

Long-Acting Penicillin G Benzathine Injectable Suspension Products (Bicillin L-A®) Shortage

- Long-acting penicillin G benzathine injectable suspension products (Bicillin L-A®), the first-line treatment for syphilis and the only recommended treatment for pregnant people and infants with syphilis, continues to be in short supply, with supply shortages likely to continue until mid-2024.
- With rising rates of syphilis and congenital syphilis in New York City (NYC), the NYC
 Department of Health and Mental Hygiene (NYC Health Department) strongly encourages
 providers to review their existing Bicillin L-A inventory and reserve Bicillin L-A for pregnant
 people with syphilis or exposure to syphilis, infants with syphilis, and for people with syphilis
 who are unable to take doxycycline if their inventory is running low.
- Doxycycline is the acceptable alternative recommendation for people who are not pregnant; providers should closely follow patients to encourage treatment completion.
- Other intramuscular formulations of penicillin, such as Bicillin C-R, are not acceptable alternatives for the treatment of syphilis.

July 10, 2023

Dear Colleague:

In April 2023, the Centers for Disease Control and Prevention (CDC) and U.S. Food and Drug Administration (FDA) listed Bicillin L-A on their drug shortage webpages, anticipating a resolution after two months. The New York State Department of Health (NYS DOH) released a health advisory on this topic on June 6, 2023. However, additional manufacturing delays have resulted in a longer recovery timeframe, now estimated to be the middle of 2024.

This is of considerable concern as NYC continues to see increased syphilis morbidity, including syphilis in pregnant people and congenital syphilis in infants. The overall rate of primary and secondary syphilis among NYC residents increased by 22% from 2017 to 2022, with an almost four-fold rise in the rate among people reported as female over the five-year period. Following several years of relatively low numbers of reported congenital syphilis cases, substantial increases were observed with 24 cases in 2021 and 19 cases in 2022 (data for 2022 is preliminary). Further, Black and Latino New Yorkers continue to have disproportionately higher rates of primary and secondary syphilis and congenital syphilis, and the Bicillin L-A shortage will compound these health inequities.

Bicillin L-A is the recommended, first-line treatment for syphilis, and the **only** recommended treatment for pregnant people and infants with syphilis. Up to 40% of infants born to pregnant people with untreated syphilis will be stillborn, suffer early infant death, or face long-term morbidity

including blindness, deafness, and bone damage. Prompt and timely treatment of syphilis in pregnancy is nearly 100% effective at preventing the devastating outcomes of congenital syphilis.

The NYC Health Department recommends the following while Bicillin L-A remains in short supply:

- 1. Inventory existing stock of Bicillin L-A.
- 2. Prioritize Bicillin L-A for pregnant patients with syphilis infection or exposure and with a congenital exposure. Treatment decisions for infants should be informed by adequacy of maternal treatment; presence of clinical, laboratory, or radiographic evidence of syphilis in the neonate; and comparison of maternal (at delivery) and neonatal nontreponemal serologic titers.
- 3. Prioritize Bicillin L-A for patients with contraindications to doxycycline (e.g., anaphylaxis, hemolytic anemia, Stevens Johnson syndrome).
- 4. If Bicillin L-A inventory is low, consider treating non-pregnant adult patients with primary, secondary, or early latent syphilis with doxycycline 100 mg PO BID x 14 days. Strongly consider treating non-pregnant adult patients with late latent syphilis or syphilis of unknown duration with doxycycline 100 mg PO BID x 28 days.
 - Perform follow-up clinical and serologic evaluation after treatment at recommended intervals, per the CDC's 2021 <u>STI Treatment Guidelines</u>. Schedule a follow-up upon the patient's post-doxycycline course to verify if treatment was completed and if there was a decline in titer, indicating that the infection was adequately treated.
- 5. Do not use other intramuscular formulations of penicillin, including Bicillin C-R, as they are not acceptable alternatives for the treatment of syphilis.
- 6. Avoid using Bicillin L-A for treatment of other infectious diseases (e.g., streptococcal pharyngitis) as alternative oral medications or other effective antimicrobials are available.
- 7. If your institution is experiencing a Bicillin L-A shortage, contact the NYC Health Department by emailing stitraining@health.nyc.gov with the name of your facility and 'Bicillin L-A shortage' in the subject line. We will notify the CDC, which is tracking shortages by jurisdiction.
- 8. Report shortages to the Pzifer Supply Continuity Team at 844-646-4398 (select 1 and then select 3).
- 9. Access current and historical syphilis test results and treatment information in the NYC Health Department's Syphilis Registry to inform diagnosis and management of syphilis in your patients.

Recommended Bicillin L-A treatment regimens		
Primary and Secondary	Benzathine penicillin G 2.4 million units IM in a single dose	
Syphilis Among Adults		
Latent Syphilis Among Adults	Early latent syphilis: Benzathine penicillin G 2.4 million units IM in a single dose	
	Late latent syphilis: Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals	

Tertiary Syphilis Among Adults	Tertiary syphilis with normal CSF examination: Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals
Syphilis Among Infants	Benzathine penicillin G 50,000 units/kg body weight IM, up to the adult
and Children	dose of 2.4 million units in a single dose

Health care providers can monitor the Bicillin L-A drug shortage on the <u>FDA Drug Shortages</u> web page. For clinical questions related to the treatment of syphilis during the Bicillin L-A shortage, please contact the <u>STD Clinical Consultation Network</u>, or the NYC Health Department at <u>stitraining@health.nyc.gov</u>.

Resources

- FDA Notice of Bicillin L-A shortage
- CDC Availability of STI Testing and Treatment Products
- CDC 2021 STI Treatment Guidelines, Syphilis
- CDC 2021 STI Treatment Guidelines, Congenital Syphilis
- CDC Syphilis information
- NYS DOH Advisory: Bicillin L-A Manufacturing and Supply Shortage Coinciding with Continued Syphilis Increases

Sincerely,

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