



METHOTREXATE PROTOCOL FOR HEALTH CENTRES

Introduction

Methotrexate is an antineoplastic drug which is commonly used in the treatment of several non-cancer conditions, including rheumatoid arthritis, psoriasis and Crohn's disease. Methotrexate is classified as a cytotoxic agent, and therefore carries potential occupational health and safety risks to the health care provider. The primary routes of exposure are through: inhalation of airborne contaminants (e.g., expulsion of air from a drug-filled syringe, vial or from a crushed tablet); absorption (e.g., spills or splashes to the skin or eyes, or sharps injuries); and ingestion. This document is intended to provide best practices for the safe transportation, preparation, administration and disposal of methotrexate, with the goal to minimize the occupational health and safety risks.

Methotrexate has been shown to have the potential to be teratogenic, therefore it is not to be given to women who are pregnant or breastfeeding, or to men or women planning to conceive. The literature is not as conclusive about the reproductive risks associated with occupational handling of cytotoxic drugs. However, since methotrexate has the potential to be teratogenic, it is recommended that all health care providers who are pregnant, breastfeeding or planning to conceive avoid handling the medication.

Policy

Registered Nurses (RN) may administer oral and parenteral methotrexate with a written physician order. The order must contain instructions for patient monitoring (such as frequency of blood work) and parameters for physician consultation.

The drawing up of methotrexate from vials into syringes for subcutaneous administration is to be done in a pharmacy in a biologic safety cabinet. If a special circumstance arises and there is a need to prepare syringes in the health centre, then the Territorial Pharmacist must first be consulted for further direction.

In order to minimize the risks of harm, parenteral route methotrexate is to be given on-site in the health centre only. In-home administration by the RN, NP or RPN may be considered on an individual basis when the patient does not have reasonable access to the health centre. These cases must be discussed with the Supervisor of Community Health Programs, Regional Home Care Manager and Territorial Pharmacist.

Patients or family members willing to self-administer the injections must receive appropriate training and supervision. Contact the Territorial Pharmacist for training material and/or guidance.

Definitions

Cytotoxic Agent: Refers to any agent that may be:

- Genotoxic (damages DNA)
- Mutagenic (induces or increases genetic changes by causing DNA changes)
- Oncogenic (giving rise to or causing cancerous tumours) or
- Teratogenic (ability to cause fetal malformations)



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Handling: Refers to the process of transportation, preparation, administration and disposal of methotrexate.

Nurse: For the purpose of this document, nurse refers to Registered Nurses and Nurse Practitioners.

Transportation

As a cytotoxic agent, methotrexate falls under the Transportation of Dangerous Goods Act. Pre-filled syringes and tablets are for personal use and are considered exempt from the regulations.

PRACTICE POINT: Pre-filled methotrexate syringes are now available from NIHB on a drug exception basis. The physician or retail pharmacist is required to contact NIHB and request the exception. It will be granted if the patient qualifies under a set list of criteria (e.g., inability to draw up medication into the syringe themselves). The drug exception number for NIHB is 1-800-580-0950.

Methotrexate in vials, however, falls under the Transportation of Dangerous Goods Act and thus requires a Transportation of Dangerous Goods certificate.

Packaging methotrexate for transportation should include a sealable plastic container with enough absorbent material to retain the volume being transported. The package is then placed in a puncture proof container for shipment. The outer container must have a warning label indicating that it contains a cytotoxic agent.

Transportation to the home: The syringes are transported with the luer end capped off and double bagged in cytotoxic bags. A home health spill kit is also required for transportation to the home.

Storage

Methotrexate must be double bagged in cytotoxic bags and stored in a bin that is clearly labeled with a cytotoxic sticker. No other medications are to be stored in this bin. The spill kit is always required to be stored with the medication and transported with the medication whenever it is moved or administered. Gloves are to be worn when unpacking the medication.

Consent

Explain the procedure, including the anticipated benefits, potential risks, and required follow up of methotrexate treatment. Obtain verbal consent. Review *Appendix C: Patient Teaching pamphlet*.

Patient Monitoring

Patients receiving methotrexate therapy require close monitoring. Routine blood work including a CBC with differential, serum creatinine and LFTs is required to help monitor for toxicity. The frequency of blood work monitoring is determined in collaboration with the prescribing physician. The goal is early detection and treatment to minimize potential toxicity.

The patient must be added to the Chronic Disease Management program in the community. It is recommended that the patient be assigned to one nurse for this ongoing management, whenever



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possible. The frequency of follow up appointments will be determined in collaboration with the prescribing physician.

PRACTICE POINT: The patient may require more frequent monitoring during the initiation of therapy, or during periods of increased risk of elevated methotrexate blood levels (e.g., dehydration).

Baseline Health Assessment:

- ✓ Conduct a general health assessment. Hold the injection and consult the physician if any of the following are noted: shortness of breath, dry, non-productive cough, mouth ulcers, nausea, or any overt signs of infection.
- ✓ If the patient is in reproductive years, counsel both men and women about the use of birth control during methotrexate therapy.

Physician Consultation

The most responsible physician must be consulted when:

- Any of the reported lab values are outside of the treatment parameters;
- The patient demonstrates any adverse effects to treatment;
- The patient exhibits shortness of breath, dry, non-productive cough, mouth ulcers, nausea, or any overt signs of infection;
- The patient becomes pregnant;
- The patient is planning to conceive;
- Anytime the nurse requires clarification of this protocol or is unsure on how to proceed.

The patient should be scheduled to see the physician during the first community visit following initiation of methotrexate therapy. The frequency intervals for follow up physician assessments shall be determined in collaboration with the physician. A documented care plan is required.

Personal Protective Equipment

Disposable Personal Protective Equipment (PPE) must be worn when handling methotrexate to avoid accidental drug exposure. See Table 1: Personal Protective Equipment Requirements.





PRACTICE POINT: Don gloves and a gown (use a face shield if there is a risk of splashing) when handling urine or other excreta from patients that have received methotrexate within the previous 48 hours.

Do not wear the PPE outside the administration area. Used PPE must be handled as cytotoxic waste and disposed of accordingly. Don and remove PPE according to guidelines in Appendix A.



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Table 1: Personal Protective Equipment Requirements

	<div>GLOVES</div> <div></div>	<div>GOWN</div> <div></div>	<div>EYE PROTECTION</div> <div></div>	<div>MASK</div> <div></div>
	<ul style="list-style-type: none">• 7-9 mm thick• Latex, nitrile, polyurethane or neoprene• Inspect gloves for visible defects• Double glove for spills• Change immediately if punctured or contaminated	<ul style="list-style-type: none">• Disposable moisture resistance• Long sleeve• Ensure outer glove extends over the cuff	<ul style="list-style-type: none">• Chemical splash goggles when there is potential for splashes into eyes• Eye wash station must be available	<ul style="list-style-type: none">• Disposable face mask for protection against aerosolized particles (e.g., N95 mask) <p>Note: Fit testing required for N95 mask</p>
PREPARATION				
Oral (intact coated tablets)	YES	NO	NO	NO
Split oral tablets	Preparation not permitted at the health centre – to be completed at the pharmacy Contact the Territorial Pharmacist for guidance.			
S/C Injection				
ADMINISTRATION				
Oral (intact coated tablets)	YES	NO	NO	NO
Feeding tube (liquid prep)	YES	YES	YES	NO
S/C Injection	YES	YES	YES if splashing possible	NO
Spill Clean Up Kit	YES	YES	YES	YES
Waste Disposal	YES	YES if waste uncontained	YES if waste uncontained	NO



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Administration

Equipment Required:

- PPE (as identified in Table 1)
- Cytotoxic bags
- Puncture and leak proof container (e.g., sharps container) that is labeled with cytotoxic sticker
- Cytotoxic alert stickers
- Home spill kit
- Storage bin for cytotoxic drugs
- Biohazardous waste bins with cytotoxic alert sticker

General Administration Procedure:

1. Verify that all blood work has been completed and evaluate the results. If any of the results are outside the specified treatment parameters, hold the injection and consult the physician.
2. Conduct a general health assessment and verify there are no contraindications – contact the physician if noted. Verify pregnancy status and plans for conception (patient of reproductive age).
3. Gather all supplies and PPE equipment (as outlined in Table 1), including the spill kit.
4. Inspect the shipment container and its contents prior to handling it. Perform all work below eye level and have access to a cytotoxic spill kit at all times when handling the medication.
5. Don PPE, as outlined in *Appendix A*, prior to removing methotrexate from the shipment container.
6. Administer the medication:

6.1 Oral Route:

- Blister packaging is preferred. Use a non-touch technique for transferring tablets from their container into disposable cup to avoid direct handling. When possible, have the patient open the package and handle the medication themselves. Instruct the patient to wash hands afterwards to reduce surface contamination.
- Dispose of the medication wrapper into the regular garbage.

PRACTICE NOTE: Instruct patients not to crush or chew the tablets. If crushing is required, contact the prescribing physician to discuss changing the prescription.

- If the patient requires split tablets, discuss with the pharmacy. Splitting the tablets in the health centre is not permitted due to the increased risk of accidental exposure to the drug.

PRACTICE NOTE: Methotrexate is available as 2.5 mg tablets. The usual adult dose is 7.5-20 mg once weekly. The usual dosing in children for rheumatologic disorders is 10-15 mg/m² (BSA-directed) or 0.5-1 mg/kg (weight-directed) once weekly, to maximum of 25 mg/week. Discuss with the physician to have the dose rounded to the nearest 2.5 mg dose. If the child requires a non-rounded dose, then recommend measuring the appropriate quantity of the parenteral form (vial) and administer it orally.

6.2 Feeding Tube Route:

- Follow administration procedure outlined the text book *Clinical Nursing Skills and Techniques* (Perry, Potter, and Ostendorf).



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- Discard empty containers into the biohazardous container.

6.3 SC or IM Route:

- Do not expel air due to risk of inhalation or spillage of medication.
- Administer the injection as outlined in the text book *Clinical Nursing Skills and Techniques* (Perry, Potter, and Ostendorf).
- Dispose of the syringe and needle into the puncture proof biohazardous container immediately following injection.

PRACTICE NOTE: Injections are absorbed best from the stomach, next from the arms, and least well from the legs and buttocks.

7. Remove and discard PPE in hazardous waste container (as outlined in *Appendix A*) and perform hand hygiene.
8. Document according to the medication standards stated in the *GN Community Health Nursing Policies, Standards, and Guidelines*.
9. Any unopened medication packages are to be returned to the pharmacy as described in the Transportation section of this policy. Never discard the medication into a drain, toilet or other receptacle.
10. Used biohazardous containers must have a cytotoxic sticker affixed to the container and shipped according to Transport Canada regulations to the regional facility for incineration.

Management of Spills

Prevention of spills of biohazardous drugs is paramount. However, even with careful handling, spills can happen. Spill kits must be available wherever methotrexate is stored, prepared, or administered. All staff required to handle methotrexate must be oriented to where the spill kit is stored and how to safely manage spills. Housekeeping staff are not to be delegated this task. Spills must be managed immediately by staff that were handling the drug and trained on spill management.

1. Notify the SCHP and anyone in the immediate area that a cytotoxic spill has occurred and instruct them to avoid the area.
2. Open the spill kit, display signs, restrict access and call for assistance as required.
3. Don PPE (gown, double gloves, N95 mask, and eye shield or goggles).
4. For liquid spills, wait a few seconds for aerosols to settle, then cover spill using absorbent material. Be careful not to cause splashes.
5. For spills involving powder, place an absorbent mat over the powder. Be careful to minimize dust disruption. Cautiously wet the mat so that the powder dissolves and is absorbed by the mat.
6. Gather absorbed material and discard into a cytotoxic waste bag.
7. Wash area several times with detergent, working from area of least contamination and rinse thoroughly with water.
8. Dry the affected area with absorbent towels and dispose into cytotoxic waste bag.
9. Discard outer gloves into the cytotoxic waste bag. Seal bag and place inside a second cytotoxic waste bag.
10. Discard contaminated PPE and inner gloves into the outer bag and seal.
11. Place cytotoxic waste bag in a biohazardous container.



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12. Wash hands with soap and water.
13. Complete the incident report and submit to the regional office as per established regional procedures.
14. Ensure the cytotoxic spill kit is replaced through established regional ordering processes.

Accidental Exposure / Contact

Eye Contact:

1. Call for help and immediately flush the affected eye(s) with copious amounts of water or normal saline for a minimum of 15 minutes. Ensure the water reaches the eyeball by gently prying the eyelids open and keeping them apart until the treatment is complete.
2. Seek medical attention.
3. Incident report and WSCC report to be completed as soon as possible.

Skin Contact:

1. Call for help and immediately remove any contaminated clothing.
2. Wash the affected area with soap and water for minimum of 15 minutes.
3. Seek medical attention.
4. Incident report and WSCC report to be completed as soon as possible.

Skin puncture:

1. Wash the puncture site thoroughly with soap and water for 15 minutes.
2. Allow wound to bleed freely.
3. Incident report and WSCC report to be completed as soon as possible.

Contamination of Clothing and PPE:

1. Immediately remove outer gloves, gown and any contaminated clothing.
2. Place disposable PPE in the biohazardous container.
3. Contaminated clothing should be separately bagged and machine washed separately and line dried.
4. Remove and dispose of inner gloves.
5. Seek medical attention.
6. Incident report and WSCC report to be completed as soon as possible.

Appendices

Appendix A: Donning and Removing Personal Protective Equipment

Appendix B: Methotrexate Frequently Asked Questions

Appendix C: Methotrexate Teaching Pamphlet



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References

1. Provincial Infectious Diseases Advisory Committee (2012). Routine Practices and Additional Precautions in all Health Care Settings, 3rd Edition.
http://www.publichealthontario.ca/en/eRepository/RPAP_All_HealthCare_Settings_Eng2012.pdf
2. The Ottawa Hospital (2014). Cytotoxic agents and hazardous drugs: Safe handling, administration, and disposal.
3. Perry, A. G., Potter, P.A., and Ostendorf, W. (2013). Clinical Nursing Skills and Techniques 8th ed. Mosby.

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Appendix A: Donning and Removing Personal Protective Equipment

PUTTING ON PPE

1. Perform Hand Hygiene



2. Put on Gown

Tie neck and waist ties securely



5. Put on Gloves

- Put on gloves taking care not to tear or puncture glove
- If a gown is worn, the glove fits over the gown's cuff



3. Put on Mask/N95 Respirator

- Place mask over nose and under chin
- Secure ties, loops or straps
- Mould metal piece to your nose bridge
- For respirators, perform seal-check



4. Put on Protective Eyewear

- Put on eye protection and adjust to fit
- Face shield should fit over brow



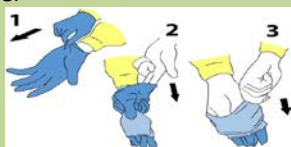
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Appendix A: Donning and Removing Personal Protective Equipment

TAKING OFF PPE

1. Remove Gloves

- Remove gloves using a glove-to-glove/skin-to-skin technique
- Grasp outside edge near the wrist and peel away, rolling the glove inside-out
- Reach under second glove and peel away
- Discard immediately into biohazardous container

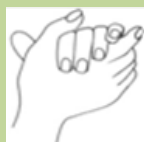


2. Remove Gown

- Remove gown in manner that prevents contamination of clothing or skin
- Starting at the neck ties, the outer 'contaminated', side of gown is pulled forward and turned inward, rolled off the arms into a bundle, then discarded immediately in a manner that minimizes air disturbance



6. Perform Hand Hygiene



3. Perform Hand Hygiene



5. Remove Mask/N95 Respirator

- Ties/ear loops/straps are considered 'clean' & may be touched with hands
- The front of the mask is considered to be contaminated
- Untie bottom tie then top tie, or grasp straps or ear loops
- Pull forward off the head, bending forward to allow mask to fall away from face
- Discard immediately into biohazardous container



4. Remove Eye Protection

- Arms of goggles and headband of face shields are considered to be 'clean' and may be touched with the hands
- The front of the goggles/face shield is considered to be contaminated
- Remove eye protection by handling ear loops, sides or back only
- Discard into waste receptacle or into appropriate container to be sent for reprocessing
- Personally-owned eyewear may be cleaned by the individual after each use

