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 PROTAMINE 10MG/ML INJ 5ML

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

- **Protamine 10mg/mL Injection 5mL**

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 **05 February 2025**.

Table 1: Provincial estimates

Province	Six Months Estimate
Correctional Services	0
EC-MT	0
EC-PE	400
FS	600
GP	3000
KZN	1200
LP	240
MP	250
NC	30
NW	340
SAMHS	20
WC	2500
Total	**8580**

Yours sincerely

KHADIJA JAMALOODIEN
CHIEF DIRECTOR: SECTOR WIDE PROCUREMENT
DATE:

SAHPRA
SOUTH AFRICAN
HEALTH PRODUCTS
REGULATORY AUTHORITY

Section 21 Response Letter

8/5/2024 5:12 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 **8/5/2024 10:23 AM** refers

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

GENERIC NAME: Protamine Sulphate 10mg/mL

TRADE NAME: Neutrahep 10mg/mL

F. QUANTITY: Protamine Sulphate 10mg/mL INJ 5mL x 9000 ampoules

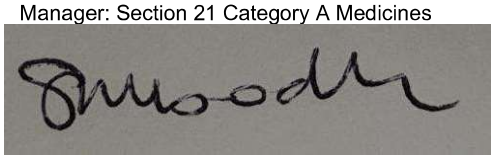
G. LETTER NUMBER: B-29442

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

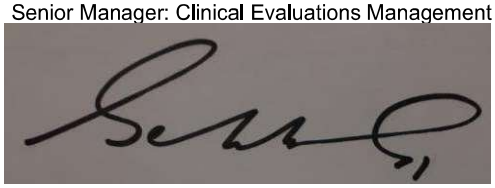
Comments:

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	**S21RFQ136**
QUOTE ENQUIRY DATE	**26/06/2024**	QUOTE CLOSING DATE			**07/07/2024**
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	**Protamine 10mg/mL Injection 5mL**		
TRADE DESCRIPTION	Neutrahep 10mg/ml (5ml amp)		
UNIT OF MEASURE	**1's**	PACK or BOX (*SIZE/ QUANTITY*)	**1's**
QUANTITY REQUIRED	**9000 Vials/Ampoules**		

TO BE COMPLETED BY THE SUPPLIER/ SERVICE PROVIDER

SUPPLIER CONTACT DETAILS (as per CSD)

COMPANY NAME	Equity Pharmaceuticals (Pty) Ltd			
SUPPLIER NUMBER	MAAA0007480			
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 20.93	TOTAL PRICE (INCL. DELIVERY & VAT)	R 188 370.00
VOLUMES AVAILABLE – 14DAYS	9 000 amps		
VOLUMES AVAILABLE – 28DAYS			
VOLUMES AVAILABLE – 56DAYS			
VOLUMES AVAILABLE – 112DAYS			
QUOTE VALIDITY PERIOD			
NORMAL LEAD/DELIVERY TIME			

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	**04/07/2024**

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.
- The only electronic GMP Certificate considered is that from EUDRA.
- 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***

04/07/2024

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 # 20240704

TO: National Department of Health

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

CONTACT PERSON / PATIENT: Buhle Mbongo

NB IMPORTED AND SUPPLIED UNDER SECTION 21 TERMS

PRODUCT CODE	DESCRIPTION	PACK SIZE	QUANTITY	PRICE EXCL	TOTAL INCL
	Neutrahep 10mg/ml	1 x 5ml	1	R 18.20	R 20.93
			9 000	**R163 800.00**	**R 188 370.00**
			9 000	**R163 800.00**	**R 188 370.00**

Valid for 180 days

Employee Signature: _____

Date: 04 July 2024

Approved by: Ehrard van Zyl / Carel Bouwer

04/07/2024

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: Section21Quotes@health.gov.za

Attention: Ms Buhle Mbongo

Dear Ms Mbongo

Re: Request for quotation – Protamine Sulphate – Section 21 Supply

Trust you are well. Please find below our quotation for *Protamine Sulphate* supplied under section 21 terms.

- Quantity: **9 000 amps**
- Delivery Time (Weeks): **1 week**
- Price (Vat Inclusive): **R 20.93 incl. vat per amp**
- Generic Name: **Protamine Sulphate**
- Trade Name: **Neutrahep 10mg/ml**
- Packaging: **5 x 5ml**
- Specifications: **10mg/ml (5ml)**
- Shelf Life: **24 months**
- Package Insert: **Please find attached**
- Manufacturer: **Gland Pharma**
- 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

PROTAMINE SULPHATE INJECTION IP

NeutraHep® न्यूट्राहेप®

Dosage Form

Sterile, pyrogen-free, injectable solution, 10mg/ml, 5ml ampoule.

Composition

Each ml contains: Protamine Sulphate BP 10mg.
It also contains following inactive ingredients: Sodium Chloride, HydrochloricAcid, Water for Injections.

Pharmaco-Therapeutic Class

Heparin Antagonist.

Therapeutic Indications

Protamine Sulphate is indicated in the treatment of heparin overdosage. Protamine Sulphate is used in the treatment of severe heparin calcium or heparin sodium over dosage. Protamine Sulphate should not be used if only minor bleeding occurs during heparin therapy, since with drawl of heparin will usually correct minor overdosage or bleeding within a few hours. However, if severe overdosage or bleeding occurs during heparin therapy, heparin should be discontinued and Protamine Sulphate administered immediately. Blood transfusions may be required in patients with massive blood loss. Protamine Sulphate is also used to neutralize heparin administered during extracorporial circulation in arterial and cardiac surgery or dialysis procedures.

Contra-indication

Protamine Sulphate is contraindicated in patients who have shown previous intolerance to the drug. Either the activated partial thromboplastin time (APTT) or the activated coagulation time (ACT) should be used to monitor the effect of Protamine Sulphate in neutralizing heparin, and additional doses of Protamine Sulphate should be administered if necessary. Coagulation tests are usually performed 5-15 minutes after administration of Protamine Sulphate. Repeat coagulation tests are not usually necessary; however because heparin rebound has been reported (e.g., after cardiac surgery) another test in 2-8 hours may be desirable. It is important to keep the patient under close observation following cardiac surgery; additional doses of Protamine sulphate should be administered if indicated by coagulation studies (e.g., heparin titration test with Protamine, plasma thrombin time).
The risk of a hypersensitivity reaction to Protamine Sulphate should be considered in patients with known sensitivity to fish, vasectomized or infertile males, and patients who have received Protamine containing insulin orprevious Protamine Sulphate therapy. Because fatal anaphylactic and anaphylactoid reaction have been reported following administration of Protamine Sulphate, the drug should be given only when facilities and equipment for the treatment of such reactions are readily available. Protamine Sulphate is contraindicated in patients with a history of intolerance to the drug.

Administration

Dosage of Protamine sulphate should be determined by the dose of heparin, its route of administration, and the time elapsed since it was given. Each ml neutralizes about 1000 units of Heparin. Since blood heparin concentrations decrease rapidly after heparin is administered IV, the dose of Protamine sulphate required in the treatment of IV heparin overdosage also decreases rapidly as time elapses. If only a few minutes have elapsed since heparin was administered by IV injection, most clinicians recommended that 1-1.5mg of Protamine sulphate be given for every 100 units of heparin administered. If 30-60 minutes have elapsed since IV injection of heparin, 0.5-0.75mg of Protamine sulphate should be given for every 100 units of heparin and, if 2 hours or more have elapsed since IV injection of heparin, 0.25-0.375mg of protamin sulphate should be given for every 100 units of heparin administered. If heparin was administered by IV infusion, some clinicians recommended that a dose of 25-50mg of Protamine sulphate be given after stopping the infusion.
If heparin was administered by deep subcutaneous injection, some clinicians recommend that 1-1.5mg of Protamine sulphate be given for each 100 units of heparin. Some clinicians have suggested that a loading dose of 25-50mg of Protamine sulphate may be administered by slow IV injection and the rest of the calculated dose administered by continuous IV infusion over 8-16 hours or the expected duration of absorption of heparin.
To neutralize heparin administered during extracorporeal circulation, 1.5mg of Protamine sulphate is usually given for each 100 units of heparin administered. Alternatively, some clinicians recommend that Protamine sulphate dosage be determined using sequential activated coagulation time (ACT) and a close response curve which correlates results of the coagulation tests and the amounts of heparin remaining in the body.

Special Warnings

Hyperheparinemia or bleeding has been reported in experimental animals and in some patients 30 minutes to 18 hours after cardiac surgery (under cardiopulmonary bypass) in spite of complete neutralization of heparin by adequate doses of Protamine sulphate at the end of operation. It is important to keep the patient under close observation after cardiac surgery. Additional doses of Protamine sulphate should be administered if indicated by coagulation studies, such as the heparin titration test with Protamine and the determination of plasma thrombin time.
Too-rapid administration of Protamine sulphate can cause severe hypotensive and anaphylactoid reactions. Facilities to treat shock should be available.

Precautions for Use

Safe and efficacy of Protamine Sulphate in children have not been established.
Pregnancy, Fertility and Lactation: Animal reproduction studies have not been performed with Protamine Sulphate. It is not known whether Protamine Sulphate can cause fetal harm when administered to pregnant women or can affect reproduction capacity. The drug should be used during pregnancy only when clearly needed. Studies have not been performed to date with Protamine Sulphate to determine the effect of the drug on fertility. Since it is not known whether Protamine Sulphate is distributed into milk, the drug should be used with caution in nursing women.

Interactions with Other Drugs and Other Forms of Interactions

Protamine Sulphate should not be mixed with other drugs without knowledge of their compatibility, because Protamine Sulphate has been shown to be incompatible with certain antibiotics, including several of the cephalosporins and penicillins.

Undesirable Effects

Rapid IV injection of Protamine Sulphate has caused acute hypotension, bradycardia, pulmonary hypertension, dyspnea, transient flushing, and a feeling of warmth. Facilities to treat shock should be available. These adverse effects are minimized when Protamine Sulphate is administrated slowly and when not more than 50mg of the drug is administered in any 10-minute period.
Hypersensitivity reactions including urticaria, angioedema, acute pulmonary hypertension, anaphylaxis, and anaphylactoid reactions have occurred occasionally after administration of Protamine Sulphate. Complement activation by the heparin-Protamine complexes, release of lysosomal enzymes from neutrophils, and prostaglandin and thromboxane generation have been associated with the development of anaphylactoid reactions. Severe and potentially irreversible circulatory collapse associated with myocardial failure and reduced cardiac out put also can occur. High-protein, noncardiogenic pulmonary edema associated with the use of Protamine sulphate has been reported in patients on cardiopulmonary bypass who are undergoing cardiovascular surgery. The etiologic role of Protamine sulphate in the pathogenesis of this condition is uncertain, and multiple factors have been present in most cases. The condition has been reported in association with administration of certain blood products, other drugs, cardiopulmonary alone, and other etiologic factors.
Hypersensitivity reactions to the drug have been reported in several individuals who were also hypersensitive to fish, and the drug probably should be used with caution in patients with a history of allergy to fish. Fatal anaphylaxis also has been reported in at least one patient with no prior history of allergies. Previous exposure to Protamine from use of Protamine sulphate for the management of heparin overdosage or from use of Protamine containing insulin may predispose susceptible individuals to the development of hypersensitivity reactions during subsequent use of Protamine sulphate.
Antiprotamine antibodies are present in the serum of infertile or vasectomized men, and the presence of these antibodies potentially may predispose individuals to Protamine sulphate–induced hypersensitivity reactions. An immediate anaphylactoid reaction has occurred in at least one vasectomized male following administration of a dose of Protamine sulphate; pretreatment with a corticosteroid and antihistamine prevented recurrence of the reaction during subsequent administration of Protamine sulphate. Vasectomy history should be determined prior to administration of Protamine sulphate in males, and the possibility of Protamine sensitivity should be considered. Some clinicians suggest that vasectomized males should be pretreated with a corticosteroid and antihistamine prior to administration of Protamine sulphate in an attempt to ameliorate or prevent such reactions. Males undergoing vasectomy should be advised of the potential risk of developing Protamine antibodies.
Systemic hypertension, nausea, vomiting, and lassitude have occurred in patients receiving Protamine sulphate. Back pain has been reported rarely in conscious patients undergoing procedures such as cardiac catheterization.
Heparin rebound with anticoagulation and bleeding has been reported occasionally several hours after heparin has been adequately neutralised by Protamine sulphate. This effect occurs most frequently when Protamine sulphate is used to neutralize heparin administered during extracorporeal circulation in arterial and cardiac surgery or dialysis procedures. Heparin rebound, when it occurs, usually is evident within 8-9 hours after Protamine sulphate administration but has been reported 30 minutes to 18 hours after cardiopulmonary bypass despite complete neutralization of heparin by adequate doses of Protamine sulphate at the end of the operation. The precise cause is unknown but this effect presumably results from release of heparin from the heparin-heparin complex or release of heparin from extravascular compartments.
Because Protamine sulphate is a weak anticoagulant, overdosage theoretically may result in bleeding. However, in one study, overdosage of 600-800mg of IV Protamine sulphate had only minimal, transient effects on blood coagulation tests.

Mutagenicity and Carcinogenicity

Studies to determine the Mutagenic or carcinogenic potential of Protamine Sulphate have not been performed to date.

Overdosage

Signs and symptoms:
Over dosage of Protamine sulphate may cause bleeding. Protamine has a weak anticoagulant effect due to an interaction with platelets and with many proteins including fibrinogen. This effect should be distinguished from the rebound anticoagulation that may occur 30 minutes to 18 hours following the reversal of heparin with Protamine.
Rapid administration of Protamine is more likely to results in bradycardia, dyspnea, a sensation of warmth, flushing, and severe hypotension. Hypertension has also occurred. The median lethal intravenous dose of Protamine sulphate is 50mg/kg in mice. Serum concentrations of Protamine sulphate are not clinically useful. Information is not available on the amount of drug in a single dose that is associated with overdosage or is likely to be life threatening.
Treatment:
In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient. Replace blood loss with blood transfusions or fresh frozen plasma. If the patient is hypotensive, consider fluids, epinephrine, dobutamine, or dopamine.

Pharmacological Properties

Pharmacodynamic properties: Although protamine is a potent antidote for heparin, its precise mechanism of action is unknown.
However, when the strongly basic protamine combines with the strongly acid heparin, a stable salt is formed lacking in anticoagulant activity. 1mg of protamine sulphate neutralises between 80 and 120 units of heparin. However, methods of standardisation and the use of heparin from different sources (mucosal, lung) may produce different responses to protamine.
Pharmacokinetic properties: The onset of action of protamine occurs within five minutes following intravenous administration. The fate of the protamine-heparin complex is unknown, but it may be partially degraded, thus freeing heparin.

Storage

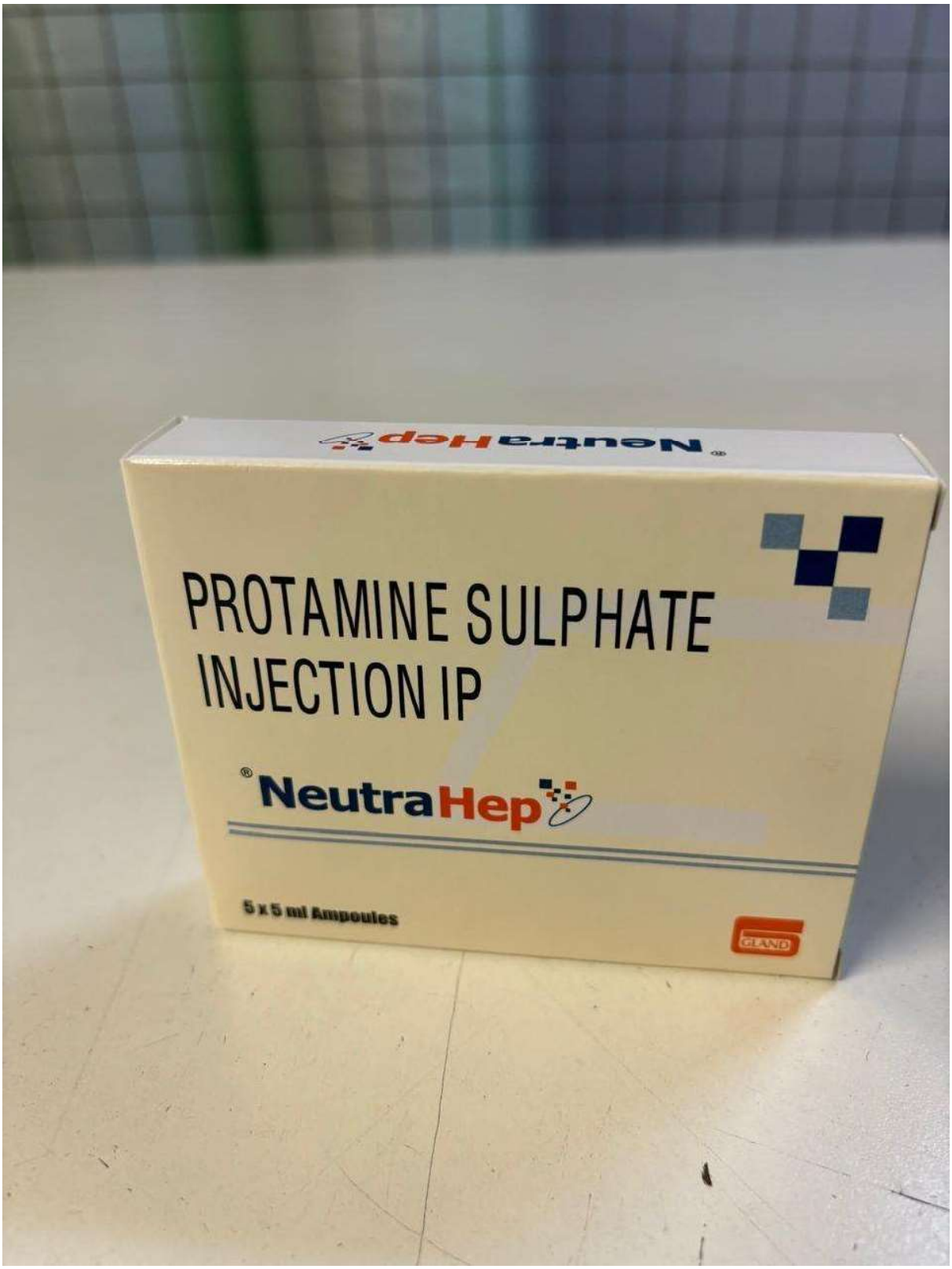
Shelf-life: 36 months.
Special storage precautions: Protamine sulphate Injection should be stored at a temperature not exceeding 25ºC. Protect from light. Keep out of reach of children.

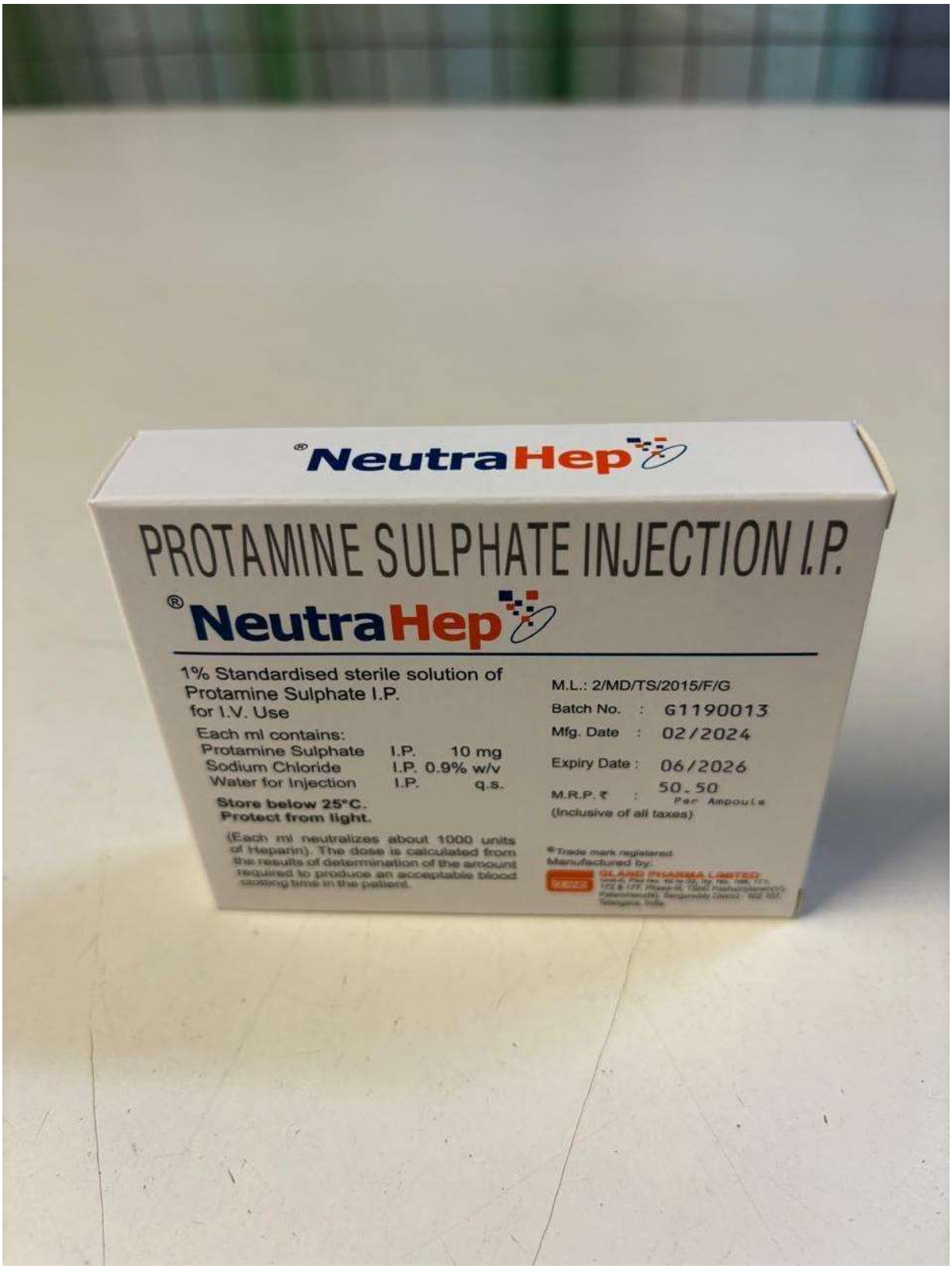
Manufactured by:
GLAND PHARMA LIMITED
D.P. Pally, Hyderabad-500043, INDIA.

100 x 180 mm (L x H)

Print Colour Black


NeutraHep
PROTAMINE SULPHATE
INJECTION IP
NeutraHep
NeutraHep


NeutraHep
PROTAMINE SULPHATE
INJECTION IP
NeutraHep
5 x 5 ml Ampoules
GLAND


®NeutraHep
PROTAMINE SULPHATE INJECTION I.P.
®NeutraHep
1% Standardised sterile solution of Protamine Sulphate I.P. for I.V. Use
Each ml contains:
Protamine Sulphate I.P. 10 mg
Sodium Chloride I.P. 0.9% w/v
Water for Injection I.P. q.s.
Store below 25°C.
Protect from light.
(Each ml neutralizes about 1000 units of Heparin). The dose is calculated from the results of determination of the amount required to produce an acceptable blood clotting time in the patient.
M.L.: 2/MD/TS/2015/F/G
Batch No. : G1190013
Mfg. Date : 02/2024
Expiry Date : 06/2026
M.R.P. ₹ : 50.50 Per Ampoule
(Inclusive of all taxes)
®Trade mark registered
Manufactured by: