

GOALS

Urgent primary care assessment and management of urinary tract infections (UTIs) in patients with multiple sclerosis (MS)

Preventing re-occurrence of UTIs

TARGET POPULATION

Adults with multiple sclerosis (MS) displaying signs and symptoms (typical and atypical) suggesting urinary tract infection (UTI)

Adults with MS living in the community; ambulatory care setting

EXCLUSIONS

Institutionalized patients, i.e., nursing homes, long term care

RECOMMENDATIONS

ASSESSMENT

- X Do not wait to assess.
 - ✓ **Same day attention** in primary care is strongly recommended.
 - ✓ Assess for indicators of urinary tract infection (UTI) in patients with multiple sclerosis (MS), including:
 - Typical signs and symptoms of lower or upper UTI
- OR
- New/worsening neurological symptoms **PLUS** one or more of the following:
 - History of UTIs or pre-existing bladder dysfunction
 - Catheterization
 - Fever, chills even without other symptoms of UTI
 - New severe fatigue or confusion

PRACTICE POINT

*MS patients with possible UTIs need **same day attention** in primary care. Do not rely on only typical signs and symptoms of UTI alone. Consider new/worsening of neurologic symptoms plus any of the following: history of UTIs, bladder dysfunction or catheterization, fever, chills, new severe fatigue or confusion.*

PRACTICE POINT

Patients presenting with new/worsening neurological symptoms in isolation require a full clinical assessment and fall outside the scope of this guideline.

Consider consulting with neurologist or MS Clinic

URGENT MANAGEMENT

Same day:

- ✓ Collect a **clean** catch midstream urine sample. For indwelling catheters, urethral or suprapubic, collect urine from a newly inserted catheter.
- ✓ Order urine for culture and susceptibility (C&S)*. Label the requisition with the following details:
“MS patient symptomatic of UTI, [indicate sample collection method]. Work up for low colony count of uropathogens. Contact immediately if sample is unsatisfactory.”
- *Note: If microscopic urinalysis is used, antibiotics should be started immediately after obtaining the urine sample and stopped only if the results are fully negative, i.e., no nitrites, leukocytes, blood, WBC, RBC or bacteria
- ✓ Start antibiotic therapy immediately after urine sample is collected. (See [Appendix A](#)) and determine treatment based on patient history and presentation)
- ✓ Tell patient to phone back if not feeling better within 48-72 hours, or sooner if symptoms worsen
- X Do not use a urine dipstick
- X Do not wait for urine culture results to start antibiotics. Treat immediately
- X Do not prescribe antibiotics without collecting a urine sample first

24-48 hours later:

- ✓ Discontinue antibiotic therapy if urine culture results indicate no growth. Inform patient that the follow-up urine culture is not required
- ✓ Adjust antibiotic if necessary, based on culture and susceptibility results

PRACTICE POINT

*Collect clean catch midstream urine sample, order urine culture and start antibiotic treatment. **Do not wait for results to begin antibiotic treatment.***

Do not use dipstick

*Label lab requisition to indicate: “MS patient, [indicate sample collection method], work up for **low colony counts**. Contact immediately if sample is unsatisfactory.”*

FOLLOW-UP

A follow-up visit should occur approximately **14 to 21 days** after the start of antibiotic therapy.

- ✓ Review symptoms to ensure UTI has resolved. Repeat urine culture is not required unless patient is symptomatic or pregnant.
- ✓ Assess for recurrent UTIs (2 infections in 6 months or ≥ 3 infections in 12 months)

- ✓ Assess overall bladder function. Ask patient: *Are you “bothered” by your bladder function?*
Consider:
 - Overactive bladder symptoms (OAB). These include frequency greater than eight times/day with urgency (possible urgency incontinence) and nocturia of greater than once
 - Incontinence (stress, urgency, overflow)
 - Impaired emptying
 - Difficulty with catheters (in and out catheter or indwelling catheter)
- ✓ Refer to appropriate specialist for follow-up if patient has recurrent UTIs and/or if patient has bladder dysfunction that you have not been able to manage. If urinary retention has not been excluded, be cautious initiating drugs to treat over-active bladder in MS. History alone cannot exclude urinary retention.
- ✓ Consider checking post-void residual using bladder scan or ultrasound if retention is suspected.
- ✓ Discuss strategies to prevent re-occurrence of UTI.
- ✓ Develop a plan to address future UTI (See [Appendix B](#) – *Multiple Sclerosis: My Bladder Management Action Plan*).

PRACTICE POINT

A follow-up visit provides an opportunity to confirm the UTI is resolved, assess overall bladder function, and develop a bladder management plan.

EVIDENCE-BASED IMPLEMENTATION STRATEGIES

- ✓ Identify patients with MS in physician practice.
- ✓ Develop a clinic plan for management of UTIs in patients with MS, during regular clinic hours and after-hours/weekends.
- ✓ Communicate plan with patients and clinic staff. Consider using the *Multiple Sclerosis: My Bladder Management Action Plan* (see [Appendix B](#)) as a communication tool.
- ✓ Consider a patient self-management plan, when appropriate.

BACKGROUND AND SUPPORTING EVIDENCE

RISKS

Urinary tract dysfunction is common in the MS population with estimates of occurrence cited upward of 70%^{1,2} and up to 100% for those with severe disability.³ While UTI is often associated with mortality in advanced disease the frequency of this association is unclear. Studies to date have been of limited scope.

Infections can trigger MS relapse. One prospective study⁴ found a significant association between systemic infections (i.e., viral and bacterial) and risk of relapse. There is also evidence to suggest that exacerbations associated with infectious episodes lead to more severe and sustained neurologic deterioration.^{5, 6}

Symptoms of UTI may be masked by underlying neurogenic bladder and sensory deficits. In addition, cognitive dysfunction (another common consequence of MS) may make it difficult for patients with MS to identify symptoms and seek medical attention. These factors may limit access to medical care at times of deterioration when help is most needed.²

Because of the potentially serious deleterious effects of untreated UTI in MS, treatment differs from that of the general population. Urgent assessment and management is essential to reduce the likelihood of disease progression. Based on expert opinion, same day assessment, collection of urine sample and initiation of antibiotics without waiting for the results of C&S are recommended.

ASSESSMENT

Classical symptoms of lower and upper UTI are well documented in the literature, including but not limited to: dysuria, frequency, urgency, suprapubic pain, fever, chills, flank pain, and hematuria.^{1,7,8,9} For patients with MS, the signs and symptoms of UTI may be absent due to sensory dysfunction or pre-existing bladder dysfunction. In addition, symptoms may include new or worsening of neurologic symptoms, change in consciousness, new delirium or confusion.^{7,10}

Patients presenting with new/worsening neurological symptoms in isolation require a full clinical assessment and fall outside the scope of this guideline.

Patients with MS represent the full range of UTIs, from a patient with uncomplicated cystitis in the early stages of MS (e.g., a young female patient presenting with first UTI), to a complicated urinary tract infection in a patient at a later stage (e.g., patient is wheelchair bound and with an indwelling catheter and has had multiple urologic procedures). Complicated UTI is defined as a “urinary infection occurring in a patient with a structural or functional abnormality of the genitourinary tract”.¹² This includes, obstruction (e.g., tumours); instrumentation (e.g., catheter); impaired voiding (e.g., neurogenic bladder); metabolic abnormalities (e.g., renal failure); and immunocompromised (e.g., renal transplant).

URINE FOR CULTURE AND SUSCEPTIBILITIES

Urine specimens should be collected prior to initiating antimicrobial therapy. It is important that patients receive and follow urine collection guidelines for clean-catch midstream urine (MSU) or catheterized urine specimens. For those patients with indwelling catheters (urethral or suprapubic), a urine sample should ideally be collected from a newly inserted catheter and never taken directly from the urine collection bag. If the first urine sample is not clean, the ability to identify potential infecting organisms in re-testing (i.e., after antibiotic treatment is initiated) will be reduced and may compromise treatment. One study reported that out of 127 laboratories, the median contamination rate was 15.0% and as high as 41.7% for those laboratories in the 10th percentile.¹¹

Urine testing for the detection of asymptomatic bacteriuria is not recommended, with the exception of pregnant patients.^{12,13}

URINE TESTING

Urine for culture and susceptibility provides the most definitive results to determine whether to continue or discontinue antibiotic therapy in symptomatic MS patients, and is the preferred method of testing for managing patients with MS. Testing for pyuria in symptomatic MS patients has a limited value. Dipstick urinalysis for pyuria is not recommended due to a wide variation of sensitivity, specificity and predictive values.¹³ Microscopic urinalysis may be helpful in ambulatory non-catheterized patients with minimal or atypical symptoms related to urinary tract. In these patients the absence of pyuria would suggest a diagnosis other than UTI, while the presence of pyuria would be compatible with the diagnosis of UTI.¹ Similarly, the absence of pyuria on microscopic urinalysis may also be helpful to rule out UTI, or to suggest other diagnosis than UTI when urine culture result is “mixed”. The urinalysis testing should be done in conjunction with urine culture. Urinalysis testing for pyuria (dipstick or microscopic) is not recommended for diagnosis of UTI in patients with an indwelling catheter.^{11, 10}

INTERPRETATION OF URINE CULTURES

Bacterial colony count criteria are used for defining significant bacteriuria. (See [Table 1](#)) Emerging evidence supports significance of lower bacterial counts (i.e., 10^6 cfu/L or even 10^5 cfu/L) in the presence of UTI signs and symptoms.^{10,13,14} When using criteria of higher bacterial counts, (i.e., $\geq 10^7$ cfu/L or 10^8 cfu/L) significant UTIs may be missed. A note on the lab requisition to “work up for low colony count” is important since some laboratories may need to modify their work up and interpretation guidelines for urine cultures in these patients. (See [Table 1](#))

Specimen Type	Significant Colony Count	Notes
Mid-stream urine: males and females	$\geq 10^6$ cfu/L	Single or 80% predominance of uropathogenic organism If single uropathogenic organism is present in lower count of 10^5 cfu/L, microbiologist should be consulted if further work-up is needed
Single catheter specimen or suprapubic aspirate	$\geq 10^5$ cfu/L	1 uropathogen Single or 80% predominant
In-dwelling catheters		
<ul style="list-style-type: none"> In-dwelling urethral: newly inserted, if old catheter was in place ≥ 14 days 	$\geq 10^6$ cfu/L	1-2 uropathogenic organism(s), either pure or 80% predominant
<ul style="list-style-type: none"> Condom catheter: clean catch with freshly applied condom device 	$\geq 10^7$ cfu/L	If ≥ 3 uropathogenic organisms are present in mixed culture, microbiologist should be consulted about the need for further work-up

Table 1: Interpretation of Urine Culture in Symptomatic MS Patients

COMMUNICATION WITH LAB

The following information is important for labs to effectively and efficiently process urine cultures and therefore should be included on the requisition: “MS patient symptomatic of UTI, [indicate sample collection method]. Work up for low colony count of uropathogens. Contact immediately if sample is unsatisfactory.”

ANTIBIOTICS

Refer to [Appendix A](#) to determine antibiotic treatment options based on patient history and presentation. When results of urine C&S are available, adjust antibiotics to match susceptibilities or discontinue the antibiotic in the absence of an infection.

FOLLOW-UP VISIT

A follow-up visit can provide value to ensure that symptoms of UTI have resolved, to assess bladder function and management of dysfunction, to assess for recurrent UTIs, to determine the need for referral to a specialist, to discuss measures to prevent re-occurrence of infection; and to develop a plan for urgent action in the event of another UTI. This appointment should occur approximately 14 to 21 days after the start of antibiotic therapy. The following suggestions, based on expert opinion, are key aspects of the follow-up visit.

ENSURE UTI IS RESOLVED

Review patient symptoms ensure UTI has resolved. Repeat urine culture is not recommended unless the patient is symptomatic. Post treatment urine culture is recommended in pregnant women, since asymptomatic bacteriuria should be treated in this specific population.¹² In the event that the patient presents for a follow-up appointment and has not had a urine culture, a urine culture should be completed.

ASSESS BLADDER FUNCTION

Asking patients whether they are “bothered” by their bladder often reveals potential issues. Assess for overactive bladder, incontinence, and difficulty with catheters.

ASSESS FOR RECURRENT UTI

Recurrent UTI has been defined in other guidelines as 2 infections in 6 months or 3 or more infections in 12 months.^{1, 8} MS patients with recurrent UTIs should be referred to a specialist for further testing to exclude predisposing underlying causes.³ For women, examination to explore features suggestive of anatomic abnormalities, pelvic floor prolapse and the level of estrogenization of vaginal tissues is important.

It is important to distinguish relapse from re-infection. Relapse usually occurs within 2 weeks of completing therapy and is caused by the same original organism and is due to persistence within the urinary tract. Re-infection occurs after two weeks after complete resolution of the initial infection and is typically a different organism. (See [Appendix A](#))

DISCUSS GENERAL MEASURES TO PREVENT UTI

Evidence for general measures to prevent the re-occurrence of UTIs is primarily derived from studies with the general population. Evidence is summarized as follows:

Intake of liquids: Patients with overactive bladder tend to lower their intake of liquids in order to reduce frequency and urgency of urination.^{1,3} A recommended daily intake between 1-2 litres a day is cited in the literature with a proviso to individualize based on body weight, dietary habits, physical activity, etc.^{1,3} However, there is no evidence to support a specific volume of fluid intake per day to reduce recurrent UTI.¹⁵ It was the expert opinion of this committee to encourage patients to drink enough water or clear fluids to keep the urine lightly coloured or clear.

Caffeine: Caffeine reduction has been shown to reduce both frequency and urgency of urination.^{1,3}

Bowel emptying: A scientific basis for recommending treatment of coexistent constipation as a means of improving bladder function is lacking but anecdotally, many practitioners, and indeed their patients, feel this is important. Further research on the effect of improved bowel management on reduction in bladder symptoms is needed.¹

Contraceptives: Discourage use of spermicide containing contraceptives.⁷

Vaginal estrogen: Vaginal estrogen should be offered to postmenopausal with recurrent UTI.⁷ There is insufficient evidence for recommending a specific type or form (i.e., cream, vaginal ring, tablets).

Cranberry juice: There is conflicting evidence on the efficacy of cranberry juice and its derivatives (i.e., tablets, capsules, powders) for the prevention of UTIs.^{16, 17} Common regimens include 500 mg tablets po bid, 500-1000 mg powder once daily or 125-250 mL juice daily (with appropriate precautions for those with underlying diabetes).

D-Mannose: Evidence supporting the use of D-Mannose is very limited but a recent study suggests that D-Mannose 200 grams in 200 mL of water daily may be effective in reducing the risk of recurrent lower UTI.¹⁸

Behaviour: Behavioural measures have not been shown to be of any benefit but are unlikely to be harmful. Specifically, there is no association between recurrent UTI and pre- and post-coital patterns, frequency of voiding, delayed voiding, douching, hot tubs, bubble baths; use of pantyhose or tights, use of tight clothing, type of clothing, and bicycle riding.

Food and alcohol: There is no research evidence found that spicy foods, alcohol or acidic foods irritate the bladder and/or increase bladder symptoms.

Smoking: Research has shown that smoking cessation may result in decreased urinary tract symptoms in men; however, there is no information on whether this is true for women.¹⁹

DEVELOP PLAN FOR URGENT MANAGEMENT

Planning ahead for management of potential UTIs is important to achieving urgent management. The first step is identifying patients with MS within the practice (i.e., panel identification) and developing clinic processes for managing these patients should a UTI concern arise. For example, the receptionist is aware that when a patient with MS phones regarding a UTI, same day attention by a primary care provider is required. Consider using the *Multiple Sclerosis: My Bladder Management Action Plan* (see [Appendix B](#)) as a communication tool. Self-management of UTIs has been reported with success⁸ although has not been studied in patients with MS. Use clinical judgment to determine if a self-management program is appropriate.

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SUGGESTED CITATION

Toward Optimized Practice (TOP) Working Group for Multiple Sclerosis and UTI. 2013 Nov. Multiple sclerosis and management of urinary tract infection: clinical practice guideline. Edmonton, AB: For more information see www.topalbertadoctors.org

GUIDELINE COMMITTEE

The committee consisted of representatives from family medicine, neurology, internal medicine, infectious disease, urology, medical microbiology and pharmacy.

November 2013

2017 minor revision

APPENDIX A

Antibiotic Considerations for Management of UTIs in MS

- Empiric antibiotic therapy is based on availability, allergies, tolerance and likelihood of resistance.
- Resistance levels should be assessed within the context of the local practice setting.
- Level of resistance to a specific agent to be empirically used in a practice setting should be $\leq 20\%$ for lower UTI and $\leq 10\%$ for upper UTI.
- In patients with recent (previous three months) antibiotic exposure, consider a different antibiotic than previously used due to increased risk of resistance. Local or regional antibiograms or [Bugs & Drugs](#) may be consulted.
- Trimethoprim (TMP) use should be limited to those allergic to sulpha since the resistance rate to TMP is generally higher than TMP-SMX. TMP-SMX susceptibility is variable from setting to setting.
- Quinolones (ciprofloxacin, levofloxacin, norfloxacin): Greater flora alteration, increased rates of C difficile, and/or resistance development. Risk of disabling and persistent serious adverse events has been recently highlighted by Health Canada.²⁰
- Complicated UTI: structural or functional abnormality of the genitourinary tract, e.g., catheterization, neurogenic bladder, renal failure.

Uncomplicated Symptomatic Lower Tract UTI		Dose	Duration	Notes
1 st line	Nitrofurantoin	50-100 mg po qid	5 days	*Fosfomycin: Reserve for high risk populations with more resistant organisms and/or failed treatments
	Nitrofurantoin macrocrystals	100 mg po bid	5 days	
	TMP-SMX	1 DS tablet po bid	3 days	
Alternates	Amoxicillin-clavulanate	500 mg po tid or 875 mg po bid	3-7 days	†Risk of disabling and persistent serious adverse reactions with fluoroquinolones. Rare cases of disabling and persistent serious adverse reactions including tendinopathy, peripheral neuropathy, and central nervous system disorders have been reported to Health Canada for fluoroquinolones when used systemically (i.e. taken by mouth or by injection). ²⁰ Avoid fluoroquinolones in patients who have previously experienced serious adverse reactions associated with them. Stop fluoroquinolone treatment if a patient reports any serious adverse reaction. Patients should be switched to an alternative treatment with a non-fluoroquinolone antibacterial drug, if needed, to complete the treatment course. ** TMP should be used with caution since susceptibility testing for TMP is not routinely available in Alberta and susceptibility cannot be inferred from TMP-SMX.
	Cephalexin	500 mg po qid	3-7 days	
	Fosfomycin* (See Note)	3 g po once	1 day	
	Ciprofloxacin† (See Note)	250 mg po bid or 500 mg XL po once daily	3 days	
	Levofloxacin† (See Note)	500 mg po once daily	3 days	
	Norfloxacin† (See Note)	400 mg po bid	3 days	
	Trimethoprim (TMP)** (See Note)	100 mg po bid	3 days	
Complicated Symptomatic Lower Tract UTI		Dose	Duration	Notes
1 st line	Amoxicillin-clavulanate	500 mg po tid or 875 mg po bid	7-14 days	If delayed response, anatomic abnormality or uncertainty if upper tract involvement, treat for 14 days **TMP should be used with caution since susceptibility testing for TMP is not routinely available in Alberta and susceptibility cannot be inferred from TMP SMX.
	TMP-SMX	1 DS tablet po bid	7-14 days	
	Ciprofloxacin† (See Note)	500 mg po bid or 1000 mg XL po once daily	7-14 days	
	Levofloxacin† (See Note)	500 mg po once daily	7-14 days	
Alternate	Cefixime	400 mg once daily	7-14 days	
	Trimethoprim (TMP)** (See Note)	100-200 mg po bid	7-14 days	

Uncomplicated or Complicated Upper Tract UTI		Dose	Duration	Notes
1 st line	Ciprofloxacin [†] (See Note)	500 mg po bid or 1000 mg XL po once daily	7 days	Use oral therapy if not ill, no significant nausea or vomiting and reasonable compliance may be expected; otherwise consider a parenteral regimen. Collection of blood culture in febrile patients is good practice. The effectiveness of oral agents is less trustworthy if previous antibiotic use and infections.
	Levofloxacin [†] (See Note)	750 mg po once daily	5 days	
	TMP-SMX	1 DS tablet po bid	14 days	
	Amoxicillin-clavulanate	500 mg po tid or 875 mg po bid	14 days	
Alternate	Cefixime	400 mg po once daily	14 days	**TMP should be used with caution since susceptibility testing for TMP is not routinely available in Alberta and susceptibility cannot be inferred from TMP SMX.
	Trimethoprim (TMP)** (See Note)	100 mg po bid	14 days	
Recurrent UTIs		Dose	Duration	Notes
Antibiotic Prophylaxis	TMP-SMX	1 SS po daily	Continuous prophylaxis for 6 months	If related to coitus, consider single dose prophylaxis: TMP-SMX, Nitrofurantoin, TMP or Cephalexin prior to or immediately post coitus. For women unable or not willing to take continuous prophylaxis, self-initiated therapy is an option – see above for uncomplicated cystitis.
	Trimethoprim (TMP)	100 mg once daily		
	Nitrofurantoin	50 -100 mg once daily		
	Cephalexin	250 mg once daily		
	Fosfomycin	3 g po every 10 days		
Alternate	Norfloxacin	200 mg once daily		Consider consulting an infectious disease specialist.
	Ciprofloxacin	125 mg once daily		

Abbreviations: TMP- trimethoprim; TMP-SMX - trimethoprim-sulfamethoxazole; po – by mouth; bid – twice a day; tid – three times a day; SS – single strength; DS - double strength; XL – extended release

APPENDIX B



NAME: _____
 FAMILY DOCTOR: _____
 PHONE: _____
 NEUROLOGIST OR MS OFFICE: _____
 PHONE: _____

This *Multiple Sclerosis: My Bladder Management Action Plan* will help you recognize early signs of bladder problems and take the appropriate steps to prevent or, if need be, treat possible bladder infection.

TIPS FOR BLADDER HEALTH

- Drink enough water or clear fluids to keep your urine lightly coloured or clear. Cranberry products (including juice) may be helpful for some.
- Decrease or avoid caffeine and smoking (which may irritate your bladder and increase symptoms).
- Pay attention to your bowel habits. Being constipated can make it harder to empty your bladder completely.



Some people also find it helpful to:

- Decrease or avoid acidic or spicy foods, alcohol and artificial sweeteners.
- Empty the bladder regularly and take the time to empty it completely.

RECOGNIZING AND TREATING POSSIBLE BLADDER INFECTIONS

People with MS may normally have some of the following symptoms. Pay attention to new or worsening symptoms. Use the following checkboxes to help track your symptoms.

SYMPTOMS OF POSSIBLE BLADDER INFECTION:

- | | |
|--|---|
| <input type="checkbox"/> Increased urinary frequency (you feel the urge to urinate/pee more often) | <input type="checkbox"/> Blood in the urine |
| <input type="checkbox"/> Incontinent of urine (dripping) | <input type="checkbox"/> Fever |
| <input type="checkbox"/> Burning, bladder spasms or pain on urination | <input type="checkbox"/> Decreased appetite or energy |
| <input type="checkbox"/> Increasing pain in low back or low abdomen | <input type="checkbox"/> More stiffness or spasms in any muscles |
| | <input type="checkbox"/> Increasing mental fogginess or confusion |

Some people also report:

- Foul smelling urine
- Sand-like material (sediment) in urine
- Very cloudy urine

Multiple Sclerosis: My Bladder Management Action Plan

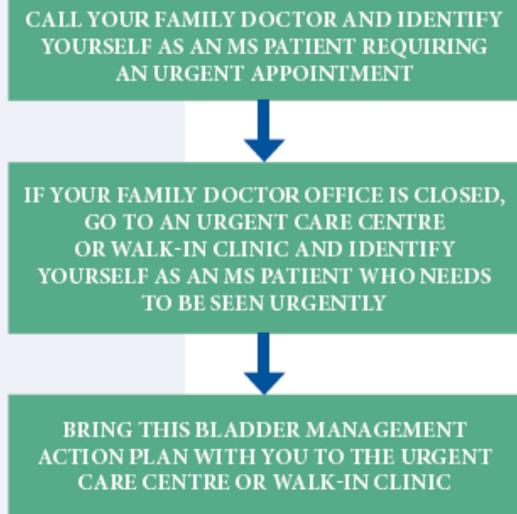
If symptoms are new or worsening, activate Plan A or B:

PLAN A

If your family doctor has given you a urine collection container and a prescription for antibiotics “just in case” of a bladder infection:



PLAN B



NOTE: If within 24 hours of starting the antibiotics your symptoms are worsening, seek medical advice immediately.

Ask someone to take you to an urgent care or emergency centre if you have one or more of the following symptoms:

- Temperature is above 39.5° C
- Trembling uncontrollably/having chills
- Increasing mental fogginess or confusion
- Moderate to severe pain in low back or low abdomen

Be sure to notify staff immediately that you have MS

Signed:

PATIENT: _____ FAMILY DOCTOR: _____
 FAMILY CLINIC CONTACT: _____ DATE: _____
 (NURSE, RECEPTIONIST)

For the complete guideline, *Multiple Sclerosis & Management of Urinary Tract Infection*, refer to the TOP website: www.topalbertadoctors.org

Multiple Sclerosis: My Bladder Management Action Plan