



health

Department:  
Health  
REPUBLIC OF SOUTH AFRICA



## South Africa National Essential Medicine List Primary Healthcare Medication Review Process Component: Sexually transmitted infections

### PROBENECID QUANTIFICATION

**Date:** 8 February 2018

**Background:** Erratic availability of benzathine benzylpenicillin globally has resulted in access of this medicine (1.2 MU and 2.4 MU strengths) through Section 21 (S21) during the past year<sup>1</sup>. Alternate options of this agent for the indications listed in the Standard treatment guidelines (STGs) and essential medicine list (EML) was reviewed and use was subsequently restricted to management of maternal and congenital syphilis<sup>2</sup>. However, further Medicines Control Council (MCC) S21 approval and continuous access of these agents has been a challenge and currently there is limited or no availability of benzathine benzylpenicillin nationwide. The National Essential Medicines List Committee (NEMLC) had subsequently reviewed the available evidence for an alternate option, and recommended amoxicillin+probenecid for syphilis in the pregnant woman, if benzathine benzylpenicillin is unavailable (doctor initiated) - see PHC Medicine Review: Amoxicillin and probenecid for syphilis in pregnancy, 15 January 2018 - <http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/404-phc-medicines-reviews>

NEMLC had raised concerns of sufficient stock availability and that pregnant women with syphilis would not present at all primary care clinic facilities. The supplier had indicated a consistent supply of 500 units of probenecid tablets (100's) per month. The question is whether this would be sufficient for the 5296 primary care facilities in the country?

**Objective:** To forecast the use of probenecid to assist National Department of Health (NDoH) with procurement.

**Data sources:** During this exercise the lack of sufficiently robust data in South Africa was verified.

#### A: MCC S21 approvals:

S21 approvals compels Provinces to procure the specified amount described in the MCC approvals. MCC had approved a total of 193885 x 1.2 MU and 409580 x 2.4 MU of benzathine benzylpenicillin doses (June and July S21 approvals). This quantity probably was sufficient until November 2017, when it was alerted that primary care clinics were turning away pregnant women with syphilis. Due to security of supply, in provinces were advised to restrict access to benzathine benzylpenicillin only in November 2017 (i.e. syphilis in pregnancy and newborns). Thus, S21 approvals cannot be used to assist with forecasting of probenecid, as a major limitation is that the initial supply of benzathine benzylpenicillin extends to syphilis in pregnancy, congenital syphilis, rheumatic fever, rheumatic heart disease, Sydenham's chorea, diphtheria as well as tonsillitis/pharyngitis (strep infection).

<sup>1</sup> MCC S21 approvals for benzathine benzylpenicillin 1.2 MU (22 June & 12 July 2017); 2.4 MU (22 June & 12 July 2017).

<sup>2</sup> NDOH Circular notice - BenzathineBenzylpenicillin\_EDP102017-01.

### B: District Health Information System (DHIS)

Programme was requested to provide data from DHIS, as data is collected for pregnant women screened for syphilis in 270 sentinel sites. However, two data dumps that were received were contradictory: The number of pregnant women with syphilis was 378 for the period April to June 2017 was 378, and for the period January 2017 to December 2017 was reported as 261. A quick overview of the data showed that most sites were not reporting. Using the DHIS extract for quantification would be problematic.

### C: Laboratory data

National analysis of National Health Laboratory Services (NHLS) laboratory data of presumptive early congenital syphilis was forwarded by NICD/NHLS<sup>3</sup>. The survey reported an incidence rate of presumptive early congenital syphilis, in 2016 of 118 cases of congenital syphilis per 100 000 live births. Extrapolating this incidence rate to 2017 live births statistics from StatsSA (1 198 481)<sup>4</sup> suggests a prevalence of 1414 cases per annum. Expert opinion advised that this would represent congenital syphilis cases delivered by symptomatic RPR+ women. Though, these congenital syphilis cases only represent live births. A systematic review done by World Health Organisation, 20% of untreated maternal syphilis results in stillbirths and 10% of results in neonatal deaths.

### **Methodology and results for quantification:**

#### a) UPDATED PHC STGS:

*For syphilis in pregnancy, and benzathine benzylpenicillin is unavailable:*

i) Early syphilis: Amoxicillin, oral, 1 g 8 hourly PLUS probenecid 250 mg 8 hourly x 14 days.

i.e. 21 tablets of probenecid 500 mg required.

ii) Late/latent syphilis: Amoxicillin, oral, 1 g 8 hourly PLUS probenecid 250 mg 8 hourly x 28 days.

i.e. 42 tablets of probenecid 500 mg required.

(Note: The currently available probenecid 500 mg tablet that is available on the market is scored).

#### b) PREGNANT WOMEN WITH SYPHILIS

For equity purposes, each clinic (i.e. 5296 PHC facilities) should stock probenecid tablets. Probenecid 500 mg tablets are available from a sole supplier (Pharmacare Limited) in pack sizes of 100. Currently, the supplier can provide 500 units per month to the South African market (public and private healthcare sectors). But, probenecid is only required if benzathine benzylpenicillin is not available and ideally pack sizes of 21 and 42 tablets are required. Thus, stocking probenecid at every PHC facility would be wasteful and fruitless expenditure.

Therefore, an estimated annual prevalence of pregnant women with syphilis was extrapolated from NHLS laboratory data, the WHO systematic review and StatsSA midyear population statistics (2017). It was estimated that 2050 pregnant women would require treatment for syphilis nationwide per annum. However, it cannot be predetermined in which Province or District these women would present.

#### c) SINGLE EXIT PRICE (SEP)

Using the SEP database (22 December 2017), the price of 21 tablets is R76.25 and for 42 tablets is R152.51. This is expensive, compared to benzathine benzylpenicillin 2.4 MU (price of a single injection accessed as S21 from Biotech Laboratories was R8.64 in 2016, adjusted using SEP adjustments for 2017 (7.5%) and 2018(1.26%) equating to R9.41).

<sup>3</sup> Mathebula R et al. Trends in presumptive early congenital syphilis in South Africa 2010- 2016: a national analysis of laboratory data, Centre for HIV and STIs National Institute for Communicable Diseases, 4 May 2017.

<sup>4</sup> StatsSA mid year population statistics, 2017

#### d) RESULTS

Assuming that all pregnant women would be treated for late/latent syphilis (i.e 42 tablets of probenecid 500 mg required per course); would require 86100 probenecid 500 mg tablets or 861 packs of probenecid 500mg, 100 tablets per annum or 72 packs per month.

#### **Conclusion:**

For treatment of syphilis in the pregnant women, if benzathine benzylpenicillin is out of stock, it is estimated that approximately 7175 probenecid 500 mg tablets would be required per month. However, it is noted that it is unknown at which primary care facility these pregnant women would present and that pack sizes of 21 or 42 probenecid 500 mg tablets are required. Furthermore, probenecid is expensive relative to benzathine benzylpicillin 2.4 MU injection.

Request is made to the Contract Management team at the National Department of Health to address these matters with the supplier, as well as how to access probenecid at the relevant primary level of care from an operational aspect.

#### *Report prepared by:*

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