Prescribing protocol SESLHDPR/592
Intramuscular lorazepam

Health
South Eastern Sydney
Local Health District

Lorazepam intramuscular injection for acute management of aggressive and agitated behaviour of patients in Mental Health Inpatient Units	
Areas where Protocol applicable	Mental Health Inpatient Units
Areas where Protocol not applicable	Outside of Mental Health Inpatient Units
Authorised Prescribers	Psychiatric medical staff
Indication for use	Management of acutely agitated and aggressive psychiatric inpatients
Clinical condition	Agitation and aggressive behaviour related to mental illness not responsive to non-pharmacological interventions.
Contra-indications	Lorazepam injection is contraindicated in patients with a known sensitivity to benzodiazepines or the product's excipients (polyethylene glycol, propylene glycol and benzyl alcohol), in patients with acute narrow-angle glaucoma, patients with sleep apnoea syndrome and patients with severe respiratory insufficiency.
Precautions	The additive central nervous system effects of other drugs, such as phenothiazines, narcotic analgesics, barbiturates, antidepressants, scopolamine, and monoamine-oxidase (MAO) inhibitors, should be borne in mind when these other drugs are used concomitantly with or during the period of recovery from lorazepam injection. Extreme caution must be used when administering lorazepam injection to elderly patients, very ill patients, or to patients with limited pulmonary reserve because of the possibility of hypoventilation and/or hypoxic cardiac arrest. Resuscitative equipment for ventilatory support should be readily available. As with all benzodiazepines, paradoxical reactions may occur in rare instances and in an unpredictable fashion. In these instances, further use of the drug in these patients should be considered with caution. There have been reports of possible propylene glycol toxicity (e.g., lactic acidosis, hyperosmolality, hypotension) and possible polyethylene glycol toxicity (e.g., acute tubular necrosis) during administration of lorazepam injection at higher than recommended doses. Symptoms may be more likely to develop in patients with renal impairment.
Place in Therapy	Second line after oral treatment according to 2007/08v3 Emergency Sedation Policy – Acute Inpatient Psychiatry Units
Dosage **(Include dosage adjustment for specific patient groups)**	Lorazepam 1- 2mg intramuscularly, repeated after one to two hours, if needed, up to a daily maximum of 8mg. Elderly and patients with hepatic disease: Lorazepam 0.5mg -1mg intramuscularly repeated after one to two hours, if needed, to a maximum of 4mg/ 24 hours. Patients with Renal Disease: dosage adjustment not needed. Dose adjustments due to drug interactions: reduce dose by 50% when co-administered with probenecid or valproate. Increased doses may be required in female patients who are concomitantly taking oral contraceptives.

Duration of therapy	As required during inpatient admission
Important Drug Interactions	**CNS depressants** Lorazepam injection, like other injectable benzodiazepines, produces additive depression of the central nervous system when administered with other CNS depressants such as alcohol, phenothiazines, barbiturates, MAO inhibitors and other antidepressants. **Scopolamine** When scopolamine is used concomitantly with injectable lorazepam, an increased incidence of sedation, hallucinations and irrational behaviour has been observed. **Loxapine** Rare reports of significant respiratory depression, stupor and/or hypotension with the concomitant use of loxapine and lorazepam. **Clozapine** Marked sedation, excessive salivation, ataxia, and, rarely, death have been reported with the concomitant use of clozapine and lorazepam. **Haloperidol** Apnoea, coma, bradycardia, arrhythmia, heart arrest, and death have been reported with the concomitant use of haloperidol and lorazepam. The risk of using lorazepam in combination with scopolamine, loxapine, clozapine, haloperidol or other CNS-depressant drugs has not been systematically evaluated. Therefore, caution is advised if the concomitant administration of lorazepam and these drugs is required. **Valproate** Concurrent administration of lorazepam (2 mg intravenously) with valproate (250 mg twice daily orally for three days) to six healthy male subjects resulted in decreased total clearance of lorazepam by 40% and decreased formation rate of lorazepam glucuronide by 55%, as compared with lorazepam administered alone. Accordingly, lorazepam plasma concentrations were about two-fold higher for at least 12 hours post-dose administration during valproate treatment. Lorazepam dosage should be reduced to 50% of the normal adult dose when this drug combination is prescribed in patients **Oral Contraceptives** Co-administration of lorazepam (2 mg intravenously) with oral contraceptive steroids (norethindrone acetate, 1 mg, and ethinyl estradiol, 50 mcg, for at least six months) to healthy females (n=7) was associated with a 55% decrease in half-life, a 50% increase in the volume of distribution, thereby resulting in an almost 3.7-fold increase in total clearance of lorazepam as compared with control healthy females (n=8). It may be necessary to increase the dose of lorazepam in female patients who are concomitantly taking oral contraceptives. **Probenecid:** Concurrent administration of lorazepam (2 mg intravenously) with probenecid (500 mg orally every 6 hours) to 9 healthy volunteers resulted in a prolongation of lorazepam half-life by 130% and a decrease in its total clearance by 45%. No change in volume of distribution was noted during probenecid co-treatment. Lorazepam dosage should be reduced by 50% when co-administered with probenecid.

Administration instructions	Via intramuscular injection into the gluteal muscle, as per SESLHDBR/052 Administration of Ventragluteal Intramuscular Injection.
Monitoring requirements	As per 2007/08v3 Emergency Sedation Policy – Acute Inpatient Psychiatry Units.
Management of complications	Treatment of over-dose is mainly supportive until the drug is eliminated from the body. Vital signs and fluid balance should be carefully monitored in conjunction with close observation of the patient. An adequate airway should be maintained and assisted respiration used as needed. With normally functioning kidneys, forced diuresis with intravenous fluids and electrolytes may accelerate elimination of benzodiazepines from the body. In addition, osmotic diuretics, such as mannitol, may be effective as adjunctive measures. In more critical situations, renal dialysis and exchange blood transfusions may be indicated. Lorazepam does not appear to be removed in significant quantities by dialysis, although lorazepam glucuronide may be highly dialyzable. The value of dialysis has not been adequately determined for lorazepam. The benzodiazepine antagonist flumazenil may be used in hospitalized patients as an adjunct to, not as a substitute for, proper management of benzodiazepine overdose.
Storage and Handling	Lorazepam injection is not marketed in Australia. It is listed under Category C of the TGA Special Access Scheme and each use must be notified to the TGA using SAS Category C form available from: https://www.tga.gov.au/form/special-access-scheme Lorazepam injection is stored in the fridge. Schedule 4D handling requirements apply according to PD2013_043 Medication Handling in NSW Public Health Facilities
Basis of Protocol/Guideline	Product information, Cochrane review (Gillies et al 2013).
Groups/individuals consulted in development of this protocol	Katie Hargreaves, Quality Use of Medicines Lead Pharmacist, SESLHD

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GOVERNANCE	
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