HOW TO USE THESE GUIDELINES

Principles

The National Drug Policy[1] makes provision for an Essential Drugs Programme which is a key component in promoting rational medicines use.

The perspective adopted in the Adult Hospital Level Standard Treatment Guidelines (STGs) is that of a competent medical officer practicing in a public sector hospital. The STGs serve as a standard for practice, but do not replace sound clinical judgment. It is important to remember that the treatments recommended are guidelines only, and are based on the assumption that prescribers can manage patients with the relevant conditions.

This includes rational prescribing in the elderly and palliative care, as the use of some medicines, especially as people get older or more ill, can cause more harm than good. Optimizing medication through targeted de-prescribing is a vital part of managing chronic conditions, avoiding adverse effects and improving outcomes. The goal of de-prescribing is to reduce pill burden, and maintain or improve quality of life.

All reasonable steps were taken to align the STGs with Department of Health guidelines that were available at the time of review. Each treatment guideline in the Adult Hospital Level STGs and Essential Medicines List (EML) was designed as a progression in care from the current Primary Health Care (PHC) STGs and EML. Where referral to a tertiary facility is recommended, the relevant medicines have either been reviewed or included in the tertiary level EML, or are in the process of being reviewed.

Each medicine was included or removed from the EML using an evidence-based review of safety and effectiveness, followed by considerations of cost and other relevant practice factors, such as availability and storage requirements. Some recommendations might not be aligned with the indications or doses included in South African Health Products Regulatory Authority (SAHPRA) approved professional information but are guided by the best available scientific evidence.

The dosing regimens provide the recommended doses used in usual circumstances. However, the prescribed dose should take into consideration drug-drug interactions and co-morbid states, notably renal or hepatic failure, critical illness, and morbid obesity.

Local formularies

A formulary is a continually updated list of medicines and related information on the diagnosis, prophylaxis, or treatment of disease and the promotion of health to satisfy the needs of the majority of the population served by a particular health establishment/s.[2]

[1] National Drugs Policy, 1996. https://www.gov.za/documents/national-drugs-policy
[2] South African National Department of Health. 2022. National Guideline for the Development, Management and Use of Formularies. Pretoria, South Africa.

All EML medicines should be available at the relevant level of care based on the package of services provided at a particular health establishment/s. PTCs should develop formularies aligned to treatment guidelines and protocols subjected to robust evidence-based interrogation and consideration of cost implications.

The EML has been developed to the generic or International Non-Propriety Name (INN) level. Each province, through the provincial PTC, is expected to review the EML and prevailing tenders and compile a formulary which:

» lists formulations and pack sizes that will facilitate care in alignment with the STGs and EML;
» selects the preferred member of a therapeutic class based on cost; and implement formulary restrictions that are consistent with the local environment.

Therapeutic classes are designated in the "Medicine treatment" sections of the STGs, which provide classes of medicines followed by an example of each class, such as 'HMG-CoA reductase inhibitors (statins), e.g., simvastatin'. Therapeutic classes are designated where none of the class members offers any significant benefit over the other registered class members. It is anticipated that by listing a class rather than a specific medicine, there is increased competition and, hence, an improved chance of obtaining the lowest possible price in the tender process. The designation of medicines into therapeutic classes may also assist with remedial actions to mitigate challenges to security of supply, by providing suggested alternatives which have already been approved by the ministerially appointed National Essential Medicines List Committee (NEMLC)[3].

Where therapeutic classes are listed in the STGs, the local formulary should be consulted to identify the specific medicine approved for the facility. A therapeutic interchange database has been developed that lists medicines grouped into a therapeutic class for a specific condition, as outlined in the policy for classifying medicines into therapeutic classes for purposes of therapeutic interchange. The database and policy are available on the National Department of Health website: **https://knowledgehub.health.gov.za/elibrary/primary-healthcare-phc-standard-treatment-guidelines-stgs-and-essential-medicines-list-em** and

https://www.health.gov.za/nhi-hpp-edp/.

Navigating the guidelines

It is important that you become familiar with the contents and layout of these guidelines in order to use the STGs effectively.

The STGs are arranged into chapters according to the organ systems of the body. In some therapeutic areas that are not easily amenable to the development of a STG, the section is limited to a list of medicines.

[3] NEMLC is tasked to formulate and revise the Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) using a peer review consultative process.

Revisions to previous recommendations are accompanied by the level of evidence that is cited and hyperlinked accordingly. All evidence is graded described in detail under Guidelines For The Motivation Of A New Medicine On The National Essential Medicines List. To further promote transparency of medicine selection decisions, NEMLC reports, medicine reviews and costing reports are available on the National

Department of Health website:
https://knowledgehub.health.gov.za/elibrary/primary-healthcare-phc-standard-treatment-guidelines-stgs-and-essential-medicines-list-em and **https://www.health.gov.za/nhi-hpp-edp/**.

The section on Patient Education in Chronic Conditions aims to assist health workers to improve patient adherence and health, generally. Information on the Central Chronic Medicines Dispensing and Distribution (CCMDD) programme is available at: **www.health.gov.za/ccmdd**.

Diagnosis codes from the International Statistical Classification of Diseases and Related Health Problems (ICD-10) are included for each condition to facilitate the accurate recording of diagnoses. The primary ICD-10 code may be accompanied by a secondary code that is bracketed to differentiate a secondary manifestation from the primary aetiology. (For example, uncomplicated broncho-pneumonia with severe penicillin allergy would be coded as: J18.0+(Z88.0)). All the rules and guidelines for using ICD-10 must be applied as per the World Health Organization (WHO), the agreed South African Morbidity Coding Standards and Guidelines document, and the South African Master Industry Table (MIT).

Available at: **https://www.health.gov.za/icd-10-master-industry-table /**.

Medicines safety

Provincial and local PTCs should develop medicines safety systems to obtain information regarding medication errors, prevalence and severity of adverse medicine events, interactions, and medication quality. These systems should support the regulatory pharmacovigilance plan and provide pharmacoepidemiology data to inform future essential medicine decisions and local interventions to improve safety.

In accordance with the SAHPRA's guidance on reporting adverse drug reactions in South Africa, healthcare workers (with the support of PTCs) should report all relevant adverse reactions to the Pharmacovigilance unit at SAHPRA. The Adverse Drug Reaction form and guidance on its use may be found at the following link: **https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/**. Additionally, healthcare professionals can report through the Med Safety App. Search for "Medsafety" on the Apple store or Google play store and install the application on your mobile device. The application can

also be downloaded onto a smart mobile phone directly from the SAHPRA website, **https://medsafety.sahpra.org.za.**

Feedback

Comments that aim to improve these treatment guidelines will be appreciated. The submission form and guidance for completing the form are included with these guidelines under Guidelines For The Motivation Of A New Medicine On The National Essential Medicines List. Motivations will be accepted from Provincial PTCs only.

These guidelines are also reviewed regularly. During the review process, comments are requested during a comment period and should be forwarded directly to the EML Secretariat. Queries may be submitted to the Essential Drugs Programme via electronic mail to **SAEDP@health.gov.za**.

THERAPEUTIC DRUG MONITORING (TDM)

Medicines with narrow therapeutic indices and those with variable pharmacokinetics should be monitored regularly to optimise dosing, obtain maximum therapeutic effect, limit toxicity, and assess adherence. Appendix II provides detailed information for specific medicines.

TDM sampling for all drugs is usually done only once steady state has been reached (i.e. after 4–5 half-lives), unless there is a specific indication to measure concentrations earlier. Seek the assistance of a clinical pharmacologist if unsure when to perform TDM sampling and how to interpret results.

Lithium

Measure serum concentrations at about 12 hours after the last dose – i.e. immediately prior to the next dose. Concentrations should be less than 1 mmol/L and should be monitored a week after each dose increment, then at one month, three months and 6-monthly[4] while on therapy. More frequent monitoring is indicated in the elderly (see Appendix II for guidance on prescribing lithium).

Aminoglycosides

Aminoglycoside TDM is not necessary when the course of extended-interval aminoglycoside dosing is not expected to exceed 3 days in patients with normal renal function. Trough concentrations, taken immediately before the next dose, are critical for identifying potential toxicity. Peak concentrations are taken 30 minutes to 1 hour after starting the infusion and are used to determine if the dose is adequate for efficacy. Toxicity may manifest as deafness or renal

[4] South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

impairment. Aminoglycosides are relatively contraindicated in renal impairment. Bedside hearing assessment and renal function monitoring is indicated in all patients treated with aminoglycosides longer than 3 days (see Appendix II for guidance on prescribing amikacin and gentamicin). Urgent referral for formal audiology testing may be warranted if bedside hearing tests are abnormal.

Anti-epileptics

Measuring concentrations may be helpful to confirm poor adherence or to confirm a clinical suspicion of toxicity. Routine measurement in patients with well-controlled seizures and no clinical evidence of toxicity is not appropriate.

PRESCRIPTION WRITING

Prescribers may initiate and/or maintain treatment with medicines as per the STGs in accordance with their scope of practice.

Medicines should be prescribed only when they are necessary for treatment following clear diagnosis. Not all patients or conditions need prescriptions for medication. In certain conditions simple advice and general and supportive measures may be more suitable.

In all cases carefully consider the expected benefit of a prescribed medication against potential risks. This is especially important during pregnancy where the risk to both mother and fetus must be considered.

All prescriptions must:

- » be written legibly in ink OR typed, and printed OR entered electronically, where such systems exist by the authorised prescriber, and signed with the date on the prescription form (NOTE: only advanced electronic signatures are acceptable, and require access to specific software packages);
- » include the full name, identification number and address of the patient;
- » specify the age and, in the case of children, the weight of the patient;
- » have prescriber details, including contact details, i.e., name, qualification, registration and/or practice number, address and contact telephone number;
- » indicate the diagnosis on the prescription, where the patient has provided consent.

In all prescriptions:

- » State the treatment regimen in full:
  - medicine name (preferably the generic name or INN), strength and formulation,
  - dose,
  - dose frequency,
  - route of administration,
  - duration of treatment,
  - e.g., amoxicillin 250 mg capsules, 8 hourly orally for 5 days.
- » Write the name of the full medicine/preparation using the generic name.
- » Avoid abbreviations to reduce the risk of misinterpretation. Avoid the Greek mu (ų): write mcg as an abbreviation for micrograms.
- » Avoid unnecessary decimal point use. If necessary, write a zero in front of the

decimal point only, e.g., 2 mg, not 2.0 mg, or 0.5 mL, not .5 mL.

- » Avoid Greek and Roman frequency abbreviations that cause considerable confusion (qid, qod, tds, tid, etc). Instead, state the frequency in terms of hours (e.g., '8 hourly') or times per day in numerals (e.g., '3x/d').
- » In the case of "as required", a minimum dose interval should be specified, e.g., 'every 4 hours as required'.
- » Most monthly outpatient prescriptions for chronic medication are for 28 days; check that the patient can access a repeat before the 28 days are completed. Repeats may be issued for Schedule 0 to 5 medicines for up to 6 months.
- » Prescriptions for Schedule 6 medicines are not repeatable and are to be issued monthly; the quantity should be expressed in words.

After writing a prescription, check that each item's dose, dose units, route, frequency, and duration are stated. Consider whether the number of items is too great to be practical for the patient, and check that there are no redundant items or potentially important drug interactions. Check that the prescription is dated and that the patient's name, identification number and diagnosis/diagnostic code are on the prescription form. Only then should you sign the prescription and provide another way for the pharmacy staff to identify the signature if there are problems (print your name, use a stamp, or use a prescriber number from your institution's pharmacy).

SECTION 21 ACCESS TO UNREGISTERED MEDICINES

Section 21 of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) as amended, allows access to unregistered medicines. The enabling provision in the Act reads as follows:

21. Authority may authorize sale of unregistered medicines, medical devices or in vitro diagnostics (IVDs) for certain purposes:
(1) The Authority may in writing authorize any person to sell during a specified period to any specified person or institution a specified quantity of any particular medicine, medical device or IVD which is not registered.

(2) Any medicine, medical device or IVD sold in pursuance of any authority granted under subsection (1) may be used for such purposes and in such manner and during such period as the Authority may in writing determine.

(3) The Authority may at any time by notice in writing withdraw any authority granted in terms of subsection (1) if effect is not given to any determination made in terms of subsection (2).

The Act needs to be read together with the relevant General Medicines Regulation and the guidelines issued by the South African Health Products Regulatory Authority (SAHPRA). General Regulation 29 lists the details that must be included in a Section 21 application and also the obligations placed on the person under whose supervision the unregistered medicine is prescribed. Two guidelines are relevant in this regard:

- SAHPGL-CEM-S21-02 Guideline For Section 21 Access To Unregistered Medicines5 (accessible at **https://www.sahpra.org.za/document/guideline-for-section-21-access-to-unregistered-medicines/**).
- SAHPGL-PEM-01 Availability of medicines for use in a Public Health Emergency6 (PHE) (accessible at **https://www.sahpra.org.za/document/availability-of-medicines-for-use-in-a-public-health-emergency-phe/).**

Application for Section 21 approval has to be made via the online portal, at **https://www.sahpra.org.za/e-services,** then navigate to "Section 21 Applications"

For further information about section 21 procedures, see **https://www.sahpra.org.za/category-a-unregistered-products/**

The SAHPRA guidelines envisage five possible scenarios:

1. Individual named patient - where access to an unregistered medicine is required for an individually named patient when conventional therapies have failed in such cases, the application is made by an individual health care provider responsible for the care of the patient. In addition, a co-applicant is needed, which is the licensed manufacturer/importer/distributor responsible for the supply of the product for which authorisation is requested.

2. Bulk stock held by a health establishment - where an unregistered medicine needs to be available urgently and an individually named patient application is not possible. In such cases, the applicant will be the health care provider who is the intended prescriber of such medicine or a health care provider who is designated as a representative of the health establishment requiring the stock. A co-applicant also needs to be identified.

3. Bulk stock held by the holder of a licence issued in terms of section 22C(1)(b) – where a licensed distributor needs to maintain stock of a particular unregistered medicine at a single point of storage for distribution on an urgent basis to one or more health care providers or health establishments.

4. State Procurement – where an unregistered medicine may need to be procured by the State for distribution on an urgent basis to one or more public sector health establishments, when all other mechanisms of supply have been exhausted and where, without intervention, a significant public health risk may be realised. In such cases, the State may designate a health care provider as a representative in order to apply for authorisation for the supply or sale of an unregistered medicine to, and by health establishments. The co-applicant will also have to be identified.

5. Public health emergency (PHE) – where access is needed to an unregistered medicine in order to respond to an extraordinary event which poses a serious

[5] South African Health Products Regulatory Authority. Guideline For Section 21 Access to Unregistered Medicines. 5 September 2022.

[6] South African Health Products Regulatory Authority. Availability Of Medicines for Use in A Public Health Emergency (PHE). August 2023.

health risk to the public or has caused or has the potential to cause an outbreak, epidemic or pandemic.

Applications in terms of scenario 1 can be made by individual prescribers in the public health sector, with the approval of the responsible Pharmaceutical and Therapeutic Committee. Applications in terms of scenario 2 would ordinarily be done at a provincial or national level. Applications in terms of scenario 4 should preferably be done at a national level, unless the unregistered medicine is only required in a specific province. Applications in terms of scenario 5 would require national decisions to activate the specific guidance.

Although a separate section 21 application is not required, approval of a clinical trial by SAHPRA includes an implicit approval for importation of an unregistered investigational agent. The reporting requirements for clinical trials are also specific to that scenario.

Notes on specific medicines

ACE-inhibitor	Angioedema is a potentially serious complication of ACE- inhibitor treatment and if it occurs it is a contraindication to continued therapy or to re-challenge.
ACE-inhibitors and angiotensin receptor blockers (ARBs)	ACE-inhibitors and ARBs can cause or exacerbate hyperkalaemia in chronic kidney disease (eGFR < 60 mL/minute). Check the serum potassium before starting these medicines, and monitor serum potassium on therapy. ACE-inhibitors and ARBs are contra-indicated in pregnancy. In impaired kidney function: GFR 10–50 mL/min, 50–100% of dose; GFR <10 mL/min, 25% of dose.
Allopurinol	Contra-indicated in patients with eGFR < 30 mL/minute. Do not stop uric acid lowering drugs during an acute attack. In impaired kidney function reduce dose to avoid toxicity. Creatinine clearance 10–20 mL/min, 100–200 mg/day; <10 mL/min, 100 mg/day or at longer intervals.
Amitriptyline + citalopram	Concomitant use of amitriptyline and citalopram may increase the risk of serotonin syndrome or neuroleptic malignant syndrome. Furthermore, there is a potential risk for QT- prolongation.
Anti-epileptic medicines	Phenytoin, phenobarbitone, and carbamazepine are potent enzyme inducing agents and should be used with caution with other medicines metabolised by the liver, especially warfarin, antiretrovirals, progestin subdermal implants, and oral contraceptives.

Antivenom	Never administer antivenom without being fully prepared to manage acute anaphylaxis.
Benzodiazepines	Benzodiazepines can cause respiratory depression. Monitor patients closely as benzodiazepines can exacerbate an abnormal mental state or mask important neurological signs of deterioration. Prolonged treatment with benzodiazepines often leads to tolerance and withdrawal symptoms if the medicine is discontinued abruptly. Combination therapy with more than one benzodiazepine is not indicated.
ß–blockers	ß–blockers should not be used in cocaine poisoning. ß–blockers may cause bronchospasm in asthmatics.
Calcineurin inhibitors	Both tacrolimus and ciclosporin may cause hyperglycaemia, hypertension, hyperlipidaemia, neurotoxicity, and nephrotoxicity. Ciclosporin may also cause hirsutism and gingival hyperplasia. Both tacrolimus and ciclosporin are prone to multiple drug-drug interactions and concomitant medications should be reviewed. Renal function, liver function, serum electrolytes, blood glucose, total cholesterol, and blood pressure should be monitored regularly on treatment. Therapeutic drug monitoring of trough concentrations of ciclosporin and tacrolimus should be used to guide dose adjustment, maintain therapeutic efficacy, and avoid toxicity.
Clindamycin	Clindamycin has good coverage against Gram positive organisms and anaerobes, so the addition of metronidazole is unnecessary.
Diuretics	Hydrochlorothiazide is contraindicated when anuric or GFR < 10 mL/minute.[7,8]
Folic acid + vitamin B12	Anaemia megaloblastic: Give vitamin B12 and folic acid together until the test results are available as giving folic acid alone in patients with a B12 deficiency may precipitate a permanent neurological deficit.
Haloperidol	Dosing may vary according to clinical circumstances, e.g. lower doses in the elderly or where HIV infection or HIV-related dementia is known or suspected. In frail and elderly patients, reduce the dose by half.

[7] Sinha AD, Agarwal R. Clinical pharmacology of antihypertensive therapy for the treatment of hypertension in CKD. Clin J Am Soc Nephrol. 2019;14(5):757-764. doi:10.2215/CJN.04330418 [PubMed 30425103]
[8] Aronoff GR. Drug Prescribing in Renal Failure: Dosing Guidelines for Adults. 4th ed. Philadelphia, Pa.: American College of Physicians, 1999

Lithium	Therapeutic drug monitoring is essential when using lithium. Clinical toxicity may occur even within the therapeutic range. Concomitant use of many medicines e.g. ACE-inhibitors, ARBs, NSAIDs and diuretics may increase the risk of lithium toxicity.
Loperamide	Contraindicated in dysentery, acute inflammatory diarrhoea, antibiotic-associated diarrhoea and amoebic dysentery; as it may result in toxic megacolon
Low molecular weight heparin (LMWH)	In morbid obesity dosing of LMWH should be individualised, in discussion with a specialist. In renal failure (eGFR < 30 mL/minute), the recommended dose of LMWH is 1 mg/kg/day. Pregnant women with mechanical prosthetic valves should not receive LMWH unless antifactor Xa levels can be monitored reliably weekly. Therapeutic range is pre-dosing level of 0.6 units/mL and a 4-hour peak level of 1–1.2 units/mL.
Metformin	Metformin should be dose-adjusted if eGFR: 30-60 mL/minute and should not be used if eGFR: < 30mL/minute).
Metronidazole	Adding metronidazole to amoxicillin/clavulanic acid is unnecessary as amoxicillin/clavulanic acid has adequate anaerobic cover.
Misoprostol (for Termination Of Pregnancy)	Misoprostol can cause uterine rupture in women with previous caesarean sections and those of high parity. In these women use 200 mcg of misoprostol or alternative methods such as extra-amniotic saline infusion without misoprostol. The dose of misoprostol, PV, decreases with increasing gestational age because of the risk of uterine rupture.
Non-steroidal anti-inflammatory drugs (NSAIDs)	Concomitant use of more than one NSAID has no additional clinical benefit and only increases toxicity. Chronic use of all NSAIDs is associated with varying degrees of gastrointestinal, renal, and cardiovascular risks. Long-term use of NSAIDs should weigh potential benefits against these risks.
Oral antidiabetic agents	Oral antidiabetic agents (sulfonylureas) should not be used in type 1 diabetes and used with caution in liver and renal impairment.
Insulin in the treatment of diabetic ketoacidosis (DKA)	Potassium will fall on insulin treatment and patients with DKA have potassium depletion even if initial potassium is normal or high. It is therefore essential to monitor and replace potassium.
Fluoroquinolones	Irrational use of fluoroquinolones contributes to the emergence of XDR-TB and potential masking of active TB.
Sodium chloride	Rapid correction of sodium, in hyponatraemia, may lead to central pontine myelinolysis, which is often irreversible. Sodium should be frequently monitored and increases should be <9 mmol/L per day.

Spironolactone	Monitoring of sodium, potassium and renal function is essential in patients taking spironolactone. Avoid if eGFR < 30 mL/minute.
Selective serotonin reuptake inhibitors (SSRIs)	Adolescents with depression may have an increased risk of suicidal ideation when initiated on SSRIs.
Streptokinase	Do not use heparin if streptokinase is given.
Sulphonylureas	Hypoglycaemia caused by a sulphonylurea can be prolonged. The patient should be hospitalised with an intravenous glucose infusion, and observed for at least 12 hours after glucose infusion has stopped.
Tricyclic antidepressants	Avoid in patients with cardiac disease and a high risk of overdose.
Testosterone	Screen hypogonadal men for prostate cancer before beginning testosterone replacement.
Unfractionated heparin	Evidence indicates that PTT monitoring is not necessary with weight-based dosing of unfractionated heparin. However, in patients with morbid obesity and renal failure (eGFR < 30 mL/minute) unfractionated heparin should be used with PTT monitoring to maintain the PTT at 1.5 to 2.5 times the control. Blood for measurement of PTT should be taken 4 hours after SC dose.
Verapamil	Never give verapamil or adenosine IV to patients with a wide QRS tachycardia as this may precipitate ventricular fibrillation. In atrial flutter, do not use verapamil as it will not convert flutter to sinus rhythm and may cause serious hypotension.
Warfarin	Warfarin use requires regular INR monitoring and dose adjustment according to measured INR. See appendix II.

PENICILLIN DESENSITISATION

This has been included for information only.

Perform only in an ICU setting or in a setting where recognition and management of anaphylaxis can be assured.

Discontinue all ß-adrenergic antagonists. Have an IV line, ECG monitor and spirometer in place. Once desensitised, treatment must not lapse as risk of subsequent allergy increases.

A history of Stevens-Johnson's syndrome, exfoliative dermatitis, erythroderma are absolute contra-indications to desensitisation (use only as an approach to IgE sensitivity).

Oral route is preferred. 1/3 of patients develop a transient reaction during desensitisation or treatment, which is usually mild.

Oral penicillin desensitisation protocol

A: Prepare stock solution of oral phenoxymethylpenicillin 250mg/ 5mL and dilutions for steps 1-7 and 8-10

B: Administer increasing doses of penicillin strictly at 15 minutes intervals

Step	Medicine mg/mL	Amount to administer (mL)
To make 0.5 mg/mL solution: Add 0.5 mL of stock phenoxymethylpenicillin solution to 49.5 mL water (total volume 50mL)		
1	0.5 mg/mL solution (1000 units/mL)	0.1 mL orally
2		0.2 mL orally
3		0.4 mL orally
4		0.8 mL orally
5		1.6 mL orally
6		3.2 mL orally
7		6.4 mL orally
To make 5 mg/mL solution: Dilute 1 mL of stock phenoxymethylpenicillin solution with 9 mL water (total volume 10mL)		
8	5 mg/mL solution (10000 units/mL)	1.2 mL orally
9		2.4 mL orally
10		4.8 mL orally
Stock phenoxymethylpenicillin 250 mg/5 mL = 50 mg/mL		
11	50 mg/mL (80000 units/mL)	1.0 mL orally
12		2.0 mL orally
13		4.0 mL orally
14		8.0 mL orally

After step 14, observe for 30 minutes, then administer desired dose of intravenous penicillin.

Intravenous penicillin desensitisation protocol

A. Prepare stock solution for intravenous administration of benzathine penicillin G of 100mg/ml and dilutions for steps 1-5, 6-8, and 9-12. Label dilutions carefully.

Use 600mg vial =1MU

a. reconstitute dry powder with 6mls water for injection to make stock of 100mg/ml (steps 13-16)
b. Take 1ml of 100mg/ml stock and reconstitute with 9ml to make a 10mg/ml solution (steps 9-12)
c. Take 1ml of 10mg/ml benzathine penicillin G and reconstitute with 9mLs water to make a 1mg/ml solution (steps 6-8)
d. Take 1ml of 1mg/ml benzathine penicillin G and reconstitute with 9mLs water to make a 0.1mg/ml solution (steps 1-5)

B. Administer increasing doses of penicillin **strictly at 15 minutes intervals**

Step	Medicine (mg/ml)	Volume to administer (ml)	Route Cumulative dose (mg)
Use 0.1 mg/mL solution			
1	0.1	0.1	0.01
2	0.1	0.2	0.03
3	0.1	0.4	0.07
4	0.1	0.8	0.15
5	0.1	1.6	0.31
Use 1mg/ml solution			
6	1	0.32	0.63
7	1	0.64	1.27

8	1	1.2	2.47
Use 10mg/ml solution			
9	10	0.24	4.87
10	10	0.48	10
11	10	1	20
12	10	2	40
Use 100mg/ml stock solution			
13	100	0.4	80
14	100	0.8	160
15	100	1.6	320
16	100	3.2	640
Cumulative dose of 640mg (1MU) given on completion of step 16. Observe the patient for 30 minutes and then administer the full therapeutic dose intravenously.			

COTRIMOXAZOLE DESENSITISATION

Attempt desensitisation in patients with a history of cotrimoxazole intolerance, unless this was life-threatening, e.g.: Stevens-Johnson syndrome. (See section 4 . 6 : Erythema Multiforme, Stevens Johnson Syndrome, Toxic Epidermal Necrolysis).). If a rash occurs during cotrimoxazole treatment, assess severity and discontinue treatment if the rash is severe or associated with systemic symptoms. For mild rashes, treatment may be continued with careful observation for deterioration. Desensitisation should be attempted using cotrimoxazole suspension 240 mg/5mL. Dilute the suspension appropriately and consult with your pharmacist if necessary.

Note: Do not administer antihistamines or steroids with this regimen.

The following protocol describes a simple approach for cotrimoxazole desensitization.

Use cotrimoxazole suspension 240mg/5ml.

Desensitisation must be conducted in hospital and should be done WITHOUT antihistamine or steroid cover.

Take 1ml co-trimoxazole suspension (240mg/5ml) and dilute to 1litre with water and shake very well (mixture A)

Now take 1ml of mixture A and dilute with water to 10ml. (mixture B).

Time	Dose	Dose in mls of undiluted cotrimoxazole suspension
Time 0	Administer 5ml of mixture B. **(Discard balance of mixture B)**	0.0005
Time 1hr	Administer 5ml of mixture A (after shaking well)	0.005
Time 2hr	Administer 50ml of mixture A (after shaking well) **(Discard balance of mixture A)**	0.05
Time 3hr	Administer 0,5ml of co-trimoxazole suspension diluted to 5ml with water	0.5
Time 4hr	Administer 5ml of cotrimoxazole suspension	5.0
Time 5hr	Administer 2 single strength (80/400mg) cotrimoxazole tablets	
Time 6hr	Start full-dose cotrimoxazole	

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