



health

Department:
Health
REPUBLIC OF SOUTH AFRICA

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Reference: 2019/10/21/AMD/EDP/01

NOTICE: UPDATED RECOMMENDED THERAPEUTIC ALTERNATIVES FOR BENZATHINE BENZYL PENICILLIN INJECTION

The Primary Health Care, Adult and Paediatric Hospital Level Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) currently recommend the use of benzathine benzylpenicillin for various indications.

There is an ongoing supply problem with benzathine benzylpenicillin, which has necessitated the use of alternative procurement methods and/or the sourcing of alternative therapeutic options.

This updated circular¹ reinforces the recommendations to restrict the use of benzathine benzylpenicillin* and recommends alternatives, including the option to use doxycycline for latent syphilis²³.

***Note:** Benzathine benzylpenicillin is the recommended treatment for syphilis in children and pregnant women. In pregnancy, azithromycin does not effectively treat syphilis in the foetus, and resistance develops rapidly to azithromycin.

It is recommended that Pharmaceutical and Therapeutics Committees implement strategies for the rational use of the limited supplies of benzathine benzylpenicillin available.

In the event that there is no benzathine benzylpenicillin injection available at your facility, the recommended therapeutic alternatives listed in the STGs and EML and on contract for use in both Adults and Paediatrics include:

Indication: Primary Healthcare Level	Current recommendation in STGs and EML	Therapeutic alternative to benzathine benzylpenicillin
Section 4.9 Rheumatic Fever, acute: Eradication of streptococci in throat	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, as a single dose: <ul style="list-style-type: none"> Children < 30kg: 600 000 IU. Children ≥30kg and adults: 1.2 MU. 	<ul style="list-style-type: none"> Phenoxymethylpenicillin, oral, 12 hourly for 10 days: <ul style="list-style-type: none"> If < 30kg: 250mg. If ≥ 30kg and adults: 500mg. OR if unavailable: <ul style="list-style-type: none"> Amoxicillin, oral, daily for 10 days: <ul style="list-style-type: none"> If < 30kg: 250 mg. If ≥ 30kg and adults: 500 mg.
4.9 Rheumatic fever, acute: Prophylaxis for rheumatic fever	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, every 21-28 days. <ul style="list-style-type: none"> Children < 30kg: 600 000 IU. Children ≥ 30kg and adults: 1.2 MU. 	<ul style="list-style-type: none"> Phenoxymethylpenicillin, oral, 12 hourly: <ul style="list-style-type: none"> Children: 125mg. Adults: 250mg. OR if unavailable: <ul style="list-style-type: none"> Amoxicillin, oral, daily: <ul style="list-style-type: none"> If < 30kg: 125 mg. If ≥30kg and adults: 250 mg.

¹Update to previous circulars, dated 11 July 2017 and 13 March 2018: Reference: EDP072017/01 and EDP032018/04, respectively.

²World Health Organisation. WHO Guidelines for the treatment of *Treponema pallidum* (syphilis), 2016.

³Centers for Disease Control and Prevention. 2015 Sexually Transmitted Diseases Treatment Guidelines. <https://www.cdc.gov/std/tg2015/>

6.2.4 Syphilis in Pregnancy	<u>Pregnant women:</u> <ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 2.4 MU weekly for 3 weeks. <u>Newborn baby, asymptomatic, well:</u> <ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 50 000 units/kg as a single dose into the lateral thigh. 	<ul style="list-style-type: none"> Alternative procurement for benzathine benzylpenicillin is available through S21 approval⁴.
12.8 Syphilis serology and treatment	<u>Early syphilis (primary/ secondary):</u> <ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 2.4 MU immediately as a single dose. <u>Latent syphilis:</u> <ul style="list-style-type: none"> Benzathine benzylpenicillin 2.4 MU weekly for 3 weeks. 	<ul style="list-style-type: none"> Alternative procurement for benzathine benzylpenicillin is available through S21 approval⁴. <p><u>In penicillin allergy patients (or in case of stock-outs of benzathine benzylpenicillin):</u></p> <p><u>Early syphilis:</u></p> <ul style="list-style-type: none"> Doxycycline, oral 100mg 12 hourly for 14 days. <p><u>Latent syphilis:</u></p> <ul style="list-style-type: none"> Doxycycline, oral 100mg 12 hourly for 28 days.
12.8 Syphilis serology and treatment, late syphilis treatment	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 2.4 MU once weekly for 3 weeks. 	<ul style="list-style-type: none"> Alternative procurement for benzathine benzylpenicillin is available through S21 approval⁴.
19.6 Tonsillitis and Pharyngitis	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, single dose: <ul style="list-style-type: none"> Children < 30kg: 600 000IU. Children ≥ 30kg and adults: 1.2MU. 	<ul style="list-style-type: none"> Phenoxymethylpenicillin, oral, 12 hourly for 10 days: <ul style="list-style-type: none"> Children 18 months-11 years: 250mg. Children >11 years and adults: 500mg. <p>OR if unavailable:</p> <ul style="list-style-type: none"> Amoxicillin, oral, daily for 10 days: <ul style="list-style-type: none"> Children 18 months-11 years: 50 mg/kg daily. Children >11 years and adults: 1000 mg 12 hourly.

Indication: Paediatric Hospital Level	Current recommendation in STGs and EML	Therapeutic alternative to benzathine benzylpenicillin
Section 4.4 Rheumatic Fever, to eradicate any streptococci	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, as a single dose: <ul style="list-style-type: none"> If < 30kg: 600 000IU. If ≥ 30kg: 1.2MU. 	<ul style="list-style-type: none"> Phenoxymethylpenicillin, oral, 250-500mg 12 hourly for 10 days. <p>OR if unavailable:</p> <ul style="list-style-type: none"> Amoxicillin, oral, 50 mg/kg, daily for 10 days.
Section 4.4 Rheumatic Fever, prevention of repeated attacks	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, every 21 days: <ul style="list-style-type: none"> If < 30kg: 600 000IU. If ≥ 30kg: 1.2MU. 	<ul style="list-style-type: none"> Phenoxymethylpenicillin, oral 250mg 12 hourly. <p>OR if unavailable:</p> <ul style="list-style-type: none"> Amoxicillin, oral, 30-50 mg/kg daily.
Section 6.1.1 Post Streptococcal Glomerulonephritis, eradication of streptococci	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 30000 units/kg/dose, 2 doses given 5 days apart. <ul style="list-style-type: none"> Maximum dose: 1.2MU 	<ul style="list-style-type: none"> Phenoxymethylpenicillin, oral 50mg/kg/24 hours in 4 divided doses (6 hourly) for 10 days. <p>OR if unavailable:</p> <ul style="list-style-type: none"> Amoxicillin, oral, 50 mg/kg, daily for 10 days.
8.8 Diphtheria, close contacts	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM single dose: <ul style="list-style-type: none"> If < 30kg: 600 000IU If ≥ 30kg: 1.2MU 	<ul style="list-style-type: none"> Macrolide* e.g. Azithromycin, oral 10mg/kg/dose for 3 days. <p>Or</p> <ul style="list-style-type: none"> Clarithromycin, oral 7.5mg/kg/dose 12 hourly for 10 days.
13.10 Sydenham's Chorea	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 1.2 MU, every 28 days (until the age of 21 years). 	<ul style="list-style-type: none"> Phenoxymethylpenicillin, oral, 250mg 12 hourly. <p>OR if unavailable:</p>

⁴ For further information regarding S21 access of benzathine benzylpenicillin, contact local district pharmacist/manager.

19.18 Syphilis, Early Congenital, asymptomatic, well baby	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 50000 units/kg as a single dose into the antero-lateral thigh. 	<ul style="list-style-type: none"> Amoxicillin, oral, 50 mg/kg, daily for 10 days. Alternative procurement for benzathine benzylpenicillin is available through S21 approval⁵.
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*Azithromycin or clarithromycin to be used due to medicine availability challenge with erythromycin suspension (refer to Notice: recommended therapeutic alternative for erythromycin suspension).

Indication: Adult Hospital Level	Current recommendation in STGs and EML	Therapeutic alternative to benzathine benzylpenicillin
Section 3.7 Rheumatic Heart Disease, acute rheumatic fever.	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 1.2 MU as a single dose. 	<ul style="list-style-type: none"> Phenoxymethylpenicillin, oral, 500mg 12 hourly for 10 days OR if unavailable: Amoxicillin, oral, 500 mg, daily for 10 days
Section 3.7 Rheumatic Heart Disease, Prevention of recurrent rheumatic fever	<ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 1.2 MU every 3-4 weeks 	<ul style="list-style-type: none"> Phenoxymethylpenicillin, oral 250mg, 12 hourly. OR if unavailable: <ul style="list-style-type: none"> Amoxicillin, oral, 500 mg, daily
6.8 Syphilis	Pregnant women <ul style="list-style-type: none"> Benzathine benzylpenicillin, IM, 2.4 MU weekly for 3 doses 	<ul style="list-style-type: none"> Alternative procurement for benzathine benzylpenicillin is available through S21 approval⁵.

Severe penicillin allergy:

Consider using a macrolide e.g. azithromycin, only where appropriate. Refer to the STGs and EML for recommendations for specific indications and doses.

Accessing Section 21 benzathine benzylpenicillin:

The National Department of Health (NDoH) has facilitated the procurement of an emergency bulk section 21 of benzathine benzylpenicillin. South African Health Products Regulatory Authority (SAHPRA) granted the following section 21 authorisation to NDoH:

Product description	Supplier	Approval date	Quantity
Benzathine Penicillin 1.2MU Injection	Equity Pharmaceuticals	16/09/2019	159 132
Benzathine Penicillin 2.4MU injection	BGM Pharmaceuticals	22/08/2019	241 898

The Provincial authorities are responsible for placing orders with authorised section 21 suppliers. Health care facilities are requested to place orders with provincial authorities in accordance with provincial standard operating procedures.

Comments may be submitted to:

Clinical queries:

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Kind regards


MS K JAMALOODIEN

DIRECTOR: AFFORDABLE MEDICINES

DATE: 23/10/2019

⁵ For further information regarding S21 access of benzathine benzylpenicillin, contact local district pharmacist/manager.