

Potentially life threatening oral methotrexate dosing errors reported in NSW hospitals

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Objective

- To determine the incidence of oral methotrexate dosing errors reported in public hospitals located in New South Wales (NSW) and review causes and possible medication safety initiatives.

Background

- Increasing use of oral once-weekly methotrexate
- Methotrexate has low oral acute toxicity¹
- Methotrexate has high chronic oral toxicity when dosed incorrectly²
- Daily dosing for 3 consecutive daily doses can cause death
- Daily dosing errors in Australia are common, but underreported in adverse event databases. Australian Poisons Information Centres recently published on over 100 incidents of daily dosing in the community, with almost 10 times the number in PIC vs TGA database.² Changes coordinated with TGA and sponsor implemented in 2018.
- Coronial inquests resulted in actions to improve medication safety³
- Morbidity and mortality reviews can supplement these recommendations⁴
- Little is published on methotrexate medication errors from hospitals

Methods

- Incident Information Management System (IIMS) is the incident reporting system for NSW Public Hospitals, data obtained from Clinical Excellence Commission (NSW Health).
- Entries involving methotrexate were extracted from 01-01-2010 to 21-04-2015, and manually reviewed.

Results

- 4 incidents where administered for 3 or more consecutive days:
 - One death after an elderly patient given 10mg daily for three consecutive days – unclear prescribing order and administration error.
 - Prescribing error by resident and drug administered from stock obtained by nurse from after-hours access to pharmacy. No follow-up.
 - Discharge prescription error dispensed by community pharmacy without verification. No adverse event outcome documented.
 - Prescribing error and administered twice daily for 3 days. No follow-up.
- 63 near misses were methotrexate charted or dispensed daily but the error was realised before three days elapsed.
- Who finds errors:
 - 24 by pharmacy staff
 - 2 by nursing staff
 - 2 by medical staff
 - 1 by the patient
 - Not stated in the remaining 34 cases
- Frequency of these reports has remained stable over the time period studied, with 11-13 reports/year.

Limitations

- Only includes identified and reported errors and likely underestimates the true frequency of these events.
- Due to the delay in clinical consequences of methotrexate errors, outcomes may be underreported.

Conclusions

- Potentially fatal errors with oral methotrexate continue to occur in NSW hospitals, despite measures implemented to reduce the risk of error.
- Highlights the role of pharmacy in medication safety and the value of timely pharmaceutical review.
- A range of strategies have been proposed for more than a decade to reduce the chance of in-hospital methotrexate errors, including mandatory policy in NSW hospitals in 2005 with revision in 2015:
 - A key change was the prohibition of methotrexate in after-hours medicine supplies (including through direct pharmacy access)
- Electronic inpatient prescribing with safety checks could help by:
 - Default weekly administration
 - Requiring verification and entry of an appropriate oncologic indication in order entry systems for daily orders
 - Prohibiting charting of methotrexate in emergency departments
 - Preventing weekend prescribing
 - Restricting methotrexate to 'designated prescribers'
 - Mandating pharmaceutical review before administration
- ISMP 2017 survey results in US hospitals show 79% now have default weekly prescribing (up from 28% in 2014)⁵
- An evaluation of incidents is planned for 2015-18, after the latest policy directive was implemented. Further opportunities for audit of oral methotrexate medication safety practices in Australia.
- Education to health professionals that minor delays in administration of methotrexate (eg several days) should not alter effectiveness. For short stays, omission of that week's dose is reasonable – particularly since renal impairment/infection are common for inpatients.
- This builds on Australian community data showing oral methotrexate dosing errors remain an issue.
- If an incident occurs, seek urgent specialist advice from a clinical toxicologist or Poisons Information Centre on 131126 regarding management including antidote dosing.



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References

- Chan et al. Clin Toxicol. 2017; 55 (2):88. What can clinicians learn from therapeutic studies about the treatment of acute oral methotrexate poisoning?
- Cairns et al. Med J Aust 2016; 204 (10): 384. A decade of Australian methotrexate dosing errors.
- Coroners Court of Victoria. June 2018. Finding - Inquest into the Death of Ian John Gilbert. Available at: <http://www.coronerscourt.vic.gov.au/home/coroners/written+findings/findings+-+inquest+into+the+death+of+ian+john+gilbert>
- Brown et al. Asia Pacific Association of Medical Toxicology Scientific Congress 2018. Poster 53. Morbidity and mortality review of methotrexate: the many lessons learnt.
- Institute for Safe Medication Practices (ISMP). August 9, 2018. Call to Action: Longstanding Strategies to Prevent Accidental Daily Methotrexate Dosing Must Be Implemented. Available at: <https://www.ismp.org/resources/call-action-longstanding-strategies-prevent-accidental-daily-methotrexate-dosing-must-be>

Policy Directive



Methotrexate - Safe use of Oral Methotrexate

Document Number PD2005_624
Publication date 26-Sep-2005
Functional Sub group Corporate Administration - Governance
Clinical Patient Services - Pharmaceutical
Clinical Patient Services - Medical Treatment
Clinical Patient Services - Nursing and Midwifery
Population Health - Pharmaceutical
Summary This policy replaces Information Bulletin 98/31. Policy and risk management strategies to reduce the risk of error when oral methotrexate is prescribed, dispensed and administered for the treatment of inpatients of outpatients. Oral methotrexate is considered a high alert medicine due to the potential for error with its once a week dosage regimen, which is unusual compared to the daily dosing of most other medicines.
Author Branch Clinical Excellence Commission
Applies to Area Health Services/Chief Executive Governed Statutory Health Corporation, Board Governed Statutory Health Corporation, Affiliated Health Organisations, Public Health System Support Division, Community Health Centres, Divisions of General Practice, Government Medical Officers, Private Hospitals and Day Procedure Centres, Private Nursing Homes, Public Hospitals
Audience Administration, medical, pharmacy, nursing

Policy Directive



High-Risk Medicines Management Policy

Document Number PD2015_029
Publication date 12-Aug-2015
Functional Sub group Corporate Administration - Governance
Corporate Administration - Records
Clinical Patient Services - Medical Treatment
Clinical Patient Services - Nursing and Midwifery
Population Health - Pharmaceutical
Summary This policy directive outlines the requirements for the safe management and use of high-risk medicines within NSW Health facilities. It defines the requirements for establishing a high-risk medicines program that includes the development of a specific high-risk medicines register and the strategies to mitigate the risks associated with those medicines. This policy includes individual policy standards for the following medicines: hydromorphone, methotrexate (oral), neuromuscular blocking agents, paracetamol, potassium (intravenous), vincristine and anticoagulants.
Replaces Doc. No. High-Risk Medicines Management (PD2012_003)
Paracetamol Use (PD2009_009)
Methotrexate - Safe use of Oral Methotrexate (PD2005_624)

Requirement	Reviewed	Status
1. Methotrexate is not available in the after-hours pharmacy	Fully (2)	Partially (2)
2. Methotrexate is not available in the after-hours pharmacy	Fully (2)	Partially (2)
3. The pharmacist writes a full oral dose of the medicine (methotrexate) that is clear from the days of the week and the methotrexate is not in the pharmacy	Fully (2)	Partially (2)
4. Methotrexate is not in the pharmacy	Fully (2)	Partially (2)
5. There is a pharmacist review of all methotrexate prescriptions	Fully (2)	Partially (2)
6. Prior to discharge, all patients receive counselling on oral methotrexate including when their next dose is due	Fully (2)	Partially (2)