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GAVIN NEWSOM
Governor

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Powdered Benzathine Benzylpenicillin (Extencilline®) for the Treatment of Syphilis

Dear Colleague,

The California Department of Public Health (CDPH) would like to inform all health care providers regarding the use of powdered benzathine benzylpenicillin (Extencilline®) for the treatment of syphilis. To address the ongoing [shortage of benzathine penicillin G injectable suspension \(Bicillin® L-A\)](#), the U.S. Food and Drug Administration (FDA) coordinated the temporary importation of [Extencilline® \(PDF\)](#) and associated diluent for reconstitution of injectable 1.2 million and 2.4 million unit doses. Benzathine benzylpenicillin is an alternative name for benzathine penicillin G, therefore Extencilline® and Bicillin® L-A are equivalent and can be used interchangeably for the treatment of syphilis.¹⁻³

For the treatment of syphilis, CDPH advises health care providers to consider the following when using Extencilline®:

- Primary, secondary and early latent syphilis: Extencilline® 2.4 million units as a single intramuscular (IM) dose.
- Late latent syphilis or syphilis of unknown duration: Extencilline® 2.4 million units IM once weekly for 3 weeks.
- Extencilline® is safe for use in pregnancy and should be administered following [standard protocols for treatment of syphilis in pregnancy \(PDF\)](#).⁴
- Extencilline® is safe for use in neonates and infants and can therefore be used for neonates/infants when Bicillin® L-A is otherwise appropriate.
- Extencilline® is not interchangeable with aqueous crystalline penicillin G as it has low penetration of the central nervous system, therefore is not appropriate in cases of suspected neuroinvasion or in the presence of pathologic cerebrospinal fluid (CSF) findings.
- Follow-up clinical and serologic evaluation should be performed after treatment at the recommended intervals per the [2021 Centers for Disease Control and Prevention \(CDC\) Sexually Transmitted Infections \(STI\) Treatment Guidelines](#).⁵

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Given the ongoing Bicillin® L-A shortage and uncertainty regarding how importation of Extencilline® will affect the available supply of injectable long-acting penicillin-based treatment, CDPH recommends the following:

- Prioritize Bicillin® L-A over Extencilline® for infants exposed to syphilis in utero due to the larger volumes required of Extencilline® injections.
- Prioritize Bicillin® L-A and Extencilline® for pregnant people with syphilis infection (or exposure).
- Prioritize Bicillin® L-A and Extencilline® for patients with contraindications to doxycycline (e.g., anaphylaxis, hemolytic anemia, Stevens Johnson syndrome).
- Conserve Bicillin® L-A and Extencilline® by using alternative drugs for the treatment of infectious diseases (e.g., streptococcal pharyngitis) where oral medications or other effective antimicrobials are available. CDPH has posted a [Health Advisory](#) with acceptable alternative regimens for treatment of primary, secondary, early/late latent syphilis and syphilis of unknown duration in non-pregnant adults.⁶

Providers should be aware of the following key differences between Extencilline® and Bicillin® L-A:

- Extencilline® is supplied as powder for reconstitution compared to prefilled disposable syringes for Bicillin® L-A. Follow the instructions for the preparation of an intramuscular injection of Extencilline® found [in this guidance document \(PDF\)](#).
- The volume of Extencilline® 1.2 million units after reconstitution is about 5 mL compared to 2 mL for Bicillin® L-A 1.2 million units. The volume of Extencilline® 2.4 million units after reconstitution is about 7 mL compared to 4 mL for Bicillin® L-A 2.4 million units. As large volume IM injections may cause pain or exceed acceptable volumes per injection, consider splitting doses to provide simultaneous bilateral injections and/or reconstitution in lidocaine as per the provided [protocol \(PDF\)](#). IM injection should follow the same protocol used for Bicillin L-A®.
- Extencilline® contains soya lecithin phospholipids and may cause hypersensitivity reactions (urticaria, anaphylactic shock) in patients with a history of allergy to soybeans, soya or peanuts. Providers should inquire about soybean allergies as such allergy is a contraindication to use.^{7,8}
- Extencilline® does not require any special storage condition. Following reconstitution, the dose should be used immediately.

Orders for Extencilline® can be placed by contacting Direct Success at Distribution@DSuccess.com or 1-877-404-3338.

The pricing, prescribing, distribution, and availability of this product is currently unclear – providers can find updates as they become available at the [FDA Drug Shortages webpage](#). Contact your [local health department](#) if you are experiencing difficulty obtaining Extencilline®.

For clinical questions related to the treatment of syphilis during the Bicillin® L-A shortage, please contact the [Sexually Transmitted Diseases \(STD\) Clinical Consultation Network](#), your local health department, or CDPH STD Control Branch at (510) 620-3400 by phone or stdcb@cdph.ca.gov by email.

Sincerely,



Kathleen Jacobson, MD
Chief, STD Control Branch
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References:

1. [Dear Healthcare Provider Letter on Temporary Importation of Extencilline® \(PDF\)](#) and [Extencilline® Protocol \(PDF\)](#)
2. CDC: [FDA Announcement of Availability of Extencilline®](#)
3. DailyMed: [EXTENCILLINE – EXTENCILLINE®- benzathine benzylpenicillin kit](#)
[EXTENCILLINE®- benzathine benzylpenicillin injection, powder, for suspension](#)
4. CDPH: [Prenatal Syphilis Screening, Staging, Treatment and Monitoring for Congenital Syphilis Prevention \(PDF\)](#)
5. [CDC STI Treatment Guidelines, 2021](#)
6. CDPH Health Advisory: [Bicillin® L-A \(Benzathine Penicillin G\) Shortage](#)
7. Barni, Simona, et al. "Adverse reaction to benzathine benzylpenicillin due to soy allergy: a case report." *Journal of medical case reports* 9.1 (2015): 1-3.
8. Electronic Medicines Compendium: [Benzylpenicillin benzathine 2.4 Million I.U. powder and solvent for suspension for injection](#)