

Methotrimeprazine HCl (Nozinan®) Injection Shortage

Suppliers of methotrimeprazine HCl injection in Canada¹:

| DIN | Brand Name | Manufacturer | Status as of 22 Jan 2019 |
|----------|-------------------|--------------|-----------------------------------------------------------|
| 01927698 | Nozinan Inj 25/ml | AVT | Currently in stock ² ; backorder is forecasted |

Health Canada-approved indications for injectable methotrimeprazine³:

- treatment of psychotic disturbances: acute and chronic schizophrenias, senile psychoses, manic-depressive syndromes
- treatment of moderate to severe pain
- treatment of nausea and vomiting of central origin
- management of insomnia

Methotrimeprazine may also be used for^{4,5}:

- control of agitation in palliative care patients or patients with acute brain injury
- sedation: pre-surgically, in ICU or in palliative care patients

Alternative dosage forms of methotrimeprazine^{1,2}:

- oral tablets: 2 mg, 5 mg, 25 mg, 50 mg (AAP)

Therapeutic Alternatives for Injectable Methotrimeprazine

1. Acute psychotic disturbance^{6,7}

| Drug/ROA | Dose | Comments |
|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Haloperidol IM | 2-5 mg (0.5-1 mg elderly) q4-8h prn. Max 20 mg/d (5 mg elderly) | Haloperidol 5 mg IM + lorazepam 2 mg IM more effective than haloperidol alone. |
| Zuclopenthixol acetate IM | 50-150 mg q2-3d prn up to 400 mg cumulative dose or 4 injections (whichever first) | Do not use in antipsychotic-naïve patients. Kinetics may allow for fewer required injections in severe acute agitation and/or aggression. |
| Olanzapine IM | 5-10 mg (2.5-5 mg elderly); if needed: 2 nd dose 5-10 mg 2h after 1 st ; 3 rd dose ≥4h after 2 nd Up to 30 mg and no more than 3 injections/24h | Has only been studied in mildly to moderately agitated patients. Efficacy ~haloperidol with less EPS. |
| Risperidone ODT* PO | 2 mg | In trial risperidone ODT 2 mg PO + lorazepam 2mg PO ~ haloperidol 5 mg IM + lorazepam 2 mg IM regarding psychotic agitation. ⁸ If patient willing & able to take PO. |

d=day; EPS = extrapyramidal symptoms; h=hour; IM=intramuscular; ODT=oral disintegrating tablet; PO = oral; prn=as needed; q=every; ROA= route of administration. * Not currently stocked at McKesson.²

2. Moderate to severe pain⁹

| Drug/ROA | Dose | Comments |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|
| Ketorolac IM or IV | 10-30 mg q4-6h up to 120 mg/d | 30 mg ~ 12 mg morphine. Limit use to 5 days. |
| Opioids: Fentanyl SL, IM, IV Hydromorphone PR*, IM, IV, SC Morphine PR, IM, IV, SC | See individual monographs | |
| Ibuprofen IV* ¹⁰ | 400-800 mg infusion q6h prn Max recommended: 2400 mg Do not exceed 3200 mg/24h | Intended as post-operative adjunct to parenteral opioids. Infuse over 30 min; Use beyond 24h needs to be justified. |
| d=day; h=hour; IM=intramuscular; IV=intravenous; min=minute; PR = rectally; prn= as needed; q=every; ROA= route of administration; SC= subcutaneous; SL= sublingual. *Not currently stocked at McKesson. ² | | |

3. Nausea and Vomiting of Central Origin¹¹

| Drug/ROA | Dose | Comments |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| Chlorpromazine IM*, IV* | 25-50 mg q3-4h prn | |
| Haloperidol IM, IV | 0.5-2 mg q12h prn | |
| Prochlorperazine PR | 5-10 mg TID-QID prn | |
| Metoclopramide IV, SC [^] | 10-20 mg TID-QID prn | |
| Ondansetron ODF, IV | PO: 16-24 mg/day divided q6-8h. IV: initial: up to 16 mg over 15 min; then: ≤ 8 mg at 4h and 8h prn | Potential serotonin syndrome or NMS-like events when combined with serotonergic or neuroleptic drugs. |
| BID=twice daily; d=day; h=hour; IM=intramuscular; IV=intravenous; min=minute; NMS=neuroleptic malignant syndrome; ODF=oral disintegrating film; PO=oral; PR= rectally; prn=as needed; q=every; QID=4 times daily; ROA=route of administration; SC=subcutaneous; TID= 3 times daily.*Not currently stocked at McKesson. ² [^] No Canadian products officially indicated for SC route ¹ but safety/efficacy have been established. ¹² | | |

4. Agitation

| Drug/ROA | Dose | Comments |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| Terminal agitation, palliative¹² | | |
| Midazolam SC [^] | 10 mg/24h CSCI and 2.5-10 mg SC prn; ↑ dose prn (10-60 mg/24h CSCI common) | |
| Lorazepam IV, SC [^] | 1-4 mg IV stat; 4-20 mg/24h CIVI or 1-2 mg SC q6-8h prn | Sometimes used instead of midazolam; generally used in conjunction with antipsychotic. |
| Haloperidol SC [^] | 2.5-10 mg stat and q1h prn (1-5 mg q1h in elderly) Maintenance: 10-15 mg/24h CSCI | Add to midazolam if >30 mg/24h required |
| Brain Injury^{13,14} | | |
| Propranolol PO | 20-40 mg/d; ↑ by 20 mg/d up to 640 mg/d | These agents have the most evidence. ¹³ If PO not possible, consider antipsychotics. |
| Carbamazepine PO | 200-300 mg BID-TID | |
| Divalproex PO | 250-500 mg TID | |
| BID = twice daily; CSCI=continuous subcutaneous infusion; CIVI=continuous intravenous infusion; d=day; h=hour; IM=intramuscular; IV=intravenous; PO= oral; prn=as needed; q=every; ROA=route of administration; SC=subcutaneous; stat=immediately; TID=3 times daily. [^] No Canadian products officially indicated for SC route ¹ but safety/efficacy have been established. ¹² | | |

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