



April 17, 2017

Dear STD Program Colleagues,

This is an update regarding the ongoing shortage of **Penicillin G benzathine (Bicillin L-A®)** and **Penicillin G procaine** in the United States. Pfizer, the sole manufacturer of Penicillin G benzathine (Bicillin L-A®) and Penicillin G procaine in the United States, continues to experience a manufacturing delay of these products.

**Penicillin G benzathine (Bicillin L-A®)**

Penicillin G benzathine (Bicillin L-A®) is the recommended treatment for syphilis and the only recommended treatment for pregnant women infected or exposed to syphilis.

Pfizer is releasing allocations of the product to wholesale distributors. Pfizer estimates that supply improvement is expected over the next several months. However, we are challenged by the current syphilis epidemic in the United States. Thus, with an estimated 33% increase of infectious syphilis cases from 2014-2016, orders are not keeping pace with projected syphilis treatment demands among patients and their sex partners. Until normal quantities of Bicillin L-A® are available, CDC has modified steps outlined in the Dear Colleague Letters dated May 23, 2016 and December 12, 2016.

- 1) **Continue to proactively take inventory at least monthly** and more frequently if product is found to be low and project future need to inform ordering of product
  - Monitor local supply of Bicillin L-A®
  - Determine local pattern of Bicillin L-A® use
  - Determine rate of increase of syphilis cases and contacts in the previous year and contact distributors to procure Bicillin L-A® based on a projection of future cases and contacts expected rather than based on prior orders. The simplest approximation of potential cases for 2017 would be to apply the percentage increase in syphilis cases from 2015 to 2016 to the number of cases of syphilis treated in 2016.
  - If product reaches a critical supply level of three weeks or less, notify **Pfizer Injectables at 844.646.4398, press 3 for Supply Continuity Team** to inquire about emergency supply.
    - Please ensure the following information is readily available when contacting the Pfizer Supply Continuity Team:
      1. Customer Name
      2. Address
      3. Point of Contact Name
      4. Point of Contact Phone
      5. Point of Contact Email address
      6. DEA number (if available)

7. NDC number
8. Average Monthly Use of Bicillin L-A®
9. Quantity requested
10. Customer's Wholesaler (include city and state)

- Alert DSTDP by contacting Roxanne Barrow, MD, Medical Epidemiologist, ([rbarrow@cdc.gov](mailto:rbarrow@cdc.gov)) and Jennifer Fuld, PhD, Chief, Program Development and Quality Improvement Branch ([jfuld@cdc.gov](mailto:jfuld@cdc.gov)) with an email clearly labeled as “report of an urgent need for BIC as supply is critical”.
- If the Supply Continuity Team is unable to facilitate provision an emergency supply, contact Dr. Barrow ([rbarrow@cdc.gov](mailto:rbarrow@cdc.gov), 404.639.8503) and Dr. Fuld ([jfuld@cdc.gov](mailto:jfuld@cdc.gov), 404.718.5983) so we can work with the FDA and Pfizer to assist in resolving the situation.

2) **Continue to implement a usage strategy, if inventory is less than 2 months of product based on projected use**

- Discourage the use of Bicillin L-A® for treatment of other infectious diseases (e.g. streptococcal pharyngitis) where other effective antimicrobials are available.
- Encourage the adherence to the recommended dosing regimen of 2.4 million units of Bicillin L-A® IM for the treatment of primary, secondary, and early latent syphilis (early syphilis) as outlined in the [2015 STD Treatment Guidelines](#). Additional doses to treat early syphilis do not enhance efficacy including patients living with HIV infection.
- Identify inventories with ample product based on the usage pattern and facilitate movement of product, if feasible, in your jurisdiction.
- Purchase product at the state level to be distributed to facilities with less than 2 months of product. CDC will continue to approve the use of STD-AAPPS funds for emergency purchases of product, if the usage strategy documents urgent need. Please send your request for approval, clearly documenting urgent need, to DSTDP by contacting Roxanne Barrow ([rbarrow@cdc.gov](mailto:rbarrow@cdc.gov), 404.639.8503) and Jennifer Fuld ([jfuld@cdc.gov](mailto:jfuld@cdc.gov), 404.718.5983)

3) **Continue to communicate with healthcare providers and pharmacists**

- Remind health care providers and pharmacists of the limited availability of Bicillin L-A® so they are aware, can plan, and forecast demand based on rate of increase of syphilis cases in your jurisdiction. Ask them to report to you any shortages when inventory is less than 2 months of product based on projected use.
- Encourage clinicians with questions about syphilis clinical management to contact the on-line National Network of STD Clinical Prevention Training Centers (NNPTC) STD Clinical Consultation Network (<https://www.stdccn.org>) or a local ID specialist.

4) **Continue to communicate with DSTDP**

- Notify Roxanne Barrow ([rbarrow@cdc.gov](mailto:rbarrow@cdc.gov), 404.639.8503) and Jennifer Fuld ([jfuld@cdc.gov](mailto:jfuld@cdc.gov), 404.718.5983) about the shortage or low inventories of Bicillin L-A® in your jurisdiction so CDC can continue to monitor this situation and provide situational awareness to FDA and Pfizer.

More information on syphilis treatment and clinical management can be found in the [2015 STD Treatment Guidelines](http://www.cdc.gov/std/tg2015/syphilis.htm) (<http://www.cdc.gov/std/tg2015/syphilis.htm>). CDC is not recommending any changes to these treatment recommendations for patients with syphilis.

Additional information on the availability of Bicillin L-A® can be found at <http://www.cdc.gov/std/treatment/drugnotices/bicillinshortage.htm> or on the [FDA's Drug Shortage website](http://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Penicillin%20G%20Benzathine%20(Bicillin%20L-A)%20Injection&st=c) ([http://www.accessdata.fda.gov/scripts/drugshortages/dsp\\_ActiveIngredientDetails.cfm?AI=Penicillin G Benzathine \(Bicillin L-A\) Injection&st=c](http://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Penicillin G Benzathine (Bicillin L-A) Injection&st=c))

### **Penicillin G procaine**

Penicillin G procaine is one of the recommended treatments for congenital syphilis and an alternative treatment for both neurosyphilis (NS) and ocular syphilis (OS).

**Penicillin G procaine is currently unavailable.** The next delivery that was expected by April 2017 is now delayed due to prioritization of Bicillin L-A®. Pfizer will evaluate the next delivery when the supply of Bicillin L-A® is more stable. Until Penicillin G procaine is available, CDC suggests the following:

- 1) Continue to use recommended options to treat congenital syphilis and neurosyphilis/ocular syphilis:

- a) **Congenital Syphilis**

- Proven or highly probable congenital syphilis**

- Recommended Regimen**

- 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

- Possible Congenital Syphilis**

- Recommended Regimens**

- 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**

- Benzathine penicillin G 50,000 units/kg/dose IM in a single dose

- b) **Neurosyphilis/Ocular Syphilis**

- Recommended Regimen**

- 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

- As an option for treating persons with neurosyphilis/ocular syphilis outside of the hospital setting, some providers use the recommended regimen of aqueous crystalline penicillin G IV through a pic line. Limited data suggest that ceftriaxone

2 g daily either IM or IV for 10–14 days may be effective as an alternative treatment. If an alternative to aqueous crystalline penicillin G is used, close follow-up is essential.

- 2) Continue to communicate with healthcare providers and pharmacists
  - a) Remind health care providers and pharmacists that Penicillin G procaine is currently unavailable so they are aware and can plan, if not already done.
  - b) Encourage clinicians with questions about congenital syphilis, neurosyphilis, and ocular syphilis clinical management to contact the on-line National Network of STD Clinical Prevention Training Centers (NNPTC) STD Clinical Consultation Network (<https://www.stdccn.org>) or a local ID specialist.

More information on congenital syphilis, neurosyphilis, and ocular syphilis treatment and clinical management can be found in the [2015 STD Treatment Guidelines](http://www.cdc.gov/std/tg2015/syphilis.htm) (<http://www.cdc.gov/std/tg2015/syphilis.htm>). CDC is not recommending any changes to these treatment recommendations for patients with congenital syphilis, neurosyphilis, and ocular syphilis.

Additional information on the availability of Penicillin G procaine can be found at <http://www.cdc.gov/std/treatment/drugnotices/procaine-peng.htm> or on the [FDA's Drug Shortage website](http://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Penicillin%20G%20Procaine%20Injection&st=c&tab=tabs-1) ([http://www.accessdata.fda.gov/scripts/drugshortages/dsp\\_ActiveIngredientDetails.cfm?AI=Penicillin%20G%20Procaine%20Injection&st=c&tab=tabs-1](http://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Penicillin%20G%20Procaine%20Injection&st=c&tab=tabs-1)).

Please keep us posted of any shortages or low inventories of Penicillin G benzathine (Bicillin L-A®) in your jurisdiction. If resources preclude forecasting demand based on syphilis surveillance and partner services trends in your jurisdiction, technical assistance is available from CDC; requests can be made through the DSTDP mailbox [STD\\_AAPPS@cdc.gov](mailto:STD_AAPPS@cdc.gov). The Center for Disease Control and Prevention's (CDC) Division of STD Prevention (DSTDP) will continue to work with the United States Food and Drug Administration's (FDA) Drug Shortage Staff and Pfizer to address this situation and will continue to provide updates as new information becomes available.

Sincerely,



Gail Bolan, MD  
Director, Division of STD Prevention  
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention