

## Overview of STD Drug Formulary Changes

In anticipation of the 2010 CDC STD Treatment Guidelines, North Carolina is recommending shifting from the use of cefixime as the first line treatment of uncomplicated gonococcal infection to ceftriaxone. Gonorrhea treatment is complicated by the ability of *N. gonorrhoeae* to develop resistance to antimicrobial therapies. As of April 2007, quinolones are no longer recommended in the U.S. for the treatment of gonorrhea and associated conditions such as PID (2007 MMWR) because of the wide dissemination of Quinolone-resistant *N. gonorrhoeae* strains throughout the U.S. and the world. Consequently, only one class of antimicrobials, the cephalosporins, is still recommended and available for the treatment of gonorrhea in the U.S. The CDC website ([http:// www.cdc.gov/std/gisp](http://www.cdc.gov/std/gisp)) or our North Carolina DHHS website (<http://www.epi.state.nc.us/epi/hiv/>) can provide the most current information.

The proportion of isolates in CDC's Gonococcal Isolate Surveillance Project (GISP) demonstrating decreased susceptibility to ceftriaxone or cefixime has remained very low over time; from 1987 through 2007 there have been a total of four isolates with decreased susceptibility to ceftriaxone and 48 isolates with decreased susceptibility to cefixime. In 2007 there were no isolates identified with decreased susceptibility to ceftriaxone (cefixime was not tested for in 2007). Although only two cases of suspected treatment failure with ceftriaxone have been reported, approximately 50 patients are thought to have failed oral cephalosporin treatment, including one possible case in Hawaii in 2001 (Wang 2001). The majority of these treatment failures to oral cephalosporins have been reported from Asian countries (Lo 2008, Yokoi 2007, Deguchi 2003, Muratani 2001). The concern for emergence of cephalosporin resistance coupled with the reliance on this single class of antibiotics for treatment has led to our recommendation to treat all uncomplicated gonococcal infections with ceftriaxone 250 mg IM as a single dose.

Ceftriaxone in a single injection of 250 mg provides sustained, high bactericidal levels in the blood. Extensive clinical experience indicates that ceftriaxone is safe and effective for the treatment of uncomplicated gonorrhea at all anatomic sites, curing 99.2% of uncomplicated urogenital and anorectal and 98.9% of pharyngeal infections in published clinical trials (Moran 2002). A 250 mg dose of ceftriaxone is recommended over a 125 mg dose given the increased geographic distribution of isolates demonstrating *in vitro* decreased susceptibility to cephalosporins, a small number of reports of ceftriaxone treatment failures, improved efficacy of ceftriaxone 250 mg in pharyngeal infection (which is often unrecognized), and the need to use simple, consistent guidance.

A cefixime 400 mg oral dose does not provide as high, nor as sustained, a bactericidal level as that provided by the 250 mg dose of ceftriaxone. In published clinical trials, the 400 mg dose cured 97.5% of uncomplicated urogenital and anorectal (lower 95% confidence interval (CI) = 95.4%) and 92.3% of pharyngeal gonococcal infections (lower 95% CI = 74.9%) (Newman 2007, Moran 2005). The advantage of cefixime is that it can be administered orally; however, ceftriaxone should be used if pharyngeal infection is suspected and is often asymptomatic.

Single-dose injectible cephalosporin regimens (other than ceftriaxone 250 mg IM) that are safe

and highly effective against uncomplicated urogenital and anorectal gonococcal infections include ceftizoxime (500 mg, administered IM), cefoxitin (2 g, administered IM with probenecid 1 g orally), and cefotaxime (500 mg, administered IM). None of these other injectible cephalosporins offer any advantage over ceftriaxone for urogenital infection, their efficacy at the pharynx is less certain (Moran 2002) and they are currently not provided by the state.

Decreased susceptibility of *N. gonorrhoeae* to cephalosporins and other antimicrobials is expected to continue to spread; therefore, state and local surveillance for antimicrobial resistance is crucial for guiding local therapy recommendations. GISP, which samples approximately 3% of all U.S. men who have gonococcal infections, is a mainstay of surveillance. However, surveillance by clinicians also is critical. Clinicians who diagnose *N. gonorrhoeae* infection in a patient with suspected cephalosporin treatment failure should perform culture and susceptibility testing of relevant clinical specimens, consult a specialist for guidance in clinical management, and report the case to CDC at (404) 639-8373 through state and local public health authorities.

In summary, our treatment recommendations are now:

### **Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum**

#### ***Recommended Regimens***

---

Ceftriaxone 250 mg IM in a single dose

OR, IF NOT AN OPTION

Cefixime 400 mg orally in a single dose

OR

Single-dose injectible cephalosporin regimens

*PLUS*

PRESUMPTIVE TREATMENT FOR CHLAMYDIA IF CHLAMYDIAL INFECTION NOT RULED OUT

---

Generic acyclovir continues to be in short supply due to manufacturing delays. Teva, the manufacturer of generic acyclovir, is planning the following dates for availability: The 800 mg tablets should have been released the week of 2/15. The 600 mg tablets are planned to be available in early March and the 200mg tablets in early April. The acyclovir capsules are anticipated to be available soon as well. We have been providing a four month supply of generic acyclovir for the suppressive treatment of Genital HSV-2 infection in newly diagnosed individuals. The state will provide generic valacyclovir until supplies of acyclovir are available to us. The recommended therapies for the treatment of Genital HSV-2 infection are:

### **First Clinical Episode of Genital Herpes**

#### ***Recommended Regimens\****

**Acyclovir** 400 mg orally three times a day for 7–10 days

**OR**

**Famciclovir** 250 mg orally three times a day for 7–10 days

**OR**

**Valacyclovir** 1 g orally twice a day for 7–10 days

\* Treatment might be extended if healing is incomplete after 10 days of therapy.

### *Suppressive therapy*

#### *Recommended Regimens*

**Acyclovir** 400 mg orally twice a day

**OR**

**Famciclovir** 250 mg orally twice a day

**OR**

**Valacyclovir** 500 mg orally once a day (for those with 10 or fewer outbreaks per year)

**OR**

**Valacyclovir** 1.0 g orally once a day

### *Episodic Therapy for Recurrent Genital Herpes*

Effective episodic treatment of recurrent herpes requires initiation of therapy within 1 day of lesion onset or during the prodrome that precedes some outbreaks. The patient should be provided with a supply of drug or a prescription for the medication with instructions to initiate treatment immediately when symptoms begin.

#### *Recommended Regimens*

---

Acyclovir 400 mg orally three times a day for 5 days

**OR**

Acyclovir 800 mg orally twice a day for 5 days

**OR**

Acyclovir 800 mg orally three times a day for 2 days

**OR**

Famciclovir 125 mg orally twice daily for 5 days

**OR**

Famciclovir 1000 mg orally twice daily for 1 day

**OR**

Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days

**OR**

Valacyclovir 500 mg orally twice a day for 3 days

**OR**

Valacyclovir 1.0 g orally once a day for 5 days

---