Appropriate Use of Benzathine Penicillin G for Treatment of Syphilis in Adults

Inappropriate use of Bicillin® C-R for Syphilis

Benzathine Penicillin G is the Drug of Choice for Syphilis

Penicillin G remains the preferred antimicrobial for the treatment of syphilis. Benzathine penicillin G (BPG; the generic name) is the recommended treatment agent for syphilis that does not involve the central nervous system. BPG must be administered via deep intramuscular (IM) injection and is available in more than one formulation. Current guidelines recommend use of formulations containing a total dose of 2.4 million units (MU) of benzathine penicillin G, such as Bicillin® L-A (or long-acting; the trade name), either as one large IM injection of 2.4 MU or 2 smaller IM injections of 1.2 MU each. For early syphilis of less than one year's duration (including primary, secondary, and early latent infections), an IM dose of 2.4 MU is recommended. For syphilis of greater than one year's duration (including late latent syphilis or syphilis of unknown duration), a regimen of three weekly 2.4 MU IM doses of BPG is recommended.[1]

Bicillin® C-R Should Not be Used to Treat Syphilis

Bicillin® C-R (or controlled-release; the trade name) is another commercially available product containing BPG. This combination product contains equal amounts of benzathine and procaine salts of penicillin G and also is delivered via deep IM injection. Bicillin® C-R has a shorter half-life compared to Bicillin® L-A and does not achieve comparable sustained blood serum levels thought to be necessary to treat the syphilis organism Treponema pallidum. Bicillin® C-R contains only 1.2 MU – or half the recommended dose – of BPG in combination with 1.2 MU of procaine penicillin G, a much shorter acting penicillin G.

Bicillin® C-R may be confused with Bicillin® L-A. Inadvertent use of Bicillin® C-R to treat syphilis may result in declines in non-treponemal test titers, as would be expected following appropriate antibiotic therapy. However, no data exist describing either the efficacy of Bicillin® C-R or the frequency of clinical failures when used for treatment of syphilis. Therefore, Bicillin® C-R is not recommended for the treatment of syphilis, regardless of stage or anatomic site of infection.

Table 1: Trade names of BPG-containing products distributed by King Pharmaceuticals.

1) Bicillin® L-A. Recommended for the treatment of syphilis. Contains either 2.4 MU of BPG in a 4 ml syringe (NDC # 60793-702-10) or 1.2 MU of BPG in a 2 ml syringe (NDC # 60793-701-10). Blue / white packaging (Figure 1)

2) Bicillin® C-R. Not indicated for the treatment of syphilis. Contains a mixture of 1.2 MU of BPG and 1.2 MU of procaine penicillin G. NDC # 61570-140-10 / 61570-142-10. Green / white packaging. (Figure 2)

3) Bicillin® C-R 900/300. Not indicated for the treatment of syphilis. Contains a mixture of 0.9 MU BPG and 0.3 MU procaine penicillin G. NDC # 61570-143-10. Green / white packaging.
Inadvertent Use of Bicillin® C-R for Syphilis is Not Uncommon

Between 1999-2004 in California, several hundred patients were treated inadvertently for syphilis with Bicillin® C-R instead of Bicillin® L-A, resulting in an effort to locate, clinically and serologically re-evaluate, and re-treat these patients and their sex partners as appropriate. [2]

A similar incident occurred in Maryland in 1998, at which time 123 of 160 doses of penicillin G given for syphilis in one county were Bicillin® C-R, involving 63 patients, including 5 pregnant women.[3] Overall, no cases of definitive treatment failure or congenital syphilis were identified. After eight weeks of follow-up efforts, 52 (82%) of 63 patients had been re-staged and re-treated; the remaining 11 patients either could not be located (1) or refused re-treatment (10). The total estimated cost to the local clinic for follow-up and re-treatment efforts related to this incident was approximately $24,000.

In March 2003, the California STD Control Branch alerted STD Controllers to the continuing problem of inadvertent Bicillin® C-R use. The STD Control Branch is also working with the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration to improve labeling, in order to avoid future confusion and inadvertent use of Bicillin® C-R for syphilis treatment. This overview was designed to supplement these efforts.

**Recommendations**

All providers in California are urged to avoid inadvertent use of Bicillin® C-R for treatment of syphilis. The following steps are suggested to alleviate confusion and possible treatment errors:

- Check current pharmacy stocks
- Re-examine pharmacy ordering procedures, dispensing logs, and protocols
- Submit written pharmacy orders for BPG, not telephone orders
- Educate staff about potential confusion between available BPG formulations
- Review syphilis treatment guidelines with providers

More information

STD treatment guidelines can be found at the State of California’s STD Control Branch web site, [www.dhs.ca.gov/ps/dcdc/STD/stdindex.htm](http://www.dhs.ca.gov/ps/dcdc/STD/stdindex.htm), and the CDC web site, [www.cdc.gov/std/treatment](http://www.cdc.gov/std/treatment).

**References**