

TB Prevention and Control Saskatchewan: An Overview for Pharmacists and Pharmacy Technicians

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What is TB Prevention and Control Saskatchewan (TBPC SK)?

TB Prevention and Control Saskatchewan is a centralized provincial program administered by the Saskatchewan Health Authority. The program is responsible for tuberculosis (TB) prevention, treatment, education and control. The program serves residents of Saskatchewan with TB and those at risk of developing it.

How are the program's services delivered?

The program is delivered by a multi-disciplinary health care team and has three offices. Saskatoon has the main office at the Royal University Hospital. Secondary locations are in Regina and Prince Albert. Additionally, mobile clinics are offered in many communities, mainly in the north, and TeleHealth clinics are also utilized.

The program operates by referral. Referrals and consults are received for individuals undergoing screening for latent TB, candidates for treatment of latent TB, and those suspected or confirmed of having active TB. A patient undergoing treatment for TB will be monitored by the TBPC SK team for the course of their treatment. All positive laboratory results for TB are automatically reported to TBPC SK. Treatment of active TB is mandatory. The decision to treat latent TB is based on individual risk factors.

What are the indications for the screening of TB?

- Exposure to persons with infectious active TB
- Immigration screening and surveillance
- Admission to a correctional facility for one year or longer
- Pediatric screening within defined areas
- Employment, travel and educational program screening
- Health care provider referral for:
 - Anyone with signs and symptoms of active TB
 - A patient with ongoing respiratory symptoms (ex. coughing for > than 3 weeks, fever lasting > 1 week, pneumonia not responding to traditional antibiotics).
- Screening of patients at increased risk of developing active TB: HIV positive, on immunosuppressant drugs, awaiting organ transplant, or prior to starting treatment with a biologic drug

Who can prescribe treatment for TB?

Only TBPC-approved physicians may prescribe treatment for TB in Saskatchewan. There are currently six TBPC physicians in the province.

What is the role of the TB Pharmacy?

All medications for the treatment of TB are dispensed from the TB Pharmacy which is located at the TB Main Office in Saskatoon. In addition to the antitubercular antibiotics, the TB pharmacy will also dispense medication to manage the side effects of antitubercular drugs (ex. antinauseants, antihistamines, analgesics). The pharmacy ships medications to the TB office or health center nearest to the patient, where local providers are responsible to administer directly-observed-therapy (DOT). The medication may be shipped to a patient's home for self-administered therapy (SAT). There is no cost to the patient for any medications or services provided by TBPC SK.

The TB pharmacist is responsible for ensuring appropriateness, efficacy, and safety of TB treatment. They will evaluate drug interactions and recommend drug dosing for all patients. Suggestions for monitoring and management of identified drug interactions will be made to the TBPC physician and nurse. The TBPC physician may manage interactions or forward the information to the patient's most responsible physician for management and monitoring. The TBPC physician or nurse may instruct patients how to self-manage minor interactions.

Are there instances when TB medications may be dispensed by other pharmacies or prescribers?

Yes. The Refugee Engagement and Community Health (REACH) Clinic in Saskatoon prescribes treatment for latent TB and the Community Clinic Pharmacy dispenses for these patients.

Refugees will have initial health assessments at REACH. If latent TB is identified, and the patient can take SAT, the REACH physician will prescribe treatment and follow this patient. The Clinic will notify TBPC SK. If the patient needs DOT or has active TB, they will be referred to TBPC SK for treatment.

You may see anti-tubercular medications prescribed by non-TBPC SK physicians to treat other species of mycobacterium, such as *Mycobacterium avium* and *Mycobacterium kansasii*. Rifampin is also used to treat various infections caused by methicillin-resistant *S. Aureus*, for prophylaxis and treatment of meningitis, and other off label indications.

Sometimes DOT is provided at a community pharmacy, especially if a patient already receives DOT for another drug. The TB Pharmacy still fills these prescriptions and delivers them to the community pharmacy for administration.

What are the most common medications and regimens used to treat tuberculosis?

Although there are many possible regimens, TBPC SK has approved the following:

Treatment of Latent TB Infection:	Treatment of Active TB disease:
1. Rifampin once daily x 4 months	6-12* months of treatment with the following drug combination†: Isoniazid +/-pyridoxine^ Rifampin‡ Ethambutol~ Pyrazinamide~ +/- Levofloxacin or moxifloxacin (if suspected resistance) Once daily or five times weekly for the 1st 2 months followed by three times weekly thereafter **DOT**
2. Isoniazid once daily x 9 months	
3. Isoniazid twice weekly x 9 months **DOT**	
4. Isoniazid, rifapentine and pyridoxine once weekly x 12 weeks **DOT**	
5. Isoniazid + rifampin twice weekly x 4 months **DOT**	
6. Isoniazid three times weekly x 9 months (used with concurrent HIV infection or renal dialysis) **DOT**	

****DOT****= directly observed therapy

*Factors that may influence duration: severity, location of disease, medical conditions, and resistance. Treatment may extend beyond 12 months in some cases.

† If allergy or resistance to primary agent then second line drugs will be substituted and/or duration may be extended.

^Pyridoxine is used with isoniazid containing regimens to decrease neuropathy in at-risk patients (ex. pregnancy, breastfeeding, malnourishment, diabetes, renal or hepatic insufficiency)

‡Rifabutin may be substituted for rifampin if too many drug interactions, ex. with anti-retroviral medications

~Ethambutol and Pyrazinamide can be discontinued after 2 months if organism is fully sensitive

How is treatment administered?

In Saskatchewan, directly observed therapy (DOT) is the standard of treatment for persons with active TB, and is commonly used when treating latent TB. Self-administered therapy (SAT) may be provided to some patients with latent TB.

Directly observed therapy helps achieve optimal adherence. Adherence is important to ensure successful treatment, decrease morbidity and mortality, decrease transmission of TB and prevent drug resistance.

Do I need to ensure adherence to TB medications?

No. TBPC SK will monitor adherence for all of their patients. You will not need to be responsible for this. If a patient reports non-adherence to you, please encourage and/or help them to follow-up with their TBPC nurse and physician.

What do I do about potential drug interactions?

The TB pharmacist will have screened for and assisted in management of drug interactions between TB medications and pre-existing prescription medications on a patient's Pharmaceutical Information Program (PIP) profile. You should not need to rescreen these. As a community or hospital pharmacist, your responsibility is to manage interactions that arise with **newly initiated** prescription or over the counter medications. If an interaction with a TB drug that cannot easily be managed is identified, the prescriber should be contacted to seek an alternative as the TB meds are generally not changed once therapy commences. If an alternative is not available or the condition requires urgent treatment then the prescriber may need to contact the TB physician.

What are some common drug interactions with antitubercular drugs?

COMMON DRUG-DRUG INTERACTIONS INVOLVING RIFAMYCINS***

Drugs Whose Concentrations May be Substantially Decreased	TB Drug	Comments
Hormone therapy: oral contraceptive pills, patches, implants and injections	Rifampin, rifapentine, rifabutin	Add a barrier method of contraception
Levothyroxine	Rifampin	Monitor TSH; may require levothyroxine dose increase
Selective Serotonin Reuptake Inhibitors (citalopram, escitalopram, sertraline)	Rifampin	Moderate risk of interaction; may require SSRI dose increase
Corticosteroids	Rifampin, rifapentine	Monitor clinically; may require a 2- 3 fold corticosteroid dose increase
Novel oral anticoagulants: (apixaban, rivaroxaban dabigatran, edoxaban)	Rifampin	Some combos contraindicated; check individual monographs
Warfarin	Rifampin, rifapentine, rifabutin,	Monitor prothrombin time; may require 2-3 fold warfarin dose increase
Methadone	Rifampin, rifapentine, rifabutin,	May require methadone dose increase, rifabutin rarely implicated
Anticonvulsants: Phenytoin Lamotrigine	Rifampin, rifapentine	May require anticonvulsant dose increase

Antiretrovirals (ARVs): Multiple classes	Rifampin, rifapentine, rifabutin,	Complex interactions beyond scope of this document. Rifabutin usually preferred drug with ARVs
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COMMON DRUG-DRUG INTERACTIONS INVOLVING ISONIAZID***

Drugs Involved	Comments
Acetaminophen	↑ risk of hepatotoxicity; limit or avoid acetaminophen
Warfarin	↑ anticoagulant effect; monitor and adjust dose as needed
Anticonvulsants: Phenytoin Carbamazepine (CBZ) Valproic acid (VPA)	↑ phenytoin levels ↑ risk of hepatotoxicity; ↑ CBZ levels; monitor and adjust dose as needed ↑ risk of hepatotoxicity; ↑ VPA levels; monitor and adjust dose as needed

*****These charts do not contain all of the known drug-drug interactions. Please consult a drug interaction reference for more information (ex. Lexi-Comp, Micromedex, RxTx, Stockley's.)**

What are some common adverse effects to be aware of?

Drug	Common Adverse Effects*	Uncommon but Important Adverse Events
Isoniazid	Rash, asymptomatic ↑ serum transaminases, hepatotoxicity, peripheral neuropathy	CNS toxicity, anemia, optic neuritis
Rifampin**	Pruritis +/-Rash	Hepatotoxicity, flu-like illness, hematologic reactions (anemia, neutropenia, thrombocytopenia)
Rifapentine**	Rash, hematologic reactions (anemia, lymphocytopenia, thrombocytopenia), arthralgia, ↑ liver enzymes	Hepatotoxicity
Rifabutin**	Myalgia, arthralgia	Uveitis, hepatotoxicity, neutropenia, thrombocytopenia, rash
Pyrazinamide	Hepatotoxicity, rash, arthralgia, photosensitivity, hyperuricemia	Acute gout
Ethambutol	Ocular toxicity (optic neuritis)	Rash

*Gastrointestinal upset, nausea, vomiting, and abdominal pain are common adverse effects with all TB drugs.

**Rifampin, rifapentine and rifabutin may cause orange/red discoloration of the tears, saliva, sweat and urine

How common is tuberculosis?

World Health Organization estimates about 23% of the world's population is infected with TB.

Canada has one of the lowest rates of active TB in the world. There were 1796 cases of active TB reported to the Public Health Agency of Canada in 2017. There is an incidence of 4.9 cases per 100,000 nationally. Despite the low overall numbers, Indigenous and foreign born Canadians continue to be disproportionately represented among TB cases.

Saskatchewan had 94 reported cases of active TB in 2017, or 8.1 cases per 100,000. TB rates in some northern Saskatchewan communities are as high as 145 per 100,000.

What are the different types of tuberculosis?

Tuberculosis occurs as active disease and latent infection. Active disease is classified as respiratory or non-respiratory.

Respiratory TB may include primary TB, pulmonary TB, tuberculous pleurisy (non-primary) and TB of intrathoracic lymph nodes, mediastinum, nasopharynx, septum or sinus. Pulmonary TB makes up the most frequently diagnosed form of active TB in Saskatchewan (61% of cases between 2008-2017).

Non-respiratory infection is localized at any site other than the lungs, such as: lymph nodes, pleura, kidney, genitalia, bones or joints, heart, nervous system (especially meninges), and intra-abdominal organs (especially terminal ileum and cecum).

Latent TB infection occurs when the immune system is able to contain the bacteria and prevent it from actively multiplying and causing disease (the bacteria are dormant). People with latent TB do not feel ill and cannot spread the bacteria to others. They can experience an activation of latent bacteria leading to active disease. The risk of this happening depends on age, sex, genetic factors and the immune-competency of the host. Approximately 10% of people infected will develop active TB, usually within 1 to 2 years of exposure. Prophylactic treatment of those with latent TB can reduce the risk of developing active TB by 90% or more.

How do I contact someone at the TB Program if I have more questions?

The TB Main Office and TB Pharmacy are open Monday-Friday from 0800-1630. If you have pharmacy specific questions you can contact the TB pharmacist directly at 306-655-2987. If you need to reach the TBPC nurse you can phone the TB Main Office at 306-655-1740 and ask to speak to the nurse clinician responsible for that patient. If there is an urgent concern after hours, there is a TB Physician on call that can be reached through the RUH Switchboard at 306-655-1000.

There was a patient with TB coughing in my pharmacy. Am I at risk of infection?

The risk of infection in this setting is extremely small. Infection may be transmitted when aerosolized respiratory droplet nuclei containing *Mycobacterium tuberculosis* are suspended in the air and inhaled by another person. Close, prolonged and frequent contact with someone with active TB disease is usually required. For this reason, TB is more so spread to family members, roommates, friends, coworkers, class mates or others that spend time daily or almost daily with the person with active TB. Transmission is less likely to occur in well ventilated rooms. If the patient is already on effective treatment for TB then the risk of transmission is even less. In general, people in the community with active TB will be on airborne precautions until they have clinical improvement and have had 2 weeks of effective TB therapy. If the patient has non-pulmonary TB there is negligible risk of transmission in this scenario. If the patient has latent TB there is no risk of transmission.

AUGUST 2019

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