health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Private Bag X828, PRETORIA, 0001 Dr AB Xuma Building1112 Voortrekker Road, Pretoria Townlands 351-JR, PRETORIA, 0187 Tel (012) 395 8000, Fax (012) 395 8918

Mr E van Zyl
Equity Pharmaceuticals (Pty) Ltd
100 Sovereign Road
Route 21 Corporate Park
Nellmapius Drive
Irene
Pretoria

Dear Mr van Zyl

Section 21 Authorization for BENZYL PENICILLIN 1MU INJECTION

Attached, please find the Authorization for exemption under Section 21 of the Medicines and Related Substances Act by SAHPRA granted for:

- **Benzyl Penicillin 1MU Injection**

The quantities for which approval was granted are only estimates based on procurement by provinces over the last 6 months. Please note that the National Department of Health (NDOH) cannot guarantee the procurement of these quantities, as NDOH has no control over orders being placed by provincial depots, and current stock holding might influence estimated quantities.

The following process will be followed to ensure the quality of the product being brought in:

1. Manufacturer will submit an assay and identification of every batch imported.
2. An additional assay of every batch will be done by a quality control laboratory.
3. A random sample will be assayed during the authorized period by a quality control laboratory.
4. Aggregate statistics to be submitted to NDOH in the first week of each month of all orders received and quantities supplied per province.
5. The NDOH needs to be advised of the quantities and date of arrival of stocks in terms of this authorization within 7 days after arrival.
6. The supplier will provide monthly reports, by the 7th of each month, using the attached format of orders received and issues done.
7. Participating Authorities (PAs) will provide a consolidated close out report of usage using the attached format on the date when an authorization lapses.
8. The full quantities imported in terms of this Section 21authorisation must be accounted for.
9. Note that this authorization DOES NOT cover supplies to the private sector.

10. Where this authorization is obtained to provide security of supply due to supply challenges from the contracted supplier, PAs are requested to buy out against contracted suppliers and ensure that related orders are cancelled accordingly to prevent over stocking once the contracted supplier gets back into stock.

It should be noted this authorization applies only for use of the product in the public sector with estimated usage quantities for a period of one month. The authorization is expected to expire on **17 March 2024**.

Table 1: Provincial estimates

Provinces	Six Month's Estimated Quantity
Correctional Services	0
EC-MT	15600
EC-PE	14000
FS	2100
GP	0
KZN	8000
LP	0
MP	17644
NC	1500
NW	3900
SAMHS	0
WC	3000
Total	**65744**

Yours sincerely

KHADIJA JAMALOODIEN
CHIEF DIRECTOR: SECTOR WIDE PROCUREMENT
DATE: 19/9/2023

SAHPRA
SOUTH AFRICAN
HEALTH PRODUCTS
REGULATORY AUTHORITY

Section 21 Response Letter

9/15/2023 1:53 PM

Khadija Jamaloodien

National Department of Health
Dr AB Xuma Building
1112 Voortrekker Rd
Pretoria Townlands 351-JR
Pretoria
0187

Buhle.Mbongo@health.gov.za

Dear Khadija Jamaloodien,

REQUEST TO USE UNREGISTERED MEDICINE IN TERMS OF SECTION 21 OF THE MEDICINES AND RELATED SUBSTANCES ACT, 1965 (ACT 101 OF 1965):

Your application dated **9/15/2023 11:40 AM** refers

A. ***STATUS: Approved***
B. ***APPLICANT: Khadija Jamaloodien***
C. ***IMPORTING COMPANY: Equity Pharmaceuticals (Pty) Ltd***
D. ***PATIENT/(S):***
E. ***UNREGISTERED MEDICINES:***

GENERIC NAME: Benzyl Penicillin 1MU INJ

TRADE NAME: Benzyl Penicillin for injection BP 1MU

F. ***QUANTITY: Benzyl Penicillin 1MU Injection x 66000 vials***

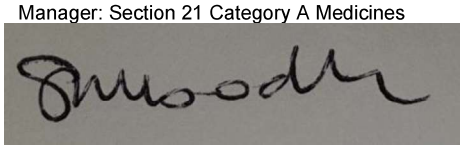
G. ***LETTER NUMBER: B-20783***

Section 21 authorization letters are valid for a period of six months from the letter date, unless otherwise specified.

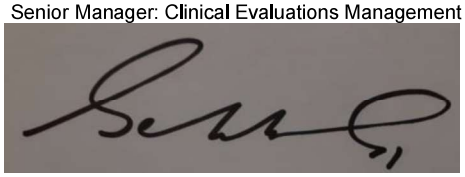
Comments:

Yours faithfully,

Dr S Munbodh
Manager: Section 21 Category A Medicines



T Sehloho
Senior Manager: Clinical Evaluations Management



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REQUEST FOR QUOTATION FORM

- **Instruction to complete this Request for Quotation (RFQ)**
  PLEASE PROVIDE A QUOTE FOR THE FOLLOWING PRODUCT(S).
  PLEASE QUOTE ON THIS RFQ FORM AND ATTACH YOUR QUOTE WITH THE REQUESTED DETAILS.
  THE SECTIONS HIGHLIGHTED IN YELLOW MUST BE COMPLETED BY THE SUPPLIER.
- **THIS DOES NOT CONSTITUTE ANY OBLIGATION TO PROCURE THE ITEM AS THIS WILL BE SUBMITTED FOR CONSIDERATION TO PROVINCIAL PROCUREMENT UNITS TO SERVE AS A BUY OUT AGAINST CURRENT NON-COMPLIANT SUPPLIERS.**

ONLY RESPONSES FROM DULY REGISTERED SUPPLIERS WILL BE EVALUATED

REFERENCE NUMBER:	NORMAL		SECTION 21	X	**S21RFQ129**
QUOTE ENQUIRY DATE	**10/08/2023**	QUOTE CLOSING DATE			**21/08/2023**
FOR CRITICAL DELIVERY, DELIVERY REQUESTED ON/BEFORE *(SCM Practitioner to Specify if applicable)*					

REQUESTING INSTITUTION CONTACT DETAILS

NAME OF REQUESTOR	Buhle Mbongo		
EMAIL ADDRESS	Buhle.Mbongo@health.gov.za		
PHONE No.	**012 395 9539**	FAX No.	**N/A**

PRODUCT INFORMATION

DESCRIPTION PER MPC	**BENZYL PENICILLIN 1MU INJECTION**		
TRADE DESCRIPTION	Benzylpenicillin for Injection BP 1MU		
UNIT OF MEASURE	**1's**	PACK or BOX *(SIZE/ QUANTITY)*	**1's**
QUANTITY REQUIRED	**66 000 VIALS/AMPOULES**		

TO BE COMPLETED BY THE SUPPLIER/ SERVICE PROVIDER

SUPPLIER CONTACT DETAILS (as per CSD)

COMPANY NAME	Equity Pharmaceuticals (Pty) Ltd			
SUPPLIER NUMBER	MAAA007480			
SECURITY CODE				
SUPPLIER CODE (NDoH)				
CONTACT PERSON 1	NAME	**Ehrard van Zyl**		
	PHONE	**012 345 1747**	FAX	**012 345 1412**
	MOBILE	*072 040 8511*		
	E-MAIL	**ehrard@equitypharma.co.za**		
CONTACT PERSON 2	NAME	**Jaco Schoeman**		
	PHONE	**012 345 1747**		

	MOBILE	*076 734 0080*
	E-MAIL	**jacos@equitypharma.co.za**

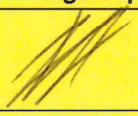
QUOTE DETAILS			
PRICE PER UNIT (INCL. VAT)	R 4.83	TOTAL PRICE (INCL. DELIVERY & VAT)	R 318 780.00
VOLUMES AVAILABLE – 14DAYS			
VOLUMES AVAILABLE – 28DAYS			
VOLUMES AVAILABLE – 56DAYS	66 000		
VOLUMES AVAILABLE – 112DAYS			
QUOTE VALIDITY PERIOD	180 days		
NORMAL LEAD/DELIVERY TIME	3 day		

DEVIATION TO SPECIFICATION

COMMENTS:

DECLARATION BY SUPPLIER

I hereby declare that in submitting this bid, there has been no consultation, communication, agreement or arrangement with any competitor/supplier regarding the price, quality, quantity, specifications and conditions or delivery particulars of the products or services to which this bid invitation relates.

NAME	**Ehrard van Zyl**
CAPACITY	**Business Unit Manager: Specialist Medicine**
SIGNATURE *(OF A DULY AUTHORISED REPRESENTATIVE OF THE SUPPLIER)*	
DATE	**21/08/2023**

Please submit quotations to **Section21Quotes@health.gov.za**

Please ensure that you include the following as part of the Quotation:

- Delivery Time (Weeks)
- Price (Vat Inclusive)
- Generic Name
- Trade Name
- Central Supplier Database Summary Report (CSD)
- Medicine Registration Certificate (Only for Locally Registered Products)
- *Artwork/Labelling
- *Package Insert: (Please attach)
- *Manufacturer Certificate: (Please attach)
- *Country of Origin: (Please indicate)

*Additional items required when submitting a quote for a Section 21 Item (Unregistered Medicine)

All of the above is required to expedite the process in considering the quotation.

Please ***SUBMIT COMPLETED RFQ FORM AND QUOTATIONS ON AN OFFICIAL COMPANY LETTERHEAD***

NB:

- The size of each individual attachment must not be more than 2MB (you may attach multiple files in one email but collectively they should not be more than 2MB in size).
- Please ensure that you provide all prescribed documentation that is outlined on page two of this RFQ.
- Kindly be advised that a picture format of an Artwork shall not be accepted. Artwork must be in pdf or word format only.
- All prices must please be submitted in two decimals.
- If submitting more than one quotation, please make sure that your subject line includes e.g., 1 of 2 or 1 of 3 etc.
- Any submission with missing documentation shall not be considered.
- Any submission with blurry relevant documents shall not be considered.
- Email subject line for responses with quotes must be kept unchanged from the originally sent RFQ email.

Please ***SUBMIT COMPLETED RFQ FORM AND QUOTATIONS ON AN OFFICIAL COMPANY LETTERHEAD***

21/08/2023

Equity Pharmaceuticals (Pty) Ltd.
1997/009942/07

+27 12 345 1747
+27 12 345 1412
equity@equitypharma.co.za

www.clinigengroup.com
www.equitypharma.co.za

QUOTATION # 20230821

TO: National Department of Health

TEL: 012 395 9539
FAX:
Email: Section21Quotes@health.gov.za

CONTACT PERSON: Buhle Mbongo

NB IMPORTED AND SUPPLIED UNDER SECTION 21 TERMS

PRODUCT CODE	DESCRIPTION	PACK SIZE	QUANTITY	PRICE EXCL	TOTAL INCL
	Benzylpenicillin for Injection BP 1MU	1's	1	R 4.20	R 4.83
			66 000	**R 277 200.00**	**R 318 780.00**
			66 000	**R 277 200.00**	**R 318 780.00**

Valid for 180 days

Employee Signature: _____

Date: 21/08/2023

Approved by: Ehrard van Zyl / Carel Bouwer

EQUITY
PHARMACEUTICALS

21/08/2023

Equity Pharmaceuticals (Pty) Ltd.
1997/009942/07

+27 12 345 1747
+27 12 345 1412
equity@equitypharma.co.za

www.clinigengroup.com
www.equitypharma.co.za

National Department of Health

Directorate: Affordable Medicines

E-mail: Buhle.Mbongo@health.gov.za

Attention: Ms Buhle Mbongo

Dear Ms Mbongo

Re: Request for quotation – Benzyl Penicillin 1MU – Section 21 Supply

Trust you are well. Please find below our quotation for *Benzylpenicillin for Injection BP 1MU* supplied under section 21 terms.

- Quantity: **66 000 vials**
- Delivery Time (Weeks): **8 Weeks after approval**
- Price (Vat Inclusive): **R 4.83 per vial**
- Generic Name: **Benzyl Penicillin for Injection BP 1MU**
- Trade Name: **Benzylpenicillin for Injection BP 1MU**
- Packaging: **1 vial**
- Specifications: **1 Million Units**
- Shelf Life: **24 months**
- Package Insert: **Attached**
- Manufacturer: **Karnataka Antibiotics & Pharmaceuticals Ltd.**
- Country of Origin: **India**

Please note that the immediate availability of the product is conditioned on the manufacturer receiving notice of our order as soon as possible. Unfortunately, the stock cannot be reserved for our purposes for too long.

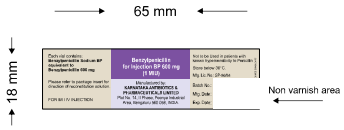
We look forward to your response.

Please contact me if you require any additional information.

Kind Regards

Ehrard van Zyl

Benzylpenicillin for Injection BP 600 mg 1.0 MIU - South Africa
Vial Sticker label
65 (L) x 18 (H) mm
4 colour (Cyan, Mazenta, Yellow, Black)
Ref. specification No.FD/VL/3LP0913/001/0422

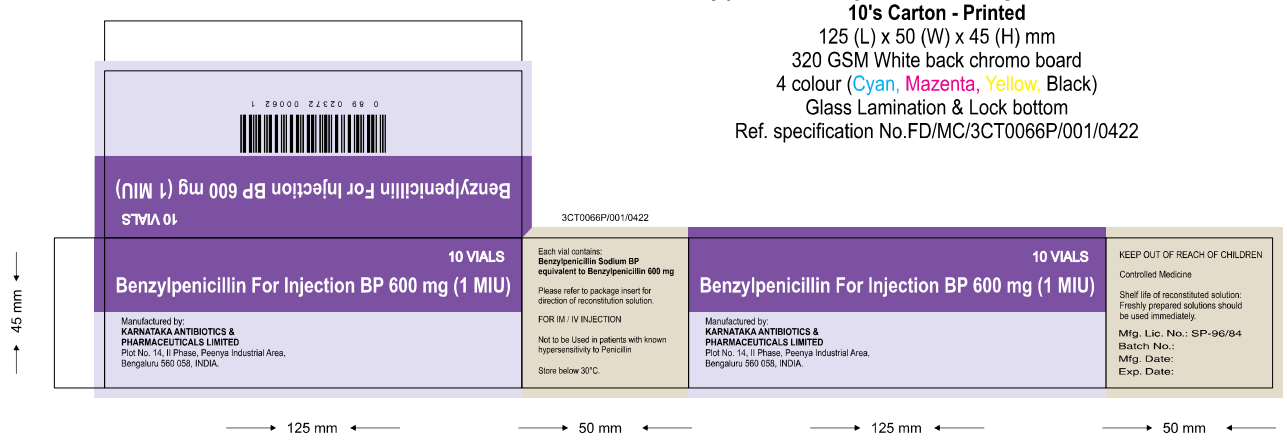


300 % Enlarged size

Each vial contains: **Benzylpenicillin Sodium BP equivalent to Benzylpenicillin 600 mg** Please refer to package insert for direction of reconstitution solution. FOR IM / IV INJECTION	**Benzylpenicillin for Injection BP 600 mg (1 MIU)** Manufactured by: **KARNATAKA ANTIBIOTICS & PHARMACEUTICALS LIMITED** Plot No. 14, II Phase, Peenya Industrial Area, Bengaluru 560 058, INDIA.	Not to be Used in patients with known hypersensitivity to Penicillin Store below 30°C. Mfg. Lic. No.: SP-96/84 Batch No.: Mfg. Date: Exp. Date: 3LP0913/001/0422

Prepared by	Checked by	Reviewed by		Approved by
AM (RNG)	E / IC - Production	E / IC - FD	DGM (RPS)	AGM (NCM)

Benzylpenicillin for Injection BP 600 mg 1.0 MIU - South Africa
10's Carton - Printed
125 (L) x 50 (W) x 45 (H) mm
320 GSM White back chromo board
4 colour (Cyan, Mazenta, Yellow, Black)
Glass Lamination & Lock bottom
Ref. specification No.FD/MC/3CT0066P/001/0422



Prepared by	Checked by	Reviewed by		Approved by
AM (RNG)	E / IC - Production	E / IC - FD	DGM (RPS)	AGM (NCM)

Benzylpenicillin for Injection BP 1.0 MU & 5.0 MU - KAPL Export Pack Insert
Open Length 340 (L) x 240(H) mm
57 GSM White Print Paper, Colour Black

Immune System Disorders
Very Common >10%)
Patients undergoing treatment for syphilis or neurosyphilis with Benzylpenicillin may develop a Jarisch-Herxheimer reaction.

Common (1-10%)
Hypersensitivity to penicillin in the form of rashes (all types), fever, and serum sickness may occur (1-10% treated patients). These may be treated with antihistamine drugs.

Rare (0.01%-0.1%)
More rarely, anaphylactic reactions have been reported (<0.05% treated patients).

Nervous System Disorders
Rare (0.01%-0.1%)
Central nervous system toxicity, including convulsions, has been reported with massive doses over 60 g per day and in patients with severe renal impairment.

Renal and Urinary Disorders
Rare (0.01%-0.1%)
Interstitial nephritis has been reported after intravenous Benzylpenicillin sodium BP at doses of more than 12 g per day.

Symptoms and Treatment ofOverdose
Symptoms of overdosage includes convulsion and neurological adverse reactions. In case of overdosage, discontinue medication, treat symptomatically and institute supportive measures as required. In patients with renal function impairment, ampicillin-class antibiotics can be removed by haemodialysis but not by peritoneal dialysis.

Presentation
One folded paper box contains 10 vials or 50 vials.

Storage Condition
Store below 30°C.

Shelf Life
Unopened vials: 36 months from the date of manufacture if kept as recommended.
Reconstituted solution: Freshly prepared solutions should be used immediately.

Manufactured by:
KARNATAKA ANTIBIOTICS & PHARMACEUTICALS LIMITED
Plot No. 14, II Phase, Peenya Industrial Area,
Bengaluru, 560 058, INDIA.
Tel: 091 (080) 23372123
Fax: 091 (080) 23371350

Date of revision of package insert
April 2022

Benzylpenicillin for Injection BP

Product Name
BENZYLPENICILLIN FOR INJECTION BP 1.0 MU
BENZYLPENICILLIN FOR INJECTION BP 5.0 MU

Product Description
A white crystalline powder in glass vials. Pale yellow solution after reconstitution.

Composition
BENZYLPENICILLIN FOR INJECTION BP *1MU*
Each vial contains Benzylpenicillin Sodium BP 600 mg.

BENZYLPENICILLIN FOR INJECTION BP *5MU*
Each vial contains Benzylpenicillin Sodium BP 3 g.

Pharmacodynamics
General Properties:
Benzylpenicillin sodium BP is a beta-lactam antibiotic. It is bacteriocidal by inhibiting bacterial cell wall biosynthesis.

Breakpoints:
The tentative breakpoints (British Society for Antimicrobial Chemotherapy, BSAC) for Benzylpenicillin sodium BP are as follows:

Organism	Susceptibility ≤ (mg/L)	Intermediate susceptibility (mg/L)	Resistant ≥ (mg/L)
Streptococcus pneumoniae Neisseria gonorrhoeae	0.06	0.12 – 1.0	2.0
Neisseria meningitides	0.06		0.12
Haemolytic streptococci Staphylococci Moraxella catarrhalis Haemophilus influenza	0.12		0.25
Rapidly growing anaerobes	1.0		2.0

Susceptibility:
The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. The following table gives only approximate guidance on probabilities whether microorganisms will be susceptible to Benzylpenicillin sodium BP or not.

Susceptible and intermediately susceptible microorganisms		
Type of Microorganism	**Microorganism**	**Range of acquired resistance**
Aerobic Gram-positive microorganism	Bacillus anthracis	0%**
	Corynebacteriumdiphtheriae	0%*
	Haemolytic streptococci (including Streptococcus pyrogenes)	0%* - 3%**
	Listeria monocytogenes	0%**
	Streptococcus pneumoniae	4%* - 40%**
	Streptococcus viridans	3 – 32%*
Aerobic Gram-negative microorganisms	Neisseria gonorrhoeae	9 – 10%*
	Neisseria meningitidis	18%*
	Pasteurellamultocida	0%***
Anaerobic microorganisms	Actinomyces israelii	8%**
	Fusobacterium nucleatum and Fusobacteriumnecrophorum	Usually sensitive
	Gram-positive sporing bacilli (including Clostridium tetani and Clostridium perfringens [welchii])	14%**
	Gram-positive cocci (including peptostreptococcus)	7%*
Other microorganism	Borrelia bigdorferi	Usually sensitive
	Capnocytophaga canimorosus	Usually sensitive
	Leptospirae	Usually sensitive
	Streptobacillusmoniliformis and Spirrillum minus	Usually sensitive
	Treponemapallidum	0%**

* UK data; ** European data, ***Global data

Insusceptible microorganisms		
Type of Microorganism	**Microorganism**	**Range of acquired resistance**
Aerobic Gram-positive microorganism	Coagulase negative Staphylococcus	71 – 81%*
	Enterococcus Spp	Resistant
	Staphylococcus aureus	79 – 87%*
Aerobic Gram-negative microorganisms	Acinctobacter	Resistant
	Bordetella pertussis	Generally resistant
	Brucella spp.	Resistant
	Enterobacteriaceae (including Escherichia coli, Salmonella, Shigella, Enterobacter, Klebsiella, Proteus, Citrobacter)	Generally resistant
	Haemophilus influenza	Resistant
	Pseudomonas	Resistant
Anaerobic microorganisms	Bacteroides fragilis	100%***

* UK data; ** European data, ***Global data

Other Information:
Known Resistance Mechanisms and Cross-resistance
Penicillin resistance can be mediated by alteration of penicillin binding proteins or development of beta-lactamases.

Resistance to penicillin may be associated with cross-resistance to a variety of other beta lactam antibiotics either due to a shared target site that is altered, or due to a beta-lactamase with a broad range of substrate molecules. In addition to this, cross resistance to unrelated antibiotics can develop due to more than one resistance gene being present on a mobile section of DNA (e.g. plasmid, transposon etc) resulting in two or more resistance mechanisms being transferred to a new organism at the same time.

Pharmacokinetics
Benzylpenicillin sodium BP rapidly appears in the blood following intramuscular injection of water-soluble salts and maximum concentrations are usually reached in 15-30 minutes. Peak plasma concentrations of about 12 mcg/ml have been reported after doses of 600 mg with therapeutic plasma concentrations for most susceptible organisms detectable for about 5 hours. Approximately 60% of the dose injected is reversibly bound to plasma protein.

In adults with normal renal function the plasma half-life is about 30 minutes. Most of the dose (60-90%) undergoes renal elimination, 10% by glomerular filtration and 90% by tubular secretion. Tubular secretion is inhibited by probenecid, which is sometimes given to increase plasma penicillin concentrations. Biliary elimination of Benzylpenicillin sodium BP accounts for only a minor fraction of the dose.

Indication
Benzylpenicillin is indicated for most wound infections, pyogenic infections of the skin, soft tissue infections and infections of the respiratory tract.
It is also indicated for the following infections caused by penicillin-sensitive microorganisms:
Generalised infections and septicaemia from susceptible bacteria.
Acute and chronic osteomyelitis, sub-acute bacterial endocarditis and meningitis caused by susceptible organisms.
Tetanus, actinomycosis, anthrax, rat-bite fever, listeriosis and severe Lyme disease.
Complications secondary to gonorrhoea and syphilis (e.g. gonococcal arthritis or endocarditis, congenital syphilis and neurosyphilis).
Diphtheria, brain abscesses and pasteurellosis.

Consideration should be given to official local guidance (e.g. national recommendations) on the appropriate use of antibacterial agents.

Susceptibility of the causative organism to the treatment should be tested (if possible), although therapy may be initiated before the results are available.

Recommended Dosage
Route of administration:
The following dosages apply to both intramuscular and intravenous injection.
Alternate sites should be used for repeated injections.

Preparation of solution:
Reconstituted solutions of Benzylpenicillin sodium BP are intended for immediate administration.

600mg vial
Dissolve the contents in 2ml or more of Sterilised Water for Injections immediately before use.

3g vial
Dissolve the contents in 10ml or more of Sterilised Water for Injections immediately before use.

Dosage and administration:
Adults
600 to 3,600 mg (1 to 6 mega units) daily, divided into 4 to 6 doses, depending on the indication. Higher doses (up to 14.4 g/day (24 mega units) in divided doses) may be given in serious infections such as adult meningitis by the intravenous route.

In bacterial endocarditis, 7.2 to 12 g (12 to 20 mega units) or more may be given daily in divided doses by the intravenous route, often by infusion.

High doses should be administered by intravenous injection or infusion, with intravenous doses in excess of 1.2g (2 mega units) being given slowly, taking at least one minute for each 300 mg (0.5 mega unit) to avoid high levels causing irritation of the central nervous system and/or electrolyte imbalance.

High dosage of Benzylpenicillin sodium BP may result in hypernatraemia and hypokalaemia unless the sodium content is taken into account.

Children aged 1 month to 12 years
100 mg/kg/day in 4 divided doses; not exceeding 4 g/day.

Infants 1-4 weeks
75 mg/kg/day in 3 divided doses.

Newborn Infants
50 mg/kg/day in 2 divided doses.

Meningococcal disease
Children 1 month to 12 years: 180-300 mg/kg/day in 4-6 divided doses, not exceeding 12 g/day.
Infants 1-4 weeks: 150 mg/kg/day in 3 divided doses.
Newborn infants: 100 mg/kg/day in 2 divided doses.
Adults and children over 12 years: 2.4 g every 4 hours

Premature babies and neonates
Dosing should not be more frequent than every 8 or 12 hours in this age group, since renal clearance is reduced at this age and the mean half-life of Benzylpenicillin may be as long as 3 hours.
Since infants have been found to develop severe local reactions to intramuscular injections, intravenous treatment should preferably be used.

Patients with renal insufficiency
For doses of 0.6-1.2 g (1-2 mega units) the dosing interval should be no more frequent than every 8-10 hours.
For high doses e.g. 14.4 g (24 mega units) required for the treatment of serious infections such as meningitis, the dosage and dose interval of Benzylpenicillin sodium BP should be adjusted in accordance with the following schedule:

Creatinine clearance (mL per minute)	Dose (g)	Dose (mega units)	Dosing interval (hours)
125	1.2 or 1.8	2 or 3	2 3
60	1.2	2	4
40	0.9	1.5	4
20	0.6	1.0	4
10	0.6	1.0	6
Nil	0.3 or 0.6	0.5 or 1.0	6 8

The dose in the above table should be further reduced to 300 mg (0.5 mega units) 8 hourly if advanced liver disease is associated with severe renal failure.
If haemodialysis is required, an additional dose of 300 mg (0.5 mega units) should be given 6 hourly during the procedure.

Elderly patients
Elimination may be delayed in elderly patients and dose reduction may be necessary.

Incompatibility
Benzylpenicillin sodium BP and solutions that contain metal ions should be administered separately.

Benzylpenicillin sodium should not be administered in the same syringe / giving set as amphotericin B, cimetidine, cytarabine, flucloxacillin, hydroxyzine, methylprednisolone, or promethazine since it is incompatible with these drugs.

Contraindication
Benzylpenicillin is contraindicated in individuals with a history of allergy to penicillins.
Hypersensitivity to any ingredient of the preparation.
Cross allergy to other beta-lactams such as cephalosporins should be taken into account.

Warnings and Precautions
600 mg Benzylpenicillin contains 1.68 mmol of sodium. Massive doses of Benzylpenicillin Sodium BP can cause hypokalaemia and sometimes hypernatraemia. Use of a potassium-sparing diuretic may be helpful. In patients undergoing high-dose treatment for more than 5 days, electrolyte balance, blood counts and renal functions should be monitored.

In the presence of impaired renal function, large doses of penicillin can cause cerebral irritation, convulsions and coma.

Skin sensitisation may occur in persons handling the antibiotic and care should be taken to avoid contact with the substance.

It should be recognised that any patient with a history of allergy, especially to drugs, is more likely to develop a hypersensitivity reaction to penicillin. Patients should be observed for 30 minutes after administration and if an allergic reaction occurs the drug should be withdrawn and appropriate treatment given.

Delayed absorption from the intramuscular depot may occur in diabetics.
Prolonged use of Benzylpenicillin may occasionally result in an overgrowth of non-susceptible organisms or yeast and patients should be observed carefully for superinfections.

Pseudomembranous colitis should be considered in patients who develop severe and persistent diarrhoea during or after receiving Benzylpenicillin. In this situation, even if Clostridium difficile is only suspected, administration of Benzylpenicillin should be discontinued and appropriate treatment given.

Interactions with Other Medicaments
The efficacy of oral contraceptives may be impaired under concomitant administration of Benzylpenicillin sodium BP, which may result in unwanted pregnancy. Women taking oral contraceptives should be aware of this and should be informed about alternative methods of contraception.

There is reduced excretion of methotrexate (and therefore increased risk of methotrexate toxicity) when used with Benzylpenicillin sodium BP.

Probenecid inhibits tubular secretion of Benzylpenicillin sodium BP and so may be given to increase the plasma concentrations.

Penicillins may interfere with:
Urinary glucose tests
Coomb's tests
Tests for urinary or serum proteins
Tests which use bacteria e.g. Guthrie test

Pregnancy and Lactation
Benzylpenicillin sodium BP has been taken by a large number of pregnant women and women of childbearing age without an increase in malformations or other direct or indirect harmful effects on the foetus having been observed.

Although it is not known if Benzylpenicillin sodium BP may be excreted into the breast milk of nursing mothers, it is actively transported from the blood to milk in animals and trace amounts of other penicillins in human milk have been detected.

Side Effects
Blood and Lymphatic System Disorders
Rare (0.01% - 0.1%)
Haemolyticanaemia and granulocytopenia (neutropenia), agranulocytosis, leucopenia and thrombocytopenia, have been reported in patients receiving prolonged high doses of benzylpenicillin sodium BP (eg. Subacute bacterial endocarditis).