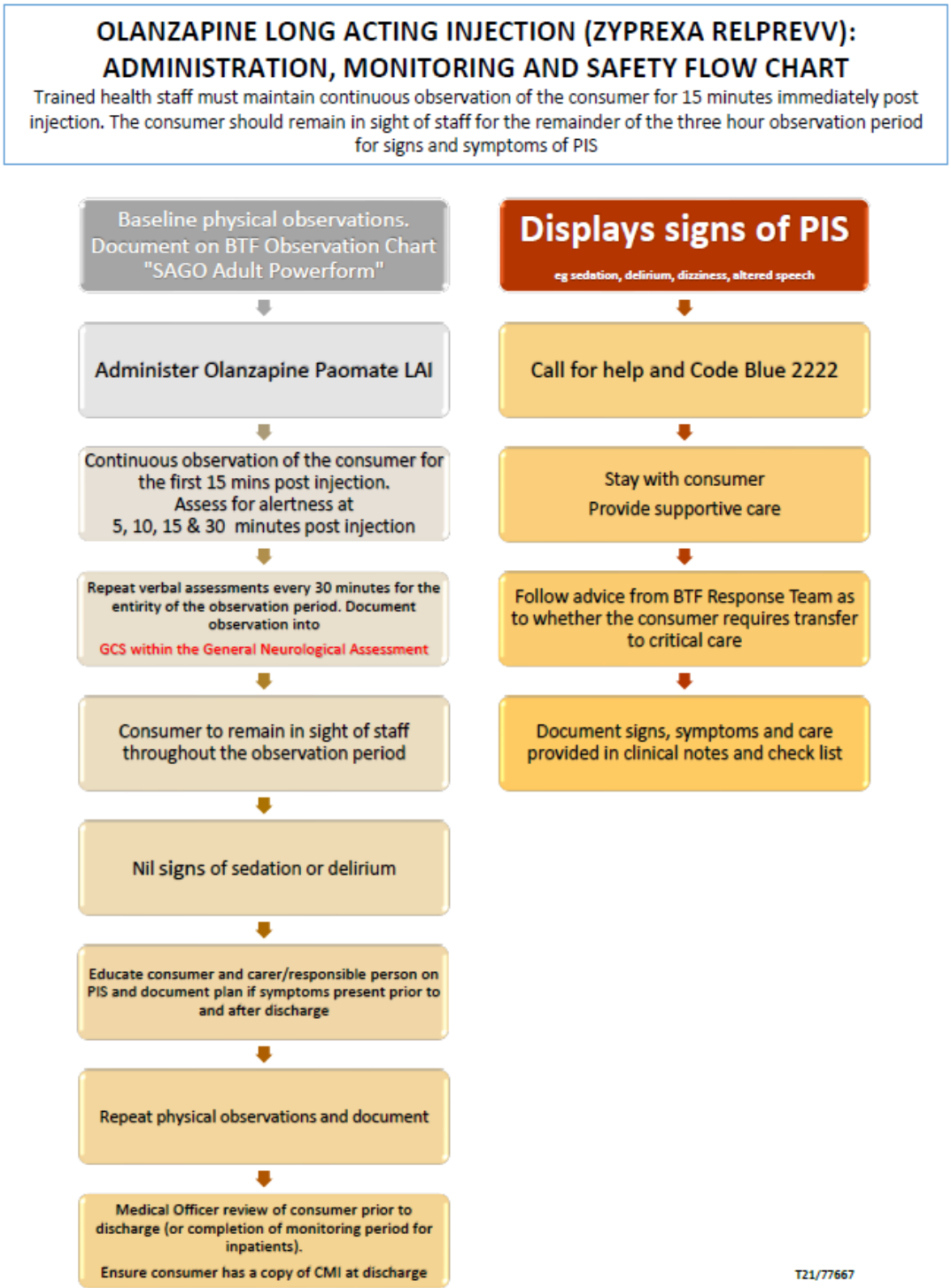
APPENDIX A: Olanzapine Long acting injection (zyprexa relprevv): Administration Monitoring and safety flow chart



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Appendix B: Consumer Informed Consent

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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 a minimum of _____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: _____

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