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

Ms MS Shaku
LHC Pharmaceuticals (Pty) Ltd
Stand No 553,33
Ghaap Street
N4 Gateway Industrial Park
Willow Park Manor
Pretoria

Dear Ms Shaku

Section 21 Authorization for BENZYL PENICILLIN 5MU INJECTION

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

- **Benzyl Penicillin 5MU 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	12400
EC-PE	10000
FS	645
GP	0
KZN	16000
LP	0
MP	6280
NC	1350
NW	400
SAMHS	0
WC	20000
Total	**67075**

Yours sincerely

K Jamaloodien

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

SAHPRA
SOUTH AFRICAN
HEALTH PRODUCTS
REGULATORY AUTHORITY

Section 21 Response Letter

9/17/2023 11:16 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 3:44 PM** refers

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

  GENERIC NAME: Benzyl Penicillin 5MU Injection

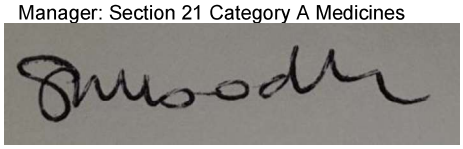
  TRADE NAME: Benzyl Penicillin for injection BP 5MU
- ***F. QUANTITY: Benzyl Penicillin 5MU Injection x 67 100 vials***
- ***G. LETTER NUMBER: B-20794***

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

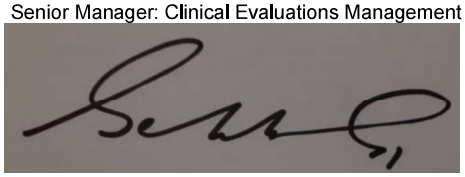
Comments:

Yours faithfully,

Dr S Munbodh
Manager: Section 21 Category A Medicines



T Sehloho
Senior Manager: Clinical Evaluations Management



LHC Pharmaceuticals (Pty) Ltd
N4 Gateway, 33 Ghaap Street
Willow Park Manor, Pretoria
0184, South Africa
Phone: 012-004-1360
Email: Sello@lhcpharma.com
Company Reg.No. 2012/009668/07
CSD Reg. No. MAAA0443063

To:	Section21Quotes@health.gov.za	From:	Avela Sidziya
Att:	Buhle Mhlongo	Ref:	S21RFQ130
Phone	012 395 9539	Phone:	012 004 1360

RE: QUOTATION: BENZYL PENICILLIN 5MU INJECTION

Dear Ms Mbongo

PRODUCT TRADE NAME	PACK SIZE	QTY	UNIT PRICE (vat incl.)	TOTAL PRICE(vat incl.)
INJPEN 5 MEGA	1s	67 100	R9.84	R660 264.00

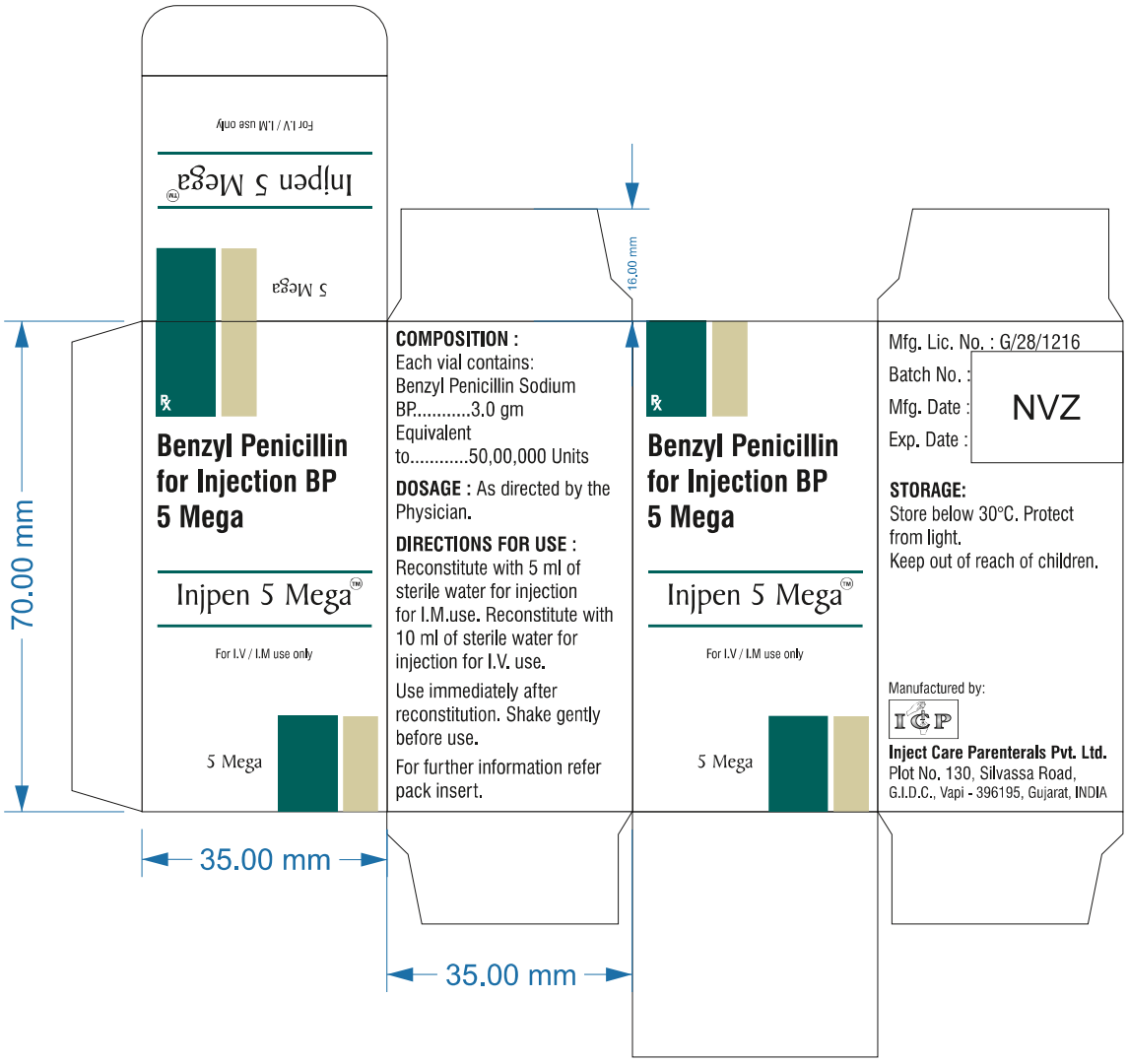
Delivery Lead Time = 60 Days
Validity = 90 Days

Should you need any further information, please contact me direct.

Regards,

Avela Sidziya
Sales Manager

Size:- L35 x W35 x H70 mm



Size:- L110 x H225 mm

Front

Injpen

1 Mega / 5 Mega

Benzyl Penicillin For Injection BP

FORMULATION:
Benzyl Penicillin Injection BP 1 Mega
Each Vial contains:
Benzylpenicillin Sodium 600 mg
Equivalent to …….…10,00,000 units

Benzyl Penicillin For Injection BP 5 Mega
Benzyl Penicillin Sodium BP……..3.0 gm
Equivalent to 50,00,000 Units

PRODUCT DESCRIPTION:
White crystalline, water-soluble sterile powder.

PHARMACOKINETIC:
Benzylpenicillin sodium 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 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 nose, throat, nasal sinuses, respiratory tract and middle ear, etc.
It is also indicated for the following infections caused by penicillin-sensitive microorganisms: Generalised infections, septicaemia and pyaemia from susceptible bacteria. Acute and chronic osteomyelitis, sub-acute bacterial endocarditis and meningitis caused by susceptible organisms. Suspected meningococcal disease. Gas gangrene, tetanus, actinomycosis, anthrax, leptospirosis, rat-bite fever, listeriosis, severe Lyme disease, and prevention of neonatal group B streptococcal infections. Complications secondary to gonorrhoea and syphilis (e.g. gonococcal arthritis or endocarditis, congenital syphilis and neurosyphilis). Diphtheria, brain abscesses and pasteurellosis.

DOSAGE AND ADMINISTRATION:
The following dosages apply to both intramuscular and intravenous injection.
Alternate sites should be used for repeated injections.
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.
Doses up to 43.2 g (72 mega units) per day may be necessary for patients with rapidly spreading gas gangrene.
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 may result in hypernatraemia and hypokalaemia unless the sodium content is taken into account.
For the prevention of Group B Streptococcal disease of the newborn, a 3 g (5 mega units) loading dose should be given to the mother initially, followed by 1.5 g (2.5 mega units) every 4 hours until delivery.
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
Suspected meningococcal disease If meningococcal disease is suspected general practitioners should give a single dose of benzylpenicillin sodium, before transferring the patient to hospital, as follows:
Adults and children over 10 years: 1,200 mg IV (or IM)
Children 1-9 years: 600 mg IV (or IM)
Children under 1 year: 300 mg IV (or IM)
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 should be adjusted in accordance with the following schedule:

Creatine clearance (ml per minute)	Dose (g)	Dose (g)	Dosing interval (hours)
125	1.2 or 1.8	2 or 3	2 or 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	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.

Back

INTERACTIONS:
The efficacy of oral contraceptives may be impaired under concomitant administration of benzylpenicillin sodium, 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.
Probenecid inhibits tubular secretion of benzylpenicillin sodium and so may be given to increase the plasma concentrations.
Penicillins may interfere with:
- Urinary glucose test
- Coomb's tests
- Tests for urinary or serum proteins
- Tests which use bacteria e.g. Guthrie test.

CONTRAINDICATION
Allergy to penicillins. Hypersensitivity to any ingredient of the preparation. Cross allergy to other beta-lactams such as cephalosporins should be taken into account.

SPECIAL WARNING & PRECAUTION
600 mg benzylpenicillin contains 1.68 mmol of sodium. Massive doses of benzylpenicillin sodium 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.

PREGNANCY AND LACTATION
Benzylpenicillin sodium 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 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.

OVERDOSE
Increased neuromuscular hyperexcitability or susceptibility to cerebral seizures can be anticipated in the event of an overdose. Countermeasures: discontinuation, clinical surveillance and symptomatic treatment, if required. {[Nationally completed name]} can be hemodialysed.

SHELF LIFE
Unopened vial 3 years
Chemical and physical in-use stability of the reconstituted and diluted product is concentration and temperature dependent. The following in-use storage times have been demonstrated:

	2°C to 8°C	below 25°C
500,000 – 910,000 IU/ml (this range includes the recommended concentration for IM injection)	48 hours	8 hours
100,000 IU/ml (the recommended concentration for IV injection/infusion)	24 hours	4 hours

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C.

SPECIAL PRECAUTIONS FOR STORAGE
Do not store above 30°C For storage conditions after reconstitution of the medicinal product, see section of Shelf life

NATURE AND CONTENTS OF CONTAINER
10 mL /20 mL Flint Glass Vial USP Type III with 20 mm butyl rubber Stopper and sealed with 20 mm aluminum seal

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING
In order to avoid hypersensitivity reactions caused by degradation products it is recommended to use the injection or infusion solution immediately after preparation. The administration should at least take place within the maximum recommended in-use shelf life. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
Preparation of a solution for IV injection or infusion: A solution for intravenous use can be prepared with the following solvents: - Sterile water for injections (SWFI) - 5% glucose solution - 0.9% sodium chloride solution
The recommended concentration for intravenous use is 100,000 IU/ml. An isotonic solution is obtained when using WFI as solvent (osmolarity of 100,000 IU/ml in WFI is 337 mOsmol/l). It should be taken in account that more concentrated solutions and solutions in 5% glucose or 0,9% sodium chloride are hypertonic and that the use of 0,9% sodium chloride leads to an additional supply of electrolytes.
For {[Nationally completed name] 500,000 IU powder for solution for injection / infusion} a one-step reconstitution in the original vial suffices.

Manufactured by:

Inject Care Parenterals Pvt. Ltd.
Plot No. 130, Silvassa Road,
G.I.D.C., Vapi - 396195. INDIA