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HEALTH

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ORAL CEPHALOSPORINS NO LONGER RECOMMENDED FOR TREATMENT OF GONOCOCCAL INFECTIONS IN THE UNITED STATES

Please distribute immediately to all Clinical Staff in Primary Care/Internal Medicine, Family Medicine, Infectious Disease, Emergency Medicine, Pediatrics, Urology, Obstetrics/Gynecology, Pharmacy, and Laboratory.

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Dear Colleagues,

On August 10, 2012, the Centers for Disease Control and Prevention (CDC) announced that oral cephalosporins are no longer recommended for treatment of infections with gonorrhea. Data from the CDC's Gonococcal Isolate Surveillance Project (GISP) provide laboratory evidence of declining cefixime susceptibility among urethral *N. gonorrhoeae* isolates collected in the United States from 2006-2011. The percentage of GISP isolates with elevated minimum inhibitory concentrations (MICs) of cefixime (MICs $\geq$ 0.25µg/mL) increased from 0.1% in 2006 to 1.5% during January – August 2011. These national data indicate that the majority of isolates with elevated cefixime MICs were from the western U.S. and from men who have sex with men (MSM), mirroring the pattern of fluoroquinolone-resistant *N. gonorrhoeae* observed in the 1990s and early 2000s. These patterns may represent the early stages of clinically significant cephalosporin resistance and raise concerns that continued use of cefixime may lead to more rapid development of resistance to ceftriaxone, the last available antibiotic which is safe and highly-effective for treatment of gonorrhea at all anatomic sites.

In response to this announcement, the New York State Department of Health recommends that clinicians follow these CDC guidelines for gonorrhea therapy, published in the Morbidity and Mortality Weekly Report[1] on August 10, 2012 (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?s_cid=mm6131a3_w):

- **CDC recommends a single intramuscular dose of ceftriaxone 250 mg PLUS either a single dose of azithromycin 1 g orally or doxycyline 100 mg twice daily for 7 days for the treatment of uncomplicated urogenital, anorectal and pharyngeal gonorrhea (box).** Dual therapy is recommended because the use of two antimicrobials with different mechanisms of action theoretically improves the efficacy of treatment and may serve to delay emerging resistance. Azithromycin is preferred over doxycycline because of convenience and observable compliance of single dose therapy and also because of increased prevalence of tetracycline resistance among GISP isolates. Furthermore, combination therapy follows recommendations to routinely treat gonorrhea infections with an antibiotic that provides coverage for Chlamydia regardless of the Chlamydia test result.

Box: Updated recommended treatment regimens for gonococcal infecitions

Uncomplicated gonococcal infections of the cervix, urethra, and rectum

Recommended regimen
Ceftriaxone 250 mg in a single intramuscular dose
PLUS
Azithromycin 1 g orally in a single dose
or doxycycline 100 mg orally twice daily for 7 days

Alternative regimens
If ceftriaxone is unavailable:
Cefixime 400 mg in a single oral dose
PLUS
Azithromycin 1 g orally in a single dose
or doxycycline 100 mg orally twice daily for 7 days
PLUS
Test-of-cure in 1 week

If the patient has severe cephalosporin allergy:
Azithromycin 2 g in a single oral dose
PLUS
Test-of-cure in 1 week

Uncomplicated gonococcal infections of the pharynx

Recommended regimen
Ceftriaxone 250 mg in a single intramuscular dose
PLUS
Azithromycin 1 g orally in a single dose
or doxycycline 100 mg orally twice daily for 7 days

- **Test-of-Cure:** Two alternative regimens are provided to address situations in which ceftriaxone is unavailable or patients have a severe cephalosporin allergy.
    - If a patient with gonorrhea is treated with an alternative regimen, the patient must return 1 week after treatment for a test-of-cure at the site of anatomic infection.
    - The test-of-cure should be performed with a culture or with a NAAT for *N. gonorrhoeae* if culture is unavailable.
    - If the post-treatment NAAT is positive, a culture should be performed. Positive cultures for test-of-cure should also have antibiotic susceptibility testing (AST) performed.

- **Treatment Failures**: Clinicians who diagnose gonorrhea in patients with persistent symptoms of gonococcal infection after treatment (treatment failure) with the recommended dual therapy should culture all anatomic sites regardless of initial infection site and request AST of isolates.
    - The treating clinician should consult NYSDOH at (518) 474-3598 for treatment advice.

- Patients who experience treatment failure after treatment with one of the alternative regimens should be re-treated with ceftriaxone 250 mg in a single intramuscular dose plus azithromycin 2 g in a single oral dose in consultation with NYSDOH.
- For all suspected treatment failures, the clinician should report the case to the local health department within 24 hours and a test-of-cure should be conducted 1 week after re-treatment.

- **Sex Partners:** Ensure that the sex partners of patients with gonococcal infection from the preceding 60 days are evaluated and treated with the recommended combination therapy.
  - Clinicians should encourage patients to refer their partners for medical evaluation and treatment.
  - In NYS, expedited partner therapy (EPT) for gonorrhea is not legal; therefore, the CDC recommendation to use EPT for heterosexual partners who cannot be clinically evaluated and treated is not an option.
  - NYSDOH partner services specialists are available for assistance with partner notification and referral.

- **Laboratory Assistance:** Providers are encouraged to contact their commercial or hospital laboratories about the availability of transport media for gonorrhea culture if resistance is suspected. With increasing use of NAAT, laboratory capacity to perform culture has declined. However, culture capacity for *N. gonorrhoeae* is essential to monitor trends in antimicrobial resistance and assessing susceptibility to guide treatment following treatment failures.

Detailed information on the gonorrhea treatment recommendations is located at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?s_cid=mm6131a3_w

Please contact the Bureau of STD Prevention and Epidemiology if you have any questions regarding these recommendations at 518-474-3598 or by e-mail at stdc@health.state.ny.us.

References:

[1] Centers for Disease Control and Prevention. Update to CDC's *Sexually Transmitted Diseases Treatment Guidelines, 2010*: Oral Cephalosporins No Longer a Recommended Treatment for Gonococcal Infection. MMWR2012;61:590-94.