INESSS
LE SAVOIR PREND FORME

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PHARMACOLOGICAL TREATMENT

STBBI

UNCOMPLICATED *CHLAMYDIA TRACHOMATIS* OR *NEISSERIA GONORRHOEAE* INFECTION

This optimal usage guide is intended for primary care physicians. It is provided for information purposes only and should not replace the judgement of the clinician who performs activities reserved under an act or a regulation. The recommendations concern persons 14 years of age and older[1]. They were developed using a systematic process and are supported by the scientific literature and the knowledge and experience of Québec clinicians and experts. For further details, go to section Guides d'usage optimal at inesss.qc.ca.

GENERAL CONSIDERATIONS

- This optimal usage guide applies to persons in whom the appropriate microbiological tests have been performed **AND** indicate the presence of *C. trachomatis* or *N. gonorrhoeae* (further details in appendix).
- For screening for *C. trachomatis* or *N. gonorrhoeae* infection, consult the following tool: *Prélèvements et analyses recommandés chez une personne asymptomatique - Infections à Chlamydia trachomatis ou à Neisseria gonorrhoeae - Lymphogranulomatose vénérienne*.
- If an infection is detected, ensure that microbiological testing has been done on **all the exposed sites**.
- If a gonococcal infection has been detected by nucleic acid amplification testing (NAAT) alone, culture specimens should be taken from the infected sites to determine the strain's susceptibility before treatment is initiated. However, obtaining these specimens should not delay treatment.
- The management of an infection caused by *C. trachomatis* with a lymphogranuloma venereum (LGV) genotype is not covered in this guide. If necessary, consult the clinical tool for LGV produced by the MSSS.
- If the person has signs and symptoms associated with these STBBIs and the microbiological test results are not yet available, consult the *Optimal usage guide on the pharmacological treatment of STBBI – Syndromic approach*.

MANAGEMENT

INTERVENTION WITH THE INFECTED PATIENT

The intervention should include:

- An appropriate treatment and a follow-up of the infected patient;
- A recommendation to abstain from sexual contact for 7 days after a single-dose treatment **OR** until the completion of a multi-dose treatment **AND** until the symptoms have resolved[2]:
  - If in doubt regarding abstinence, a recommendation to use barrier methods for all types of sexual contact (genital, oral-genital, anal or oral-anal);
- Support for the infected patient in the procedure aimed at notifying and treating his/her sexual partners. The regional public health department (DSP) can provide support during this procedure.

INTERVENTION WITH SEXUAL PARTNERS

Partners should be contacted if they have had sexual contact with the infected patient:

- Within the 60 days preceding the onset of symptoms or specimen collection; **OR**
- While the patient had symptoms; **OR**
- Before the completion of a multi-dose treatment or less than 7 days after a single-dose treatment.

In certain situations, checking for partners over a longer period of time may be warranted.

The intervention should include:

- A clinical assessment, including identifying STBBI risk factors;
- Screening for the infection to which the patient was exposed and for other STBBI, based on the risk factors identified. Consult the tool *ITSS à rechercher selon les facteurs de risque décelés*;
- If there are no signs or symptoms, an epidemiological treatment without waiting for the screening test results: decision algorithm;
- If there are signs or symptoms: a syndromic approach;
- Support for the person in the procedure aimed at notifying and treating his/her sexual partners if the microbiological test results are positive.

For further information, consult the following tools: *Personne exposée à une ITSS : que faire?* and *Soutenir la personne atteinte d'une ITSS pour qu'elle avise ses partenaires : quatre étapes.*

Accelerated partner therapy (APT):

- It is preferable to assess the sexual partner's health condition before prescribing so that he/she receives the best preventive care.
- In certain circumstances, accelerated partner therapy (APT) may be used after carefully weighing the pros and cons. However, APT is an exceptional measure.

For additional information, consult the *quick-reference guide for clinicians* and the *quick-reference guide for pharmacists*.

1. For cases of suspected sexual abuse, refer to the *Guide d'intervention médicosociale pour répondre aux besoins des victimes d'agression sexuelle*.
2. If the individual does not comply with the abstinence instructions, consult an experienced colleague to determine the appropriate management.

Québec

CHLAMYDIA TRACHOMATIS INFECTION

TREATMENT PRINCIPLES

Note concerning the choice of treatment for the infected patient or the asymptomatic partner in the absence of pregnancy:

- Treatment with doxycycline should always be preferred, especially for rectal infections or in cases where rectal exposure is reported.

TREATMENT

INFECTED PATIENT

URETHRAL, ENDOCERVICAL, PHARYNGEAL[1] OR RECTAL INFECTION

Doxycycline[2] 100 mg PO BID x 7 days

OR

Azithromycin[3] 1 g PO in a single dose:
Should be used only in patients in whom a treatment compliance problem is anticipated.

If the patient has a rectal infection and tests positive for *C. trachomatis* with an LGV genotype, initiate or continue treatment with doxycycline[2] 100 mg PO BID for a total of 21 consecutive days. For further details, consult the clinical tool for LGV.

ASYMPTOMATIC PARTNER OF THE INFECTED PATIENT

ANY TYPE OF EXPOSURE

Doxycycline[2] 100 mg PO BID x 7 days

OR

Azithromycin[3] 1 g PO in a single dose:
Should be considered only if the partner is to be treated with APT or if a treatment compliance problem is anticipated.

PREGNANT WOMEN

URETHRAL, ENDOCERVICAL, PHARYNGEAL[1] OR RECTAL INFECTION (INFECTED PATIENT) AND ANY TYPE OF EXPOSURE (ASYMPTOMATIC PARTNER OF THE INFECTED PATIENT)

1st CHOICE
Azithromycin[3] 1 g PO in a single dose

2nd CHOICE
Amoxicillin[4] 500 mg PO TID x 7 days

1. Although there is no indication for *C. trachomatis* screening in the throat, cases of pharyngeal *C. trachomatis* infection can be detected because *N. gonorrhoeae* screening is done using a NAAT that also detects *C. trachomatis*.
2. Doxycycline is contraindicated in pregnant women. It is compatible, if necessary, with breastfeeding if the duration of treatment is less than 3 weeks.
3. If the person vomits within an hour after taking azithromycin, administer a prophylactic antiemetic and then another dose of azithromycin.
4. Not approved by Health Canada for this indication.

NEISSERIA GONORRHOEAE INFECTION

TREATMENT PRINCIPLES

- The prevalence of co-infection with *C. trachomatis* is high. When ceftriaxone is used as monotherapy, treatment for *C. trachomatis* infection should be prescribed if such an infection cannot be ruled out.
- When the combined cefixime and azithromycin regimen is used and the patient has a **rectal *C. trachomatis* infection together with a urethral, endocervical or rectal *N. gonorrhoeae* infection**, use **triple therapy** by adding doxycycline[1] (100 mg PO BID x 7 days) to the recommended treatment for *N. gonorrhoeae* infection.

TREATMENT[2]
(including pregnant or breastfeeding woman)

INFECTED PATIENT

URETHRAL, ENDOCERVICAL OR RECTAL INFECTION	PHARYNGEAL INFECTION
Ceftriaxone 250 mg IM in a single dose **OR** Cefixime 800 mg PO in a single dose **AND** Azithromycin[3] 2 g PO in a single dose	Ceftriaxone 250 mg IM in a single dose

ASYMPTOMATIC PARTNER OF THE INFECTED PATIENT

NO ORAL EXPOSURE	ORAL EXPOSURE	
Ceftriaxone 250 mg IM in a single dose **OR** Cefixime 800 mg PO in a single dose **AND** Azithromycin[3] 2 g PO in a single dose	Option A Ceftriaxone 250 mg IM in a single dose	Option B Cefixime 800 mg PO in a single dose **AND** Azithromycin[3] 2 g PO in a single dose

Option A : The availability of ceftriaxone and the person's acceptance of the IM route of administration.

Option B : It is expected that the person will attend a follow-up visit if the screening test result is positive. Option B is appropriate only if throat specimens for a NAAT and a culture have been collected from the partner.

HISTORY OF ALLERGIC REACTION[4]

TO A PENICILLIN ANTIBIOTIC[5]	TO A CEPHALOSPORIN
Clic here to view the algorithm specific to *N. gonorrhoeae* infection for help in choosing the antibiotic therapy.	Refer to the treatment option presented below.

Gentamicin[6] 240 mg IM (in two 3-ml injections)
AND
Azithromycin[3] 2 g PO in a single dose

1. Doxycycline is contraindicated in pregnant women. It is compatible, if necessary, with breastfeeding if the duration of treatment is less than 3 weeks.
2. In cases of allergy or resistance to azithromycin or resistance to cephalosporins, consult a medical specialist.
3. If the person vomits within an hour after taking azithromycin, administer a prophylactic antiemetic and then another dose of azithromycin.
4. Consideration can be given to quinolones to treat adults aged 18 years and older (with the exception of pregnant or breastfeeding women) only if the strain's susceptibility to quinolones has been demonstrated with susceptibility testing. In such case, the recommended treatment is ciprofloxacin 500 mg PO in a single dose.
5. Penicillin G or V, ampicillin, amoxicillin, cloxacillin or piperacillin.
6. Not approved by Health Canada for this indication.

TESTS OF CURE

	C. TRACHOMATIS INFECTION	*N. GONORRHOEAE* INFECTION
INDICATIONS	A test of cure **is not recommended** in cases of *C. trachomatis* infection, except in the following situations: ▶ Persistence or appearance of signs or symptoms ▶ Pregnancy ▶ An anticipated treatment compliance problem ▶ A treatment regimen other than one of those recommended is being used ▶ Rectal *C. trachomatis* infection treated with azithromycin ▶ *C. trachomatis* infection of genotype $L_{1\text{-}3}$ (LGV)	A test of cure **is recommended in all cases** of gonococcal infection, especially in the following situations: ▶ Persistence or appearance of signs or symptoms ▶ Pregnancy ▶ An anticipated treatment compliance problem ▶ A treatment regimen other than one of those recommended is being used ▶ A pharyngeal infection (even if treated with ceftriaxone) ▶ The use of a treatment regimen combining gentamicin and azithromycin, given a history of allergic reaction ▶ Known resistance or reduced susceptibility[1] to one of the antibiotics used ▶ Partner of a person in whom resistance or reduced susceptibility[1] to one of the antibiotics used has been demonstrated
SPECIMENS AND TESTS	NAAT performed as soon as possible, starting from 3 weeks after the completion of treatment	**In the case of a pharyngeal infection[2] :** NAAT[3] and culture performed as soon as possible, from 2 weeks after the completion of treatment, **OR** culture[4] done as soon as possible, from 3 days and up to 2 weeks after the completion of treatment. **In the case of a non-pharyngeal infection[2]:** NAAT performed as soon as possible, from 2 weeks after the completion of treatment[5]. If the patient presents with symptoms at the follow-up visit, obtain a culture specimen as well. A culture performed as soon as possible, from 3 days and up to 2 weeks after the completion of treatment, can also be considered.

1. Cut-off for reduced susceptibility to cefixime set at a minimum inhibitory concentration (MIC) ≥ 0.125 mg/L.
2. If a follow-up appointment is scheduled for 2 weeks after the completion of treatment, the patient should be advised to return earlier if symptoms persist or appear. In such case, culture specimens should be obtained.
3. A NAAT performed on a throat specimen may be associated with false-positive results. For positive follow-up pharyngeal NAATs, see Appendix 4 of the INSPQ's explanatory guide for further details on management.
4. An additional NAAT specimen can be taken from 2 weeks onwards at the clinician's discretion.
5. If the follow-up NAAT result is positive, it is advisable to obtain a culture specimen, provided this does not delay treatment.

ANTIBIOTIC RESISTANCE

N. gonorrhoeae resistance to the different antibiotics is increasing rapidly, and the recommended treatments may eventually be modified according to the strains' changing susceptibility to these drugs. Close vigilance by practitioners is required. Here is a summary of *N. gonorrhoeae* antibiotic resistance in Québec. For further details, go to the LSPQ's website.

- Resistance to quinolones and tetracyclines is well established.
- Resistance to azithromycin is rapidly on the increase.
- Resistance to third-generation cephalosporins is emerging.

REINFECTION

To check that there is no reinfection, recommend to all persons infected with *C. trachomatis* or *N. gonorrhoeae* that they have a screening test 3 to 6 months after the treatment of the initial infection. Screening following a documented infection is in addition to the previously performed test of cure, if indicated.

ADDITIONAL INFORMATION

NOTIFIABLE DISEASES (MADO)

The clinician is required to report laboratory-confirmed cases of *C. trachomatis*, *N. gonorrhoeae* and LGV infection to the regional DSP (further details in appendix).

MEDICATION FREE OF CHARGE

For persons registered with the Québec health insurance plan (RAMQ) and who have a valid health insurance card, claim slip or temporary proof of eligibility for medication: enter on the prescription the code **K** (for the infected patient), **L** (for partners) or **M** (for APT-treated partners). The cost of 1% lidocaine without epinephrine is covered by the free program in the context of treating STIs or an associated syndrome when "diluent for ceftriaxone" is noted on the prescription.

STBBI-RELATED PREVENTIVE INTERVENTIONS

When a person consults a medical practitioner, for instance, about an STBBI or contraception or for a routine clinical examination, the practitioner should:

- Inquire about STBBI risk factors and screen accordingly, as many people are asymptomatic and do not know that they are infected;
- Inform the person about safer sexual practices and encourage consistent use;
- Vaccinate against hepatitis A and B and the human papillomavirus as indicated in the *Protocole d'immunisation du Québec*.

Preexposure prophylaxis (PrEP) may be considered in certain populations at risk for contracting HIV. If necessary, consult the following tool produced by the MSSS: *Guide PPrE pour les professionnels de la santé du Québec*.

A variety of STBBI-related preventive intervention tools are available on the MSSS's website, such as:

- *ITSS à rechercher selon les facteurs de risque décelés*
- *Prélèvements et analyses recommandés chez une personne asymptomatique - Infections à* Chlamydia trachomatis *ou à* Neisseria gonorrhoeae *- Lymphogranulomatose vénérienne*
- *Prélèvements et analyses recommandés chez une personne asymptomatique - Syphilis, hépatites B et C, VIH*
- *Personne exposée à une ITSS : que faire?*
- *Soutenir la personne atteinte d'une ITSS pour qu'elle avise ses partenaires : quatre étapes*
- *Site Internet, dépliants et brochures à l'intention des patients* (e.g., *Entre caresses et baisers, une ITSS s'est faufilée… Il faut en parler)*
- *Estimation du risque associé aux activités sexuelles*
- *Vaccination et ITSS*
- *Ressources – Intervention préventive relative aux ITSS*
- *Intervention préventive relative aux ITSS : outil d'aide à la pratique, visite initiale et visite subséquente*
- *Guide québécois de dépistage des ITSS*
- *Recrudescence de la lymphogranulomatose vénérienne au Québec : détection et traitement*
- Accelerated partner therapy: *quick-reference guide for clinicians* and *quick-reference guide for pharmacists*

REFERENCES

To consult the references, see the report in support of the OUG and the systematic review report.

Institut national d'excellence en santé et en services sociaux
Québec

UNCOMPLICATED *NEISSERIA GONORRHOEAE* INFECTION

ASSESS THE SEVERITY OF THE INITIAL REACTION

SEVERITY OF PREVIOUS ALLERGIC REACTION TO PENICILLIN ANTIBIOTICS

Vague history

or

Unconvincing history reported by patient or family

Non-severe reaction

Immediate reaction[1]

Isolated cutaneous involvement

(urticaria and/or angioedema)

or

Delayed reaction[2,3]

Isolated cutaneous involvement

(Rash and/or urticaria and/or angioedema)

Reaction in childhood[3]

Reaction in adulthood

Distant past (≥ 10 years)

Recent

Severe reaction

Immediate reaction

Anaphylaxis[4]

or

Delayed reaction

Severe skin reaction

(desquamation, pustules, vesicles, purpura with fever or joint pain, but **no** DRESS, SJS/TEN, or AGEP)

Serum sickness[3]

or

Penicillin allergy CONFIRMED[5]

(severe or non-severe reaction only)

Very severe reaction

Immediate reaction

Anaphylactic shock

(with or without intubation)

or

Delayed reaction

Hemolytic anemia
Kidney damage
Liver damage

DRESS, SJS/TEN, AGEP

DECISION-MAKING FOR CHOOSING A BETA-LACAM AND THE CONDITIONS OF ADMINISTRATION

THE FOLLOWING CAN BE PRESCRIBED SAFELY

DISSIMILAR cephalosporins

Cefixime **OR** Ceftriaxone according to treatment recommendations

PRESCRIBE THE FOLLOWING WITH CAUTION

DISSIMILAR cephalosporins

Cefixime **OR** Ceftriaxone according to treatment recommendations

The 1st dose should **always** be administered under medical supervision.

If history of :

- **Immediate reactions,** a drug provocation test should be performed;
- **Delayed reactions,** the patient or his/her family should be informed of the possible risk of recurrence in the days following initiation of the antibiotic.

!

IF A BETA-LACTAM[6] CANNOT BE ADMINISTERED, THE FOLLOWING CAN BE PRESCRIBED...

according to the treatment recommendation in case of a history of allergic reaction

AVOID PRESCRIBING

A beta-lactam[6]

Choose another class of antibiotics.

and

PRESCRIBE THE FOLLOWING

according to the treatment recommendation in case of a history of allergic reaction

1. Immediate reaction (type I or IgE-mediated): generally occurs within 1 hour following the **first dose** of an antibiotic.
2. Delayed reaction (type II, III or IV): can occur at any time, starting 1 hour following the administration of an antibiotic.
3. The delayed skin reactions and serum sickness-like reactions that appear in children receiving antibiotic therapy are generally non-allergic and can be of viral origin.
4. Anaphylaxis without shock or intubation: requires increased vigilance.
5. With no recommendations concerning other beta-lactams.
6. Penicillins, cephalosporins and carbapenems.

AGEP : acute generalized exanthematous pustulosis;
DRESS : drug reaction with eosinophilia and systemic symptoms;
SJS : Stevens–Johnson syndrome;
TEN : toxic epidermal necrolysis.

For further information on the clinical manifestations, consult the interactive tool and the decision support tool.

Further information on pharyngeal NAATs positive for *N. gonorrhoeae*

- For pharyngeal *N. gonorrhoeae* infections detected by NAAT, the specimen is sent to the LSPQ for confirmation. See the INSPQ's explanatory guide for the recommendations concerning management in light of a positive preliminary NAAT result for *N. gonorrhoeae* on a pharyngeal specimen. These recommendations are grouped together in the INSPQ guide in the form of a management algorithm:
  - Appendix 3: « Algorithme clinique pour la prise en charge des infections à *N. gonorrhoeae* ; prélèvement initial ».

Further information on notifiable diseases (MADO)

- When the specimen is sent to the LSPQ to confirm the *N. gonorrhoeae*-positive NAAT result, the microbiology laboratory immediately reports the case to the DSP, based on the preliminary result.
- The LSPQ will send the final confirmatory test result to the DSP. The initial notifier does not have to submit a second form, regardless of the result of the confirmatory test.