Wyoming Department of Health

Public Health Division
122 West 25th Street, 3rd Floor West
Cheyenne, WY 82002
(307) 777-6004 • 800-599-9754
Fax (307) 777-8687 • www.health.wyo.gov

Stefan Johansson
Director

Mark Gordon
Governor

State Health Advisory
Bicillin Shortage for Syphilis Treatment
Wyoming Department of Health
October 2, 2023

Summary
Amidst a significant increase in syphilis, including congenital syphilis, cases across the country, there is a concurrent shortage of Penicillin G Benzathine injectable suspension products (Bicillin L-A) which is the first line treatment for syphilis and the only available treatment for certain individuals, including pregnant women. The Bicillin L-A shortage is expected to last until at least the second quarter of 2024.

The Wyoming Department of Health (WDH) requests that providers prioritize Bicillin L-A for the following groups of individuals:

- Pregnant women diagnosed with or exposed to syphilis and meet criteria for presumptive treatment
- Partners of pregnant women diagnosed with or exposed to syphilis and meet criteria for presumptive treatment
- Immunocompromised individuals diagnosed with or exposed to syphilis and meet criteria for presumptive treatment
- Persons diagnosed with or exposed to syphilis with contraindications to doxycycline
- Persons diagnosed with or exposed to syphilis who are unlikely to be compliant with a doxycycline course
- Infants or children with congenital or acquired syphilis who meet criteria for Bicillin L-A treatment
- Persons diagnosed with tertiary syphilis

WDH asks that providers consider using doxycycline as an alternative to Bicillin L-A for persons diagnosed with or exposed to syphilis who are not in one of the above groups. WDH also asks providers to consider using antibiotics other than Bicillin L-A for other conditions, such as group A streptococcal pharyngitis.

Epidemiology
Syphilis cases, including congenital syphilis, are increasing nationwide. From 2018 to 2022, Wyoming has seen a 54% increase in reported syphilis cases. In 2022, 65% of cases were male

and 35% female, 68% were diagnosed in later stages of syphilis, and the age range for cases was 16-65 years. In 2022, 6.1% of cases were among pregnant women.

Clinical Presentation

Syphilis is a sexually transmitted disease which can cause serious complications including blindness, heart and other tissue damage, and death if not detected and treated. Syphilis infection has different stages and is sexually transmissible during the primary and secondary stage.

- During the primary stage, painless chancres can appear in the genital area or oral cavity. These chancres may be confused with herpes and can disappear on their own without treatment despite continued infection.
- The secondary stage is marked with non-pruritic mucocutaneous lesions, often on the palms of the hands, soles of the feet, and around the trunk of the body. Other conditions that may be present during the secondary stage include condyloma lata (wart-like lesions), lymphadenopathy, mucous patches, alopecia, and fever.
- Early latent syphilis, late latent, and syphilis of unknown duration may have no symptoms.
- Neurological, ocular and otic manifestations of syphilis can appear at any stage.
- Tertiary syphilis refers to gummas, cardiovascular syphilis, psychiatric manifestations, or late neurosyphilis

Staging syphilis and the presence of neurologic, ocular or otic manifestations impact treatment recommendations; WDH can assist providers with staging.

Details regarding the presentation of congenital syphilis can be found here: https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm

Screening and Diagnosis

Routine screening is recommended for populations at risk for acquiring syphilis and for all pregnant women. Providers are encouraged to take a complete sexual history which includes number of sex partners, previous sexually transmitted infections (STIs), and drug use. Providers should routinely test for syphilis in persons who meet any of the following criteria:

- Are pregnant, for all women at the first prenatal visit AND repeat testing throughout pregnancy if the pregnant woman or partner(s) have other sexual partners, use injection or intranasal drugs, have unprofessional or homemade tattoos or piercings, or have other ongoing risks for syphilis transmission
- Are sexually active
- Are men who have sex with men
- Have been diagnosed with other STIs
- Are living with HIV and are sexually active
- Have a current or past history of injection or intranasal drug use, experiencing homelessness, or residency in a detention or correctional facility

Providers should also test for syphilis in persons who report having sexual contact with a person diagnosed with syphilis and who have signs or symptoms suggestive of syphilis.

Two tests are required to diagnose syphilis:

- A non-treponemal test with titer (Rapid Plasma Reagin [RPR] or Venereal Disease Research Laboratory [VDRL] test)
  AND
- A treponemal test (Fluorescent treponemal antibody absorbed [FTA-ABS] test or *Treponema pallidum* passive particle agglutination [TP-PA] assay).

Details regarding syphilis testing algorithms can be found here:
https://health.wyo.gov/wp-content/uploads/2021/09/3.-TESTING-ALGORITHMS.pdf

Additional evaluation is required for patients with clinical signs of neurosyphilis, ocular syphilis, or otosyphilis: https://www.cdc.gov/std/treatment-guidelines/neurosyphilis.htm

Recommendations for evaluation of potential congenital syphilis can be found here:
https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm

If a patient is at risk for syphilis they are also at risk for infection with other STIs, including HIV, and should be tested. If a patient tests positive for an STI, it is imperative to treat the patient's sex partner(s) if indicated. Providers should encourage patients to work with the Wyoming Department of Health Communicable Disease Unit for partner services.

Treatment

Penicillin G, administered parentally, is the preferred drug for treating patients in all stages of syphilis. The preparation used (i.e., benzathine, aqueous procaine, or aqueous crystalline), dosage, and length of treatment depend on the stage and clinical manifestations of the disease. For certain individuals, including pregnant women and certain children, Bicillin L-A is the only available treatment; there are no alternative regimens for pregnant women and certain children diagnosed with or exposed to syphilis.

There is a current nationwide shortage of benzathine penicillin G (Bicillin L-A) that is expected to last until at least the second quarter of 2024. WDH requests that providers prioritize Bicillin L-A for the following groups of individuals:

- Pregnant women diagnosed with or exposed to syphilis and meet criteria for presumptive treatment
- Partners of pregnant women diagnosed with or exposed to syphilis and meet criteria for presumptive treatment
- Immunocompromised individuals diagnosed with or exposed to syphilis and meet criteria for presumptive treatment
- Persons diagnosed with or exposed to syphilis with contraindications to doxycycline
- Persons diagnosed with or exposed to syphilis who are unlikely to be compliant with a doxycycline course
- Infants or children with congenital or acquired syphilis who meet criteria for Bicillin L-A treatment
- Persons diagnosed with tertiary syphilis

In order to help conserve Bicillin L-A for patients with no other treatment options, WDH asks that providers consider using doxycycline as an alternative to Bicillin L-A for persons diagnosed with or exposed to syphilis who are not in one of the above groups. WDH also asks providers to consider using antibiotics other than Bicillin L-A for other conditions, such as group A streptococcal pharyngitis.

The table below describes treatment regimens based on syphilis stage. Please note that as there is no acceptable alternative treatment regimen for pregnant women, pregnant women who have a penicillin allergy should be desensitized and treated with penicillin. Penicillin form and dosing for pregnant women is the same as other adults based on stage and symptoms. The treatment of children with acquired (non-congenital) syphilis is not covered in this table; a child suspected to have acquired syphilis should be referred to a pediatric infectious disease specialist and evaluated for sexual abuse.

Syphilis Stage	Priority Groups	Other Groups
Primary and Secondary and Early Latent Syphilis (Adolescents and Adults)	Bicillin L-A (benzathine penicillin G) 2.4 million units IM in a single dose	Consider doxycycline 100 mg orally twice a day for 14 days as an alternative to Bicillin L-A
Late Latent syphilis, Syphilis of Unknown Duration (Adolescents and Adults)	Bicillin L-A (benzathine penicillin G) 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals	Consider doxycycline 100 mg orally twice a day for 28 days as an alternative to Bicillin L-A
Tertiary Syphilis with no evidence of neurosyphilis (Adolescents and Adults)	Bicillin L-A (benzathine penicillin G) 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals	N/A
Neurosyphilis, Ocular Syphilis, or Otosyphilis in any stage (Adolescents and Adults)	Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion for 10-14 days. An alternative regimen, if compliance with therapy can be ensured, consists of procaine penicillin G 2.4 million units IM daily plus probenecid 500 mg orally 4 times per day, both	Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion for 10-14 days. An alternative regimen, if compliance with therapy can be ensured, consists of procaine penicillin G 2.4 million units IM daily plus probenecid 500 mg orally 4 times per day, both

	medications for 10-14 days. After completion, consider additional doses of Bicillin L-A 2.4 million units IM once per week for 1-3 weeks to provide a comparable total duration of therapy as for latent syphilis.	medications for 10-14 days. After completion, consider additional doses of Bicillin L-A 2.4 million units IM once per week for 1-3 weeks to provide a comparable total duration of therapy as for latent syphilis.
Confirmed proven or highly probable congenital syphilis	Aqueous crystalline penicillin G 100,000-150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days OR procaine penicillin G 50,000 units/kg/dose IM in a single daily dose for 10 days	N/A
Possible congenital syphilis	Aqueous crystalline penicillin G 100,000-150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days OR procaine penicillin G 50,000 units/kg/dose IM in a single daily dose for 10 days OR Bicillin L-A 50,000 units/kg/dose IM in a single dose	N/A
Congenital syphilis less likely	Bicillin L-A (benzathine penicillin G) 50,000 units/kg/dose in a single dose	N/A
Congenital syphilis unlikely	No treatment is required. Providers can consider Bicillin L-A (benzathine penicillin G) 50,000 units/kg/dose in a single dose	N/A

Management of Sex Partners

Sexual transmission of syphilis is thought to occur only when mucocutaneous syphilitic lesions are present. Such manifestations are uncommon after the first year of infection. Persons exposed through sexual contact with a person who has primary, secondary, or early latent syphilis should be evaluated clinically and serologically and treated according to the following recommendations:

- Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis <90 days before the diagnosis should be treated presumptively for early syphilis, even if serologic test results are negative.
- Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis >90 days before the diagnosis should be treated presumptively for early syphilis if serologic test results are not immediately available and the opportunity for follow-up is uncertain. If serologic tests are negative, no treatment is needed. If serologic tests are positive, treatment should be based on clinical and serologic evaluation and syphilis stage.
- Long-term sex partners of persons who have late latent syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the evaluation's findings.
- The following sex partners of persons with syphilis are considered at risk for infection and should be confidentially notified of the exposure and need for evaluation: partners who have had sexual contact within 3 months plus the duration of symptoms for persons who receive a diagnosis of primary syphilis, within 6 months plus duration of symptoms for those with secondary syphilis, and within 1 year for persons with early latent syphilis.

WDH conducts partner services for all patients diagnosed with syphilis in Wyoming.

Further Information: Detailed guidelines for the diagnosis and treatment of syphilis can be found from the Centers for Disease Control and Prevention here: https://www.cdc.gov/std/treatment-guidelines/syphilis.htm

Contact Information: Syphilis is a reportable disease in Wyoming; providers should report patients diagnosed with syphilis to WDH by faxing reports to 307-777-5279 or submitting reports online at https://health.wyo.gov/publichealth/infectious-disease-epidemiology-unit/reporting/. For additional information or with questions about this advisory, providers can contact Katelyn Hoff, Communicable Disease Epidemiologist at WDH at 307-777-2434 or katelyn.hoff@wyo.gov.